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Original Article

COMBINED TREATMENT OF RHIZATHROSIS WITH LOCAL INFILTRATIONS OF OXYGEN-OZONE AND TOPICAL APPLICATIONS OF ALFA-LIPOIC ACID, CAPSAICIN, CANNABIDIOL, BETA-CARYOPHYLLENE, AND MYRRH

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ABSTRACT

We describe our experience in the combined treatment of rhizarthrosis with local oxygen-ozone infiltrations and topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh. From March 2022 to December 2023, we selected 58 patients with a diagnosis of rhizarthrosis confirmed by both clinical examination and radiographic findings with standard radiograms of the metacarpal trapezius joint. We treated 43 females and 15 males aged between 49 and 79 years (mean 61.9). Of the patients included, 13 treatments of rhizarthrosis were carried out in both hands (22.41%). The patients included in the study were treated with oxygen-ozone (O_2-O_3) infiltrations of the trapezium metacarpal joint – six to ten treatments every two weeks – followed by topical treatment by self-applying the cream on the affected parts three times a day, massaging delicately until completely absorbed. Clinical outcomes were measured using the Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire and the Visual Analogue Scale (VAS) scale. The analysis of the results of the DASH questionnaire showed improvement in the perceived disability associated with the symptoms (M = 81.00; SD = 1.77 pre-treatment; M = 17.94; SD = 1.60 after treatment). The VAS questionnaire also showed satisfactory clinical results after treatment (M = 8.31; SD = 0.73 pre-treatment; M = 2.90; SD = 0.73 after treatment). Of 58 patients, 6 (10.34%) reported no benefit and were candidates for possible surgery. These findings suggest that oxygen-ozone therapy with topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh can be considered an ideal treatment for rhizarthrosis.

KEYWORDS: *oxygen ozone, ozone therapy, rhizarthrosis; thumb osteoarthritis; trapeziometacarpal joint*

INTRODUCTION

Rhizarthrosis is a very common and painful pathology: it consists of degenerative arthritis of the base of the thumb with inflammation, joint swelling, and pain caused by joint instability.

This very common pathology, first described by Forestier in 1937 (1), affects approximately 20% of the adult population, especially women (female:male ratio 4:1, between the fifth and seventh decade of life). In women, it appears more frequently after menopause, while in men, it is more linked to overuse (2-6).

Rhizarthrosis commonly affects one side. The trapezoid-metacarpal joint plays a fundamental role: all gripping actions lead to overloading the trapezoid-metacarpal joint since the thumb axis exerts force and fulcrum at this point. This force transmits stress in a radial direction to the base of the first metacarpal, which over time causes a reduction in the tension of the capsulo-ligamentous apparatus, joint hyperlaxity, and subluxation of the first metacarpal on the trapezium.

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The preternatural movement of the bone heads alters the articular surface, and there is a progressive reduction in cartilaginous thickness, the appearance of pain, and arthrosis.

Patients complain of pain at the base of the thumb when performing daily activities such as turning a key, opening a car door, picking up a book, or threading a needle. People who suffer from this pathology tend to drop objects and feel a loss of strength between their thumb and forefinger. Joint deformity is very painful and can even prevent sleep. Therefore, normal functions of the thumb, such as gripping and fine joint movements like drawing and embroidery, are compromised, significantly impacting the patient's quality of life.

Conservative management includes the administration of anti-inflammatory drugs, splints to immobilize the joint, or intra-articular cortisone injections temporarily. A specific palmar splint may be of therapeutic use to block the joint, at least at night. Analgesics like paracetamol and non-steroidal anti-inflammatory drugs may also be helpful in the most painful stages. Local treatment with hyaluronic acid injections has also proved effective (7-16). In case of failure, surgery is performed. The most satisfying surgery is the so-called biological arthroplasty (17-25).

Rhizarthrosis can be so painful that, in the most severe cases, it is necessary to resort to surgery. Pain can regress after many years, at the cost of stiffness in adduction of the first metacarpal and hyperextension of the phalangeal metacarpal of the thumb.

The diagnosis of rhizarthrosis is clinical and radiographic, with the use of anteroposterior and oblique radiographs and the Kapandji projection to evaluate the thumb base joint (Fig.1-3), according to the Eaton-Littler setup modified by Brunelli (Table I).

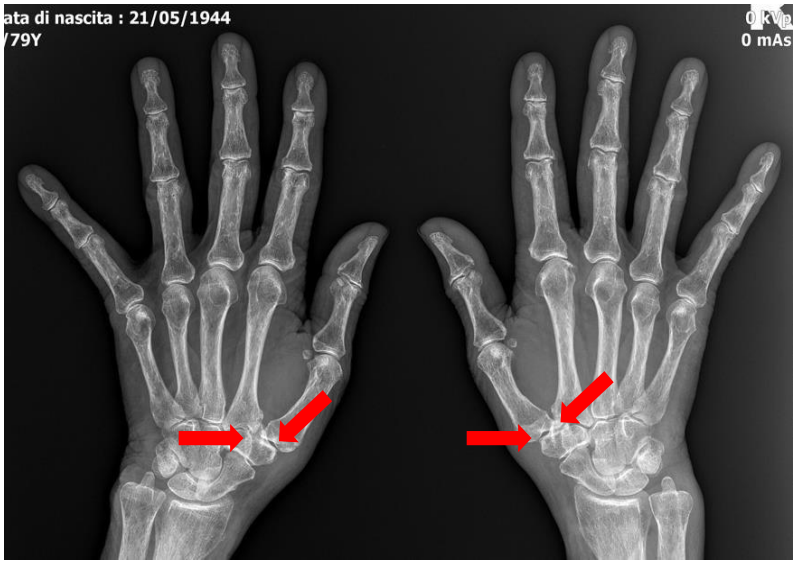

Fig. 1. *Antero-posterior radiograph projection of both hands documenting grade 2 bilateral rhizarthrosis with slight reduction of joint space (**arrows**).*

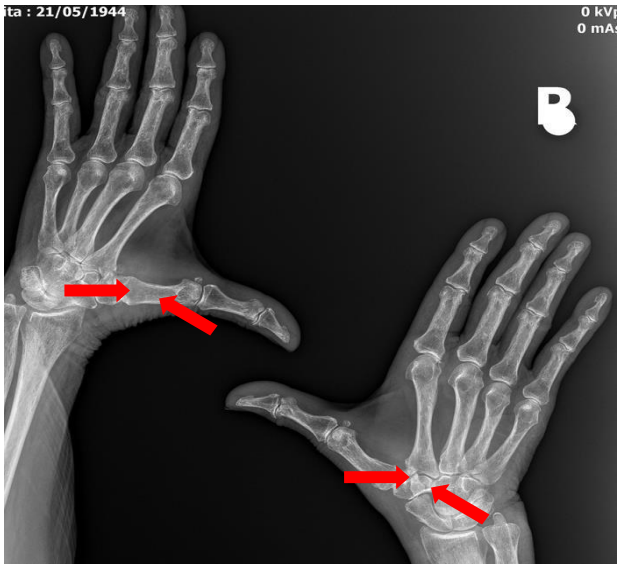

Fig. 2. *Kapandji radiographic projections of both hands documenting grade 2 bilateral rhizarthrosis with slight reduction of joint space (**arrows**).*

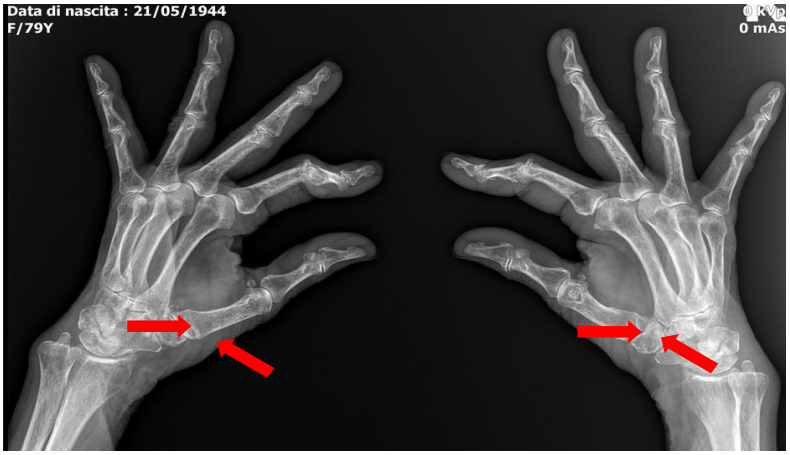

Fig. 3. *Latero-lateral radiographic projection of both hands documenting grade 2 bilateral rhizarthrosis with slight joint space reduction.*

Table I. *Radiographic staging according to Eaton-Littler.*

Grade 1	Normal joint surfaces, with increased joint space due to synovitis
Grade 2	Reduction of joint space due to deficit or laxity of the ligaments
Grade 3	Marked narrowing of the joint rim, subchondral cystic formations, bone sclerosis, and subluxation of the first metacarpal with respect to the trapezium greater than 2 mm. Trapezoid scaphoid joint intact.
Grade 4	Complete joint deterioration, associated with involvement of the trapezoid-scaphoid.

Over the years, natural products have contributed enormously to developing important therapeutic drugs currently used in modern medicine.

Alpha-lipoic acid (ALA), which, as is known, is a natural sulfur compound produced in small concentrations by all cells. ALA is a key compound in some mitochondrial enzyme complexes (pyruvate dehydrogenase and ketoglutarate dehydrogenase), which play a central role in oxidative metabolism. ALA can reduce oxidative stress, preventing damage caused by oxygen free radicals. Unlike other antioxidants that fully function in aqueous or fatty tissues, ALA exerts its antioxidant function in water and fats. This property gives lipoic acid a broad spectrum of antioxidant action (26-31).

Capsaicin is an organic compound in chili peppers, which is responsible for their spicy flavor. There are various beneficial properties attributed to capsaicin; it can bind to some pain receptors, desensitizing them, so much so that it has now consolidated pain-relieving properties.

Cannabidiol (CBD) is a non-psychotropic component of Cannabis with proven anti-inflammatory action (32-34). ß-caryophyllene (BCP) is a plant compound, a member of bicyclic sesquiterpene. In nature, it mainly occurs as trans-caryophyllene (E)-BCP mixed with small amounts of its isomers, (Z)-ß-caryophyllene (iso-caryophyllene) and a-humulene (a-caryophyllene), as well as its oxidation derivative, ß-caryophyllene oxide (BCPO). BCP-induced effect of analgesia is obtained with endocannabinoid system (ECS) involvement. BCP binds to peripheral cannabinoid receptor type 2 (CB2), leading to ß-endorphin release from keratinocytes and activation of opioid receptors (35-36).

Myrrh is a natural compound secreted by shrubs of the *Commiphora genus* of the Burseraceae, whose analgesic effect has long been known. Myrrh is a dry extract with a high content of bioactive furanodienes obtained through a patented extraction process, which allows the preservation of all the properties of the original raw material (37).

Excellent results were recently obtained with treatment with oxygen-ozone therapy in rhizarthrosis. The rationale for anti-inflammatory treatment by intraarticular oxygen-ozone infiltration is based on an attempt to relieve the inflammation with analgesic action. The oxygen-ozone gas mixture injected is thought to normalize the level of cytokines and prostaglandins, increase superoxide dismutase (SOD), minimize reactive oxidant species (ROS), and improve local circulation with a eutrophic effect (38-45).

In this observational study, we wanted to evaluate the clinical results obtained in the treatment of 58 selected patients diagnosed with rhizarthrosis treated with oxygen-ozone therapy and topical applications of alfa-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh.

MATERIALS AND METHODS

We describe our experience treating rhizarthrosis by administering oxygen-ozone (O_2-O_3) and topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh.

We treated 58 patients between March 2022 and December 2023. with a diagnosis of rhizarthrosis confirmed both by clinical examination and by radiographic findings with standard hand radiographs; in particular, we treated 43 females and 15 males between 49 years and 79 years (average age: 61.9).

Subject to informed consent to the treatment, we proposed a therapeutic path with local injection with oxygen-ozone at a concentration of 20 µg /ml and topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh.

For the treatment with O_2-O_3, we used 25 G 5/8 orange Terumo code needles, injecting the gaseous mixture at a concentration of 20 µg/ml directly into the trapezoid metacarpal joint. The first treatment was always performed under CT guidance to ensure perfect joint access and control the distribution of the gas mixture (Fig. 4).

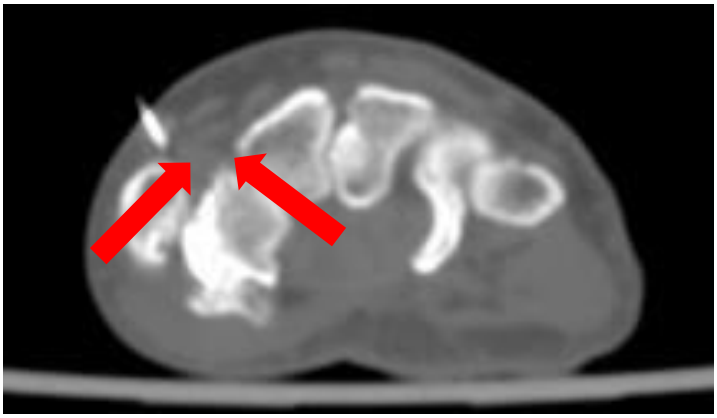

Fig. 4. *The first treatment is performed with CT guidance to identify the trapezium and base of the first metacarpal correctly. The infiltration point is marked with a dermographic pencil. Using CT, it is possible to verify the correct positioning of the needle (**arrows**).*

Once the correct entry point was identified, it was marked on the skin with a dermographic pencil, and this point remained constant for subsequent treatments (Fig. 5, 6). On average, six to ten oxygen-ozone injections were given twice a week, depending on the severity: 26 (44.8 %) patients received six treatment sessions, 11 (19%) received eight, and the remaining 21 (36.2 %) had ten injections. Since the area to be treated is susceptible, local anesthesia was administered via ethyl chloride spray before infiltration.

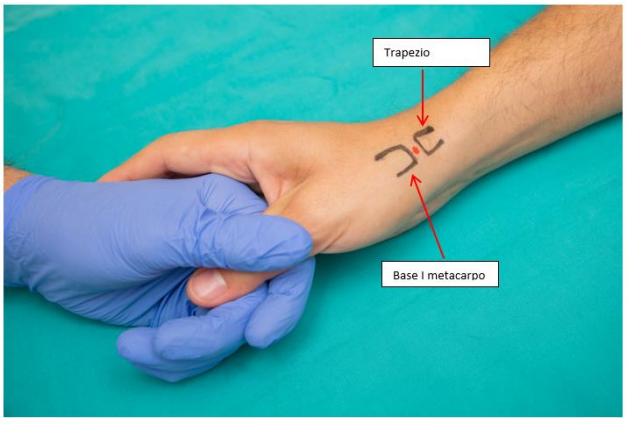

Fig. 5. *With a dermographic pencil, identify the trapezium and the base of the first metacarpal*,
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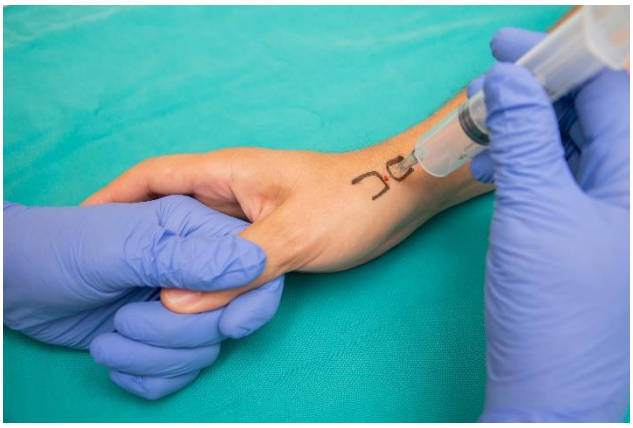

Fig. 6. *Infiltration with an oxygen-ozone mixture.*

All patients tolerated the injections well and then underwent clinical follow-up one month after the end of treatment. Following the treatment with oxygen-ozone, topical application of a cream containing alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh was carried out on the affected parts, massaging delicately until completely absorbed. The applications were carried out 3 times a day, approximately every 8 hours. They were always well-tolerated, with an immediate sensation of relief on the skin thanks to the calming effect linked to the antioxidant properties of alpha-lipoic acid and the hydrating properties.

To fully evaluate the experience of pain, it is important to assess patients' perceived disability associated with the symptoms and involve them actively in rating their algic experience. To this regard, we decided to adopt two self-report surveys, both of which have demonstrated adequate metric properties in literature, both in terms of validity and reliability.

During the treatment period, we consensually decided with the patient to suspend any anti-inflammatory therapies in progress. Every participant was asked to fill out the DASH (46-48) questionnaire before starting treatment with O_2-O_3 – on the occasion of the first medical consultation – and one month after the end of the treatment (Table II). The experience of pain was assessed before and after treatment using the VAS scale (49-51), with the same timing applied to the DASH.

Table II. *DASH questionnaire.*

Disabilities of the Arm, Shoulder and Hand

Please rate your ability to do the following activities in the last week by circling the number below the appropriate response.

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE
1. Open a tight or new jar.	1	2	3	4	5
2. Write.	1	2	3	4	5
3. Turn a key.	1	2	3	4	5
4. Prepare a meal.	1	2	3	4	5
5. Push open a heavy door.	1	2	3	4	5
6. Place an object on a shelf above your head.	1	2	3	4	5
7. Do heavy household chores (e.g., wash walls, wash floors).	1	2	3	4	5
8. Garden or do yard work.	1	2	3	4	5
9. Make a bed.	1	2	3	4	5
10. Carry a shopping bag or briefcase.	1	2	3	4	5
11. Carry a heavy object (over 10 lbs).	1	2	3	4	5
12. Change a lightbulb overhead.	1	2	3	4	5
13. Wash or blow dry your hair.	1	2	3	4	5
14. Wash your back.	1	2	3	4	5
15. Put on a pullover sweater.	1	2	3	4	5
16. Use a knife to cut food.	1	2	3	4	5
17. Recreational activities which require little effort (e.g., cardplaying, knitting, etc.).	1	2	3	4	5
18. Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g., golf, hammering, tennis, etc.).	1	2	3	4	5
19. Recreational activities in which you move your arm freely (e.g., playing frisbee, badminton, etc.).	1	2	3	4	5
20. Manage transportation needs (getting from one place to another).	1	2	3	4	5
21. Sexual activities.	1	2	3	4	5

DISABILITIES OF THE ARM, SHOULDER AND HAND

	NOT AT ALL	SLIGHTLY	MODERATELY	QUITE A BIT	EXTREMELY
22. During the past week, *to what extent* has your arm, shoulder or hand problem interfered with your normal social activities with family, friends, neighbours or groups? *(circle number)*	1	2	3	4	5

	NOT LIMITED AT ALL	SLIGHTLY LIMITED	MODERATELY LIMITED	VERY LIMITED	UNABLE
23. During the past week, were you limited in your work or other regular daily activities as a result of your arm, shoulder or hand problem? *(circle number)*	1	2	3	4	5

Please rate the severity of the following symptoms in the last week. *(circle number)*

	NONE	MILD	MODERATE	SEVERE	EXTREME
24. Arm, shoulder or hand pain.	1	2	3	4	5
25. Arm, shoulder or hand pain when you performed any specific activity.	1	2	3	4	5
26. Tingling (pins and needles) in your arm, shoulder or hand.	1	2	3	4	5
27. Weakness in your arm, shoulder or hand.	1	2	3	4	5
28. Stiffness in your arm, shoulder or hand.	1	2	3	4	5

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	SO MUCH DIFFICULTY THAT I CAN'T SLEEP
29. During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand? *(circle number)*	1	2	3	4	5

	STRONGLY DISAGREE	DISAGREE	NEITHER AGREE NOR DISAGREE	AGREE	STRONGLY AGREE
30. I feel less capable, less confident or less useful because of my arm, shoulder or hand problem. *(circle number)*	1	2	3	4	5

DASH DISABILITY/SYMPTOM SCORE = $\left[\frac{(\text{sum of n responses})}{n} - 1\right] \times 25$, where n is equal to the number of completed responses.

A DASH score may not be calculated if there are greater than 3 missing items.

RESULTS

All patients included in the study were clinically evaluated before treatment and one month after the end of the therapy. Analyzing the results of the first access to the clinic, the DASH evaluation reported, in most of the skills tested, considerable difficulties and very significant disability (e.g., unscrewing a tightly closed lid) with an average score of 81.00 (SD = 1.77) out of 100. After the therapy with local infiltrations of oxygen-ozone and topical applications of alfa-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh, the skills in daily activities were generally reported in association with lower complications (Mean DASH score after treatment: 17.94; SD = 1.60).

Regarding the experience of pain measured by the VAS scale, the ratings before treatment ranged from 7 to 9, with a mean score of 8.31 (SD = 0.73), while after treatment, the mean score was 2.90 (SD = 1.36). Only 6 patients (10.34%) reported no benefit and were candidates for possible surgery (Tables III-VIII).

Table III. *DASH and VAS test results before treatment.*

Instrument Scale	*Mean Score (Standard Deviation)*	*Range Of Scores*
DASH	81.00 (1.77)	76-87
VAS	8.31 (0.73)	7-9

Table IV. *DASH and VAS test results after treatment.*

Instrument Scale	*Mean Score (Standard Deviation)*	*Range Of Scores*
DASH	17.94 (1.60)	12-20
VAS	2.90 (1.36)	1-6

Table V. *DASH pre-treat.*

Standard Deviation	**s = 1.7671466**
Variance	s^2 = 3.122807
Count	n = 58
Mean	$\overline{x}$ = 81
Sum of Squares	SS = 178

Table VI. *DASH post-treat.*.

Standard Deviation	**s = 1.6050623**
Variance	s^2 = 2.576225
Count	n = 58
Mean	$\overline{x}$ = 17.948276
Sum of Squares	SS = 146.84483

Table VII. *VAS pre-treat.*

Standard Deviation	**s = 1.3852564**
Variance	s^2 = 1.9189353
Count	n = 58
Mean	$\overline{x}$ = 2.8965517
Sum of Squares	SS = 109.37931

Table VIII. *VAS post-treat.*

Standard Deviation	**s = 0.7304624**
Variance	s^2 = 0.53357532
Count	n = 58
Mean	$\overline{x}$ = 8.3103448
Sum of Squares	SS = 30.413793

DISCUSSION

Considering our experience in oxygen-ozone therapy and the well-known mechanism of action of the oxygen-ozone gas mixture in the analgesic purposes of treatment of rhizarthrosis, we aimed to evaluate the results of the action of local oxygen-ozone therapy and topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh (52-55).

In rhizarthrosis, the arthrosis process causes the cartilage that lines the two bones in contact between them (trapezius and first metacarpal bone) to always thin, causing friction, further wear, and pain. In the first phase of the disease, conservative treatment did not propose a single protocol. The main symptom is pain, which appears when the patient performs simple gripping and gripping movements with your thumb, for example, removing the lid of a jar, turning the key in a lock, grasping a door handle, and opening the door of the car.

Studies have demonstrated the beneficial properties of alpha-lipoic acid, capsaicin, cannabidiol, β-Caryophyllene, and myrrh regarding the treatment of musculoskeletal pathologies and the perception of pain associated with it, even in joint treatments with oxygen-ozone therapy infiltrations.

In this observational study, we found that treatment with O_2-O_3 + topical application of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh allowed to obtain excellent results also confirmed with DASH and VAS evaluations.

In recent years, several studies have demonstrated the usefulness of oxygen-ozone therapy in the treatment of rhizarthrosis as well as the known analgesic potential of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh, acting as biological modulators, favoring the physiological response of fabrics. The curative possibility, therefore, of oxygen-ozone, which is in this regard high due to the improvement of local circulation being able to normalize the level of cytokines and prostaglandins with anti-inflammatory and pain-relieving action, associated with the topical use of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh justifies the excellent result.

From the results obtained, it can be deduced that from the first treatment to the clinical control at thirty days, the association of a minimally invasive therapy such as oxygen-ozone therapy and the topical administration of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh can be considered an excellent therapeutic solution capable of further improving the good final clinical result with better control of symptoms, particularly in the first phase of the disease, to offer a valid conservative alternative to a possible surgical solution.

The results of the present study align with what is reported in the literature, confirming the beneficial effects of the joint action of these therapies, both in terms of pain perception and improvement of the functionality of the trapezium-metacarpal joint.

CONCLUSIONS

Our findings suggest that oxygen-ozone therapy with topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh can be considered an ideal rhizarthrosis treatment. Although ours is a small cohort, oxygen-ozone treatment of trapezius metacarpal rhizarthrosis appears to be a valid alternative to NSAIDs and/or steroids, especially in the early stage of illness. Further studies could investigate these factors in greater detail in broader samples and randomized controlled studies.

In our opinion, the brilliant results obtained in our series are linked to some of the main activities of oxygen-ozone therapy. The improvement of intra- and trans-tissue oxygenation with consequent improvement of both hypoxia and venous stasis and lymphatic in addition to the well-known anti-inflammatory, analgesic, and eutrophicating activities of ozone. Given these results, we can conclude that oxygen-ozone therapy, associated with topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh – can be considered an excellent therapeutic approach for patients afflicted with rhizarthrosis.

These promising data, therefore, suggest the usefulness of carrying out a randomized and controlled study to definitively ascertain the efficacy of the topical use of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh in addition to O_2-O_3 therapy for the treatment of rhizarthrosis.

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Original Article

ROOT COMPRESSION TREATMENT WITH OZONE THERAPY UNDER TOMOGRAPHIC NAVIGATION IN 345 CASES

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ABSTRACT

The objective of the present work was to demonstrate the safety and effectiveness of percutaneous nucleolysis with O_2/O_3 in symptomatic root compression under the Maximum Intensity Projection (MPR) tomographic navigation technique. A prospective observational study was carried out on 345 patients with root compression at the cervical, thoracic, and lumbar levels in men and women with symptomatic disc herniation who underwent percutaneous nucleolysis peridural and foraminal block with O_2/O_3 during a period from May 2021 to May 2023. All nucleolysis was performed under MRP tomographic navigation with asepsis, antisepsis, and local anaesthesia measures. O_2/O_3, epidural, and foraminal were administered from 3 ml to 7 ml at a 15 µg/ml concentration. The effectiveness of the treatment was based on pain control according to the visual analog scale (VAS), the baseline at 3, 6, and 12 months after nucleolysis and through the Lattinen index and a treatment satisfaction survey that was evaluated before and after nucleolysis, at the end of the study. For the 345 patients, the initial VAS was 7.78±0.99 and the evolution at 3, 6, and 12 months was 2.43±2.19, 1.80±2.31 and 2.07±2.49, respectively, with significant differences ($p<0.05$) with respect to the initial value. The initial Lattinen index was 13.02±2.95 and increased to 6.7±2.14 at 3 months, 3±1.95 at 6 months, and 1.3±0.8 at 12 months with a statistically significant reduction ($p<0.05$). Regarding the satisfaction expressed by the patients at the end of the treatment, it was: "good" for 320 (92.7%), "regular" for 20 (5.6%), and "bad" for 5 (1.4%) who were referred to surgery. No patient had adverse effects. Percutaneous nucleolysis with O_2/O_3 was an effective and very safe technique in the treatment of pain due to a herniated disc with radiculopathy.

KEYWORDS: *oxygen, ozone, percutaneous, nucleolysis, radiculopathy*

INTRODUCTION

The worldwide incidence of root compression in the spine at the cervical, thoracic, and lumbar levels may vary by region, population, and risk factors. There is no exact global incidence figure, as this condition may be underdiagnosed or not always recorded systematically in all areas. It is estimated that in the US, cervical and lumbar pain represent 67% and 80%, respectively, of primary and emergency consultations (1).

The incidence of root compression is estimated in specific studies of different regions and populations. For example, in countries with aging populations, cases of root compression at the lumbar level due to degeneration of the

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spine with age are more likely to be reported. However, availability, access to medical care, and awareness of the condition may influence case reporting. Although epidemiological studies may vary, the incidence of low back pain is estimated to be 5% to 10%, with a lifetime prevalence of 60% to 90%. Most episodes of low back pain are self-limiting and will resolve without intervention after brief periods of rest, modification of the activity that caused it, and physical therapy. Approximately 50% of cases will be resolved within 1 to 2 weeks; 90% will resolve in 6 to 12 weeks (2).

Pain management in lumbar radicular syndrome, which is often related to compression of a nerve root in the lumbar spine, can be multifaceted and usually involves a combination of medical and therapeutic approaches such as rest, physical therapy, spinal traction, anti-inflammatories, analgesics, antidepressants, infiltrations, nerve blocks, surgery, among others (3). Ozone has been used to relieve low back pain related to radicular syndrome. In this direction, different systematic studies and meta-analyses have suggested that ozone therapy can alleviate pain and reduce inflammation with a low rate of side effects (4-6).

The objective of the present work was to demonstrate the safety and effectiveness of percutaneous nucleolysis with O_2/O_3 in symptomatic root compression under the Maximum Intensity Projection (MPR) tomographic navigation technique. The work includes a case series of 345 patients with radicular pain.

MATERIALS AND METHODS

The study was carried out between January 2021 and January 2023 in patients with root compression at the cervical, thoracic, and lumbar levels who attended the private consultation at the Caracas Professional Clinical Centre (Av. Panteón, Piso 4, Cons. 415. San Bernardino, Caracas, Venezuela). The study protocol was endorsed by the Institutional Ethics Committee (Act 05-2023) and was in line with the ethical principles referred to by the World Medical Assembly (7). Before enrolling in the study, patients received verbal and written consent about the characteristics of the study.

The inclusion criteria were as follows:

- the subject was willing to give informed consent to participate in the study;
- man or woman, from 18 to 80 years old;
- subjects who did not participate in other clinical trials within the three months prior to this study;
- patients who, according to the researcher's criteria, were able and willing to comply with all the study requirements;
- patients with a herniated disc at the cervical, thoracic, or lumbar level.

The exclusion criteria were as follows:

- female participant who was pregnant, breastfeeding, or planning a pregnancy during the study;
- with significant kidney or liver failure;
- elective surgery or other procedures requiring general anesthesia during the study. Have participated in another research study on a trial product within the last 12 weeks;
- polymorphism for the G-6PD (favism). Patients who used immunosuppressants continuously or who would undergo an organ transplant within 6 months;
- patients with uncontrolled hyperthyroidism;
- patients with abnormal coagulation, thrombocytopenia, or active bleeding;
- severe anemia or hypocalcemia;
- period of severe instability of cardiovascular diseases;
- uncontrolled diabetes;
- any situation that does not allow to proceed safely.

The ozone application procedures and concentrations were suggested in the Madrid Declaration (8). Via epidural-foraminal, 3 to 7 ml of O_2/O_3 was administered at a 15 μg/ml concentration under tomographic navigation. After 10 to 12 lumbar paravertebral sessions was applied 2 times a week at a concentration of 10 μg/ml. A 27G x 40 mm needle was used in the cervical and dorsal area, and the lumbar needle used was 23G x 60 mm. Ozone was generated by a CE class IIb medical device (Ozonette, SEDECAL, Spain). The procedure was followed under the tomographic navigation technique by MPR. For this, a SIMIENS SOMATOM Emotion 16 tomograph was used.

The efficacy of the treatment was based on pain control according to the visual analog scale (VAS), the baseline at 3, 6, and 12 months after nucleolysis, and using the Lattinen index (9, 10) and a treatment satisfaction survey (classified

the subjective evolutionary criteria as good, regular or bad that was evaluated before and at the end of the study. The Lattinen index comprised five Likert-type subscales which were quantified with values from 0 to 4, the following aspects:

1) pain intensity;
2) pain frequency;
3) consumption of painkillers;
4) degree of disability;
5) hours of sleep (Table I).

Events that could be associated with side effects of the treatment were recorded in the medical history.

Table I. *Criteria followed for the evaluation of the Lattinen index.*

Criterion	Qualitative evaluation	Value
Pain intensity	Null	0
	Light	1
	Modest	2
	Intense	3
	Unbearable	4
Pain frequency	No	0
	Rarely	1
	Frequent	2
	Very common	3
	Continuous	4
Painkiller consumption	Does not take	0
	Occasionally	1
	Regular / Little	2
	Regular / A lot	3
	A lot of	4
Inability	No	0
	light	1
	Moderate	2
	Need help	3
	Total	4
Hours of sleep	As usual	0
	worse than usual	1
	Wakes up frequently	2
	less than 4 hours	3
	Need hypnotics	4
TOTAL		

For the statistical analysis of the data, the preliminary test was applied for the detection of OULIERS errors/outliers. Subsequently, the data were analyzed with a one-way analysis of variance (ANOVA) followed by a homogeneity of variance test (Bartlett-Box). Additionally, a multiple comparison test (Duncan test) was used. The results will be presented as mean±standard deviation.

Continuous and categorical variables are presented as median (IQR) and n (%). The Mann-Whitney U test, $\chi 2$ test, or Fisher's exact test is used to compare differences between before-and-after values. A two-sided α of less than 0.05 was considered statistically significant. Unless otherwise noted, statistical analyses were conducted using SPSS Statistics software (version 2015).

RESULTS

Patients who participated in the study (345) were followed for 12 months. Demographic and clinical data are shown in Table II. The main location of the hernia was at the lumbar level. The patients' evolution was accelerated in the first 3 months and gradually improved over the following months until the final follow-up time at 12 months (Fig. 1, 2).

Table II. *Demographic data of the subjects in the study*.

Variable		Value
n		345
Age, Average (Min.-Max.) years		30-67
Smokers n (%)		85 (24%)
Comorbidities n (%)		
	Hypertension	57 (16%)
	Obesity	35 (10%)
	Diabetes	28 (8%)
Blood pressure (mm Hg)		
	Systolic, Average (Min.-Max.)	120 -135
	Diastolic, Average (Min.-Max.)	75 - 85
Hernia level		
	Cervical n (%)	72 (21%)
	Thoracic n (%)	10 (3%)
	Lumbar n (%)	263 (76%)

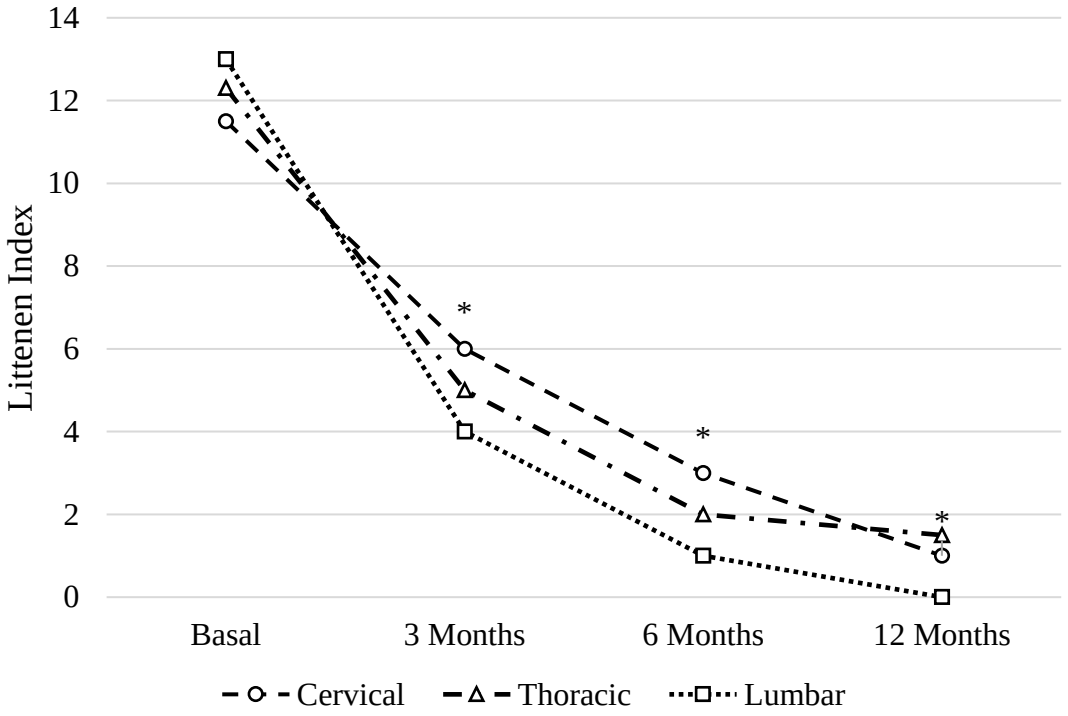

Fig. 1. *Evolution of patients according to the Lattinen scale and according to the location of the hernia;* ***represents significant differences (p<0.05) compared to baseline time. No significant differences (p>0.05) were found between the 3 locations evaluated in each time period.*

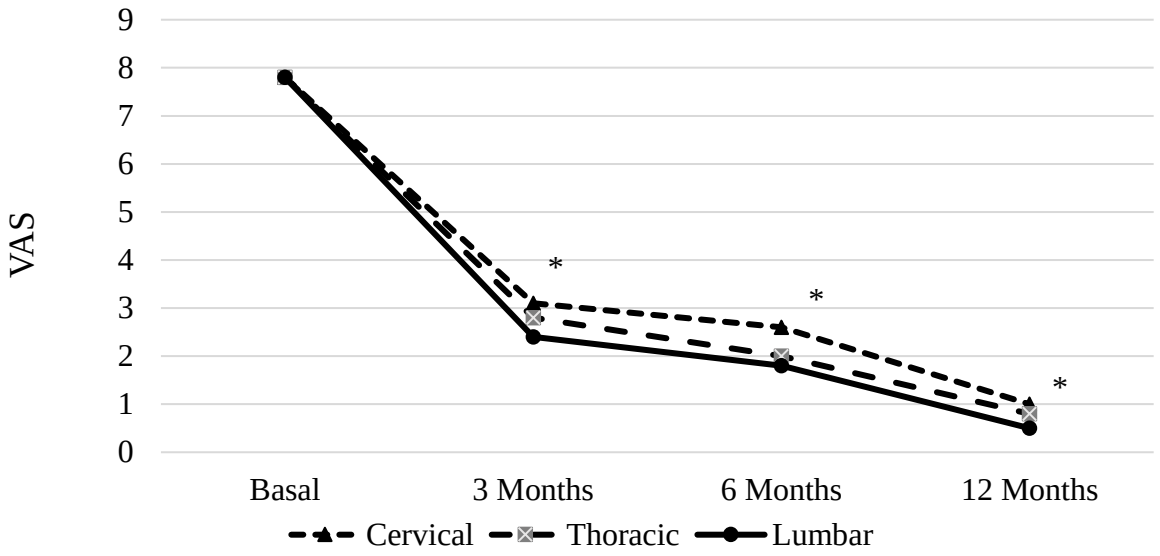

Fig. 2. *Evolution of patients according to the VAS scale; *****represents significant differences (p<0.05) compared to baseline time. No significant differences (p>0.05) were found between the 3 locations evaluated in each time period.*

The initial VAS for the 3 locations was 7.78±0.99 and the evolution at 3, 6, and 12 months was: 2.43±2.19, 1.80±2.31 and 2.07±2.49, respectively, with significant differences (p<0.05) with respect to the initial value and without significant differences between the locations. The initial Lattinen index for all locations was 13.02±2.95 and changed to 6.7±2.14 at 3 months, 3±1.95 at 6 months, and 1.3±0.8 at 12 months with a statistically significant reduction ($p < 0.05$). The initial Lattinen index in cervical hernia was 11.25±2.0, 6.0±1.3 at 3 months, 3.1±1.0 at 6 months, and 1.2±1.1 at 12 months. For the dorsal location, the initial Lattinen index was 12.0±3.0, at 3 months 5.1±2.2, at 6 months 20±3.0, at 12 months 1.50±0. ,7. In the case of lumbar hernia, the initial Lattinen index was 13.0±2.7, at 3 months 4.1±1.5, at six months 1.3±1.1, at 12 months 0.1±0.7.

According to the patient's subjective criteria, the therapy was most successful in patients whose location of the hernia was lumbar (95%), followed by 86% in the cervical location and 80% in the thoracic location (Table III). No side effects to the therapy were reported during the treatment time, the most frequent side effect was local pain at the time of application, which appeared in 65% of the patients and presented as a transient event. Representative follow-up photographs of the evolution of the patients are shown in Fig. 3.

Table III. *Subjective criterion of patient evolution after 12 months.*

Location of the hernia	**Subjective criterion**		
	Bad	Regular	Good
Cervical	3	7	62
Thoracic	1	1	8
Lumbar	1	12	250
Total	5	20	320

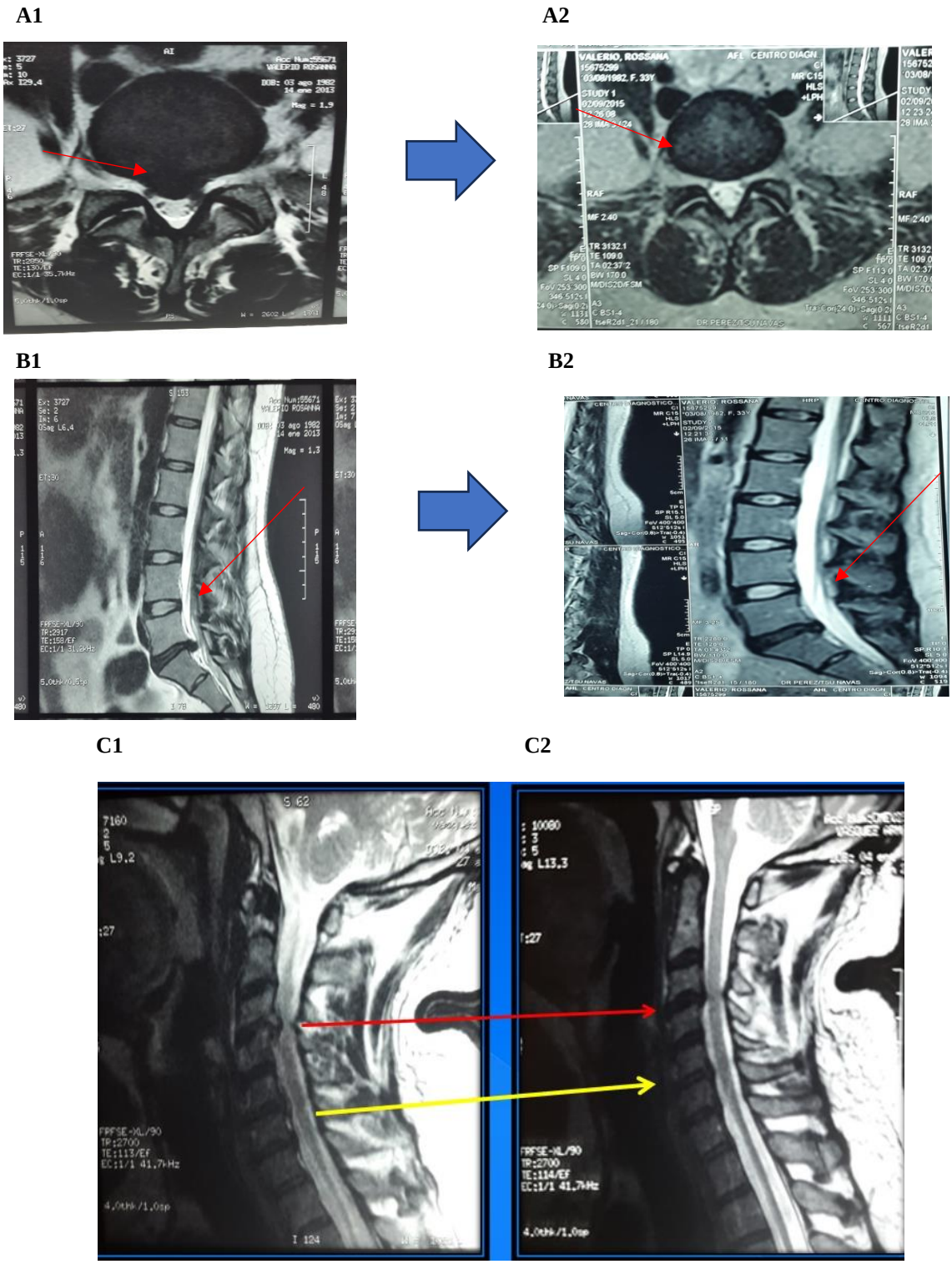

Fig. 3. *Representative photographs of the evolution of patients with herniated discs.* ***A1****): patient with L5-S1 disc herniation axial cut T2 pretreatment;* ***A2****): patient A1 post-treatment (6 months post-dicolysis);* ***B1****): patient with herniated disc L5-S1 sagittal cut T2 pre-treatment;* ***B2****): patient B1 post-treatment (6 months post-dicolysis);* ***C1****), patient with cervical disc herniation C3-C4/C5-C6 sagittal cut T2 pretreatment;* ***C2****): patient C1 post-treatment (6 months post-dicolysis). The arrows indicate the location of the hernia.*

DISCUSSION

Radicular pain is caused by discharges emanating from an inflamed or injured dorsal root or ganglion. The pain generally radiates down the leg from the back and buttocks in a dermatomal distribution. A herniated disc is the most common cause, and inflammation of the affected nerve, rather than its compression, is the most common pathophysiological process (11). Radicular pain radiates along the nerve root without causing neurological deterioration. Although it is a nociceptive pain, it differs from usual nociception because in radicular pain, the axons are not stimulated along their path or in their peripheral terminals but from the perineurium (12).

Ozone can relieve pain at least through the following molecular mechanisms: direct oxidation of pain mediators or pain receptors (13), inhibition of purinergic receptors P2X3 and P2X7 (14), modulation of caspase pathways (15), inhibition of tissue autophagy (via inhibition of LC3B and Beclin1), apoptosis (via inactivation of Caspase 3, phosphodiesterase A2 and NFκB p65 signals) (16), and activating 5'-adenosine monophosphate-activated protein kinase (AMPK) (17). Additionally, ozone treatment modifies key genes, including DCST1 and AIF1L, and metabolites, such as aconitic acid, L-glutamic acid, UDP-glucose, and tyrosine. These changes suggest a complex interplay of molecular pathways and specific regional mechanisms underlying the analgesic effects of ozone therapy (18). Additionally, ozone can modify long non-coding RNA (lncRNA) and small nucleolar RNA host gene 16 (Snhg16) to influence the improvement that occurs during neuropathic pain (19).

In addition to preclinical studies that delve into the mechanisms by which ozone can reduce pain and inflammation, numerous clinical studies demonstrate this effect, particularly those focused on controlling low back pain (20-23). In all cases, the most recent clinical studies on the subject and meta-analyses coincide with the results found in the present study. As could be seen, the evolution of the patients was gradual and progressive; additionally, no relevant adverse events were reported.

CONCLUSIONS

Ozone disc nucleolysis an optimally effective and less invasive treatment option for lumbar, cervical, and thoracic intervertebral disc herniation with a significant reduction in disability and a minimal and transient adverse effect rate. Larger clinical studies are needed to confirm these results.

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Evaluation Study

A FULLY DIGITAL PLANNING AND MANUFACTURING OF AN AESTHETICALLY CONCEIVED AND GUIDED FULL-ARCH IMPLANT-SUPPORTED REHABILITATION

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ABSTRACT

In the rapidly evolving implant dentistry scenario, integrating digital technologies has significantly advanced the precision and efficiency of treatments, especially in full arch implant-supported rehabilitations. Despite these advancements, a completely digital approach to complex cases remains difficult and very challenging, necessitating a hybrid approach that utilizes both digital and traditional techniques. This technical note delineates a combined digital workflow for aesthetically guided, full arch implant-supported rehabilitations in the upper jaw, avoiding the need for interim dentures. Integrating a precise analogical plaster implant impression, advanced digital scanning and planning, mandibular movement registration (ITAK®), and face scans are possible by detecting a reference area defined by the palatine wrinkles. This approach aims to maximize aesthetic, functional, and biomechanical outcomes and addresses the ongoing debate about the accuracy of intraoral scanner scans versus traditional impression methods for full arch restorations. Although digital methods are increasingly favored for their efficiency and potential for trueness and precision, our procedure underscores the relevance of detecting an anatomical area as a reference. Through a detailed technical note, this paper showcases a reproducible protocol that combines the effectiveness of analogic plaster impressions with the benefits of digital planning and Computer-Aided Manufacturing, representing a step towards the future of implant dentistry where digital processes may fully supplant traditional procedures for the immediate loading and the further final prosthetic restoration, enhancing patient outcomes through more accurate and efficient treatment modalities.

KEYWORDS: *full upper arch, hopeless teeth, aesthetic analysis, intraoral scanner, IOS, scanface, ITAKA® comfort position, CBCT, Exocad®*

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INTRODUCTION

Implant dentistry has witnessed remarkable advancements driven by technological innovation and an expanding understanding of mechanical and biological aspects. The treatment of complex cases, historically challenged by anatomical constraints, prosthetic considerations, and patient expectations for functionality and aesthetics, has evolved significantly. Traditionally, rehabilitating patients presenting hopeless teeth involved creating a removable denture from an initial impression and a facebow registration. This denture, worn post-extraction, was a practical method to evaluate aesthetics, phonetics, and functional integration.

Literature reports various methods to assess the correct Vertical Dimension of Occlusion (VDO) for a patient (1), acknowledging it as an adaptability range from which clinicians choose a value to balance aesthetic and functional requirements (2). However, it is also noted that no universal, well-established rules exist for determining VDO once it is lost, mainly due to inter-patient variations (3,4). If teeth are present or a removable denture has already been fabricated and the current VDO is deemed correct, pre-extraction records have been suggested because teeth represent an index.

Digital technologies have heavily influenced how specific tasks are performed in dentistry, including full arch implant-supported restorations. As reported in a recent paper by Feng et al. (5), the traditional systems to transfer information from the dental clinic to the dental laboratory are time-consuming and prone to cumulative errors. At the same time, digital methods are faster and less prone to data modification during the transferring phase. The same Authors, in their report on a dentate patient, noted that intraoral scanners (IOS), facial scanners, 3D low-dose radiographic exams like cone beam computed tomography (CBCT), and digital dynamic occlusion registration can nowadays be blended into specific planning software to create a virtual patient and make many manual steps outdated, especially if they decide to consider the palatine wrinkles as an anatomical reference.

Given the effectiveness of digital technologies, it is possible to integrate different files derived from several digital devices into a single project due to the coupling of the same anatomical reference, even if many elements are still required to streamline the digital protocol completely. Detecting a common anatomical reference among all the different files (intraoral scans during the diagnostic phase, digital wax-up proposal, master cast derived from the plaster impression) is pivotal in a stable, reliable, reproducible information transferring among all the phases.

Moreover, despite some authors (6, 7) reporting potentially comparable results in full arch implants IOS vs. plaster impressions, many are still cautious in considering digital scans on full arch implant-supported restorations as a substitute for the current gold standard (8–10). On the other hand, some authors recently reported no significative difference when comparing computer-aided manufacturing (CAM) produced full arch frameworks derived from digital impressions with the plaster impression counterparts (11). Discrepancies in reports might be attributable to the evolution of scanning equipment, acquisition protocols, and operator experience (12, 13). Nevertheless, digital planning and CAM integration hold promise, particularly as full-arch frameworks produced via Computer Numerical Control (CNC) machining have shown greater precision than traditional casting, given that an accurate impression is provided (14).

This paper details the author's approach to digital upper jaw full arch implant-supported rehabilitations. This method exploits digital technologies to prevent the need for physical dentures and facebow registrations while maximizing integration in patient aesthetics thanks to new technologies. By creating a virtual patient, this protocol enhances treatment accuracy and capitalizes on the benefits of CAD/CAM while retaining the precision of analog plaster impressions. As digital impression precision continues to improve, this protocol represents a step towards a future where digital processes can fully replace traditional methods in implant dentistry, thereby enhancing patient outcomes through more accurate and efficient treatment modalities.

CASE REPORT

In this case study, a 38-year-old female dental-phobic patient (with a traumatic dental background and long-standing phobia regarding dental check-ups and treatments) sought dental treatment at our private practice, aiming for a fixed rehabilitation and aesthetic restoration of the hopeless upper and lower arches. The patient presented an unremarkable medical history, classifying her as ASA I, and prioritized aesthetics while expressing a desire for swift rehabilitation. She emphasized avoiding any visible void in the aesthetic zone following extractions. She sought a solution to restore her full masticatory function, which had been significantly impaired and limited to her anterior teeth.

The first clinical step aimed to gather all the relevant information for the author’s digital workflow. Extraoral, smiling, non-smiling, and intraoral photographs were acquired using a standardized protocol (Fig. 1), highlighting the lack of soft tissue support and Posterior Bite Collapse (PBC). Subsequently, a CBCT exam was acquired to gather anatomical information, primarily bone availability and maxillary sinus morphology, and a double arch digital impression,

including palatine wrinkles for the upper jaw, with a virtual occlusal record was acquired as a prosthetic reference (Fig. 2).

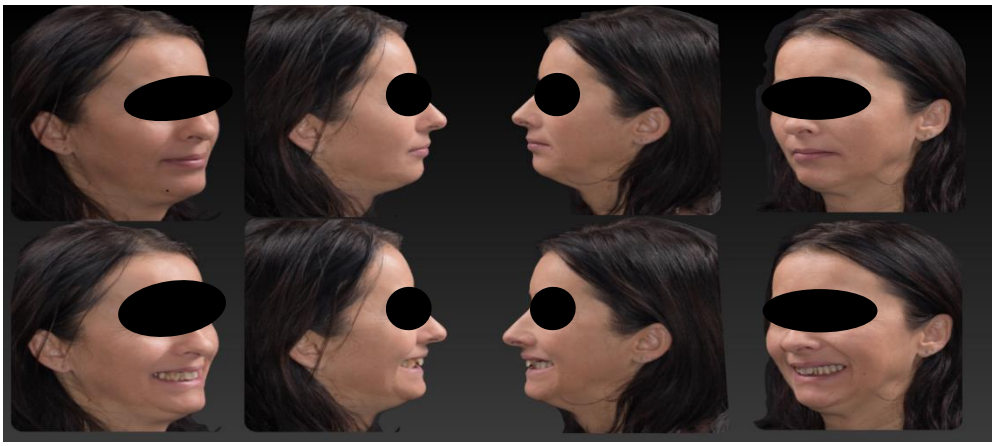


Fig. 1. *Patient panel reporting the initial extraoral condition.*

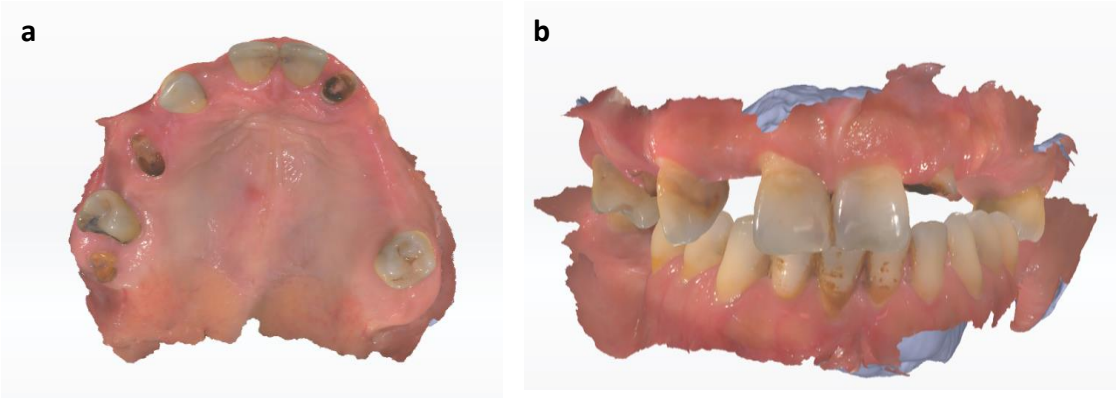


Fig. 2. *Digital scans of the individual jaws and the upper one with the palatine wrinkles (**a**) and arches articulated one another (**b**).*

During the initial consultation, a comprehensive clinical examination was carried out, revealing a significant occlusal deficiency due to the loss of multiple posterior teeth in both arches, resulting in a condition identified as PBC (Fig. 3). Given the absence of any previous records to define the patient's original occlusal schema, a detailed facial registration (MetiSmile, SHINING 3D Tech Co., Ltd., Hangzhou, China) (Fig. 4) alongside dynamic occlusion measurements, specifically called jaw kinematic analysis, (Cyclops, Itaka Way Med SRL, Marcon, Venice, Italy) were obtained (Fig. 5). A surface electromyography examination was executed (Teethan®, Teethan S.p.A, Milan, Italy) to evaluate the current occlusal schema and verify the absence of parafunctional loads. These assessments were instrumental in establishing the optimal occlusal relationship for the forthcoming rehabilitation process.

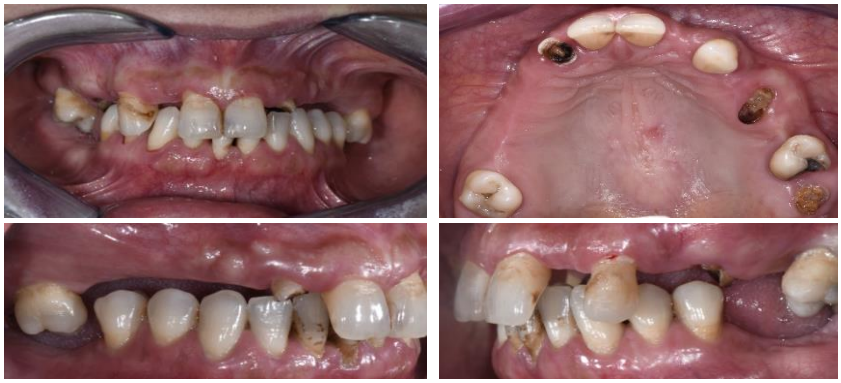


Fig. 3. *Patient's composite reporting the starting intraoral condition.*

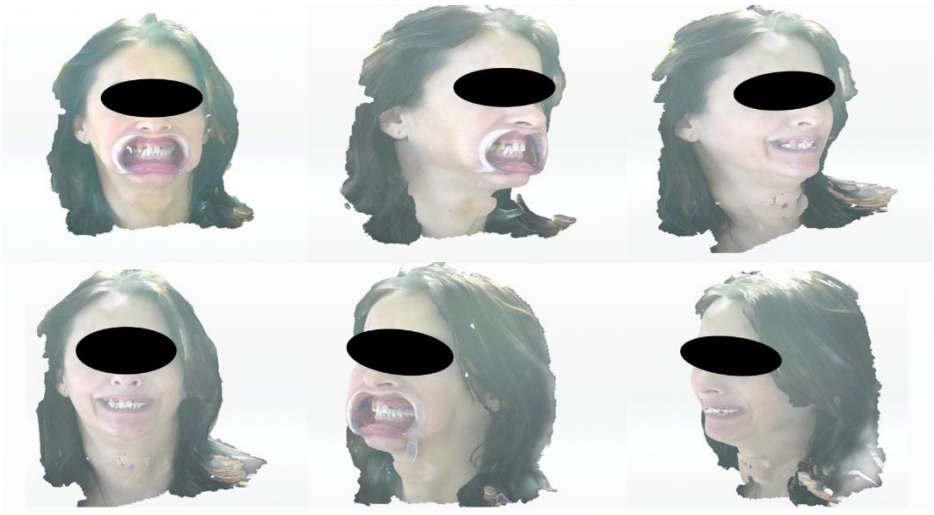
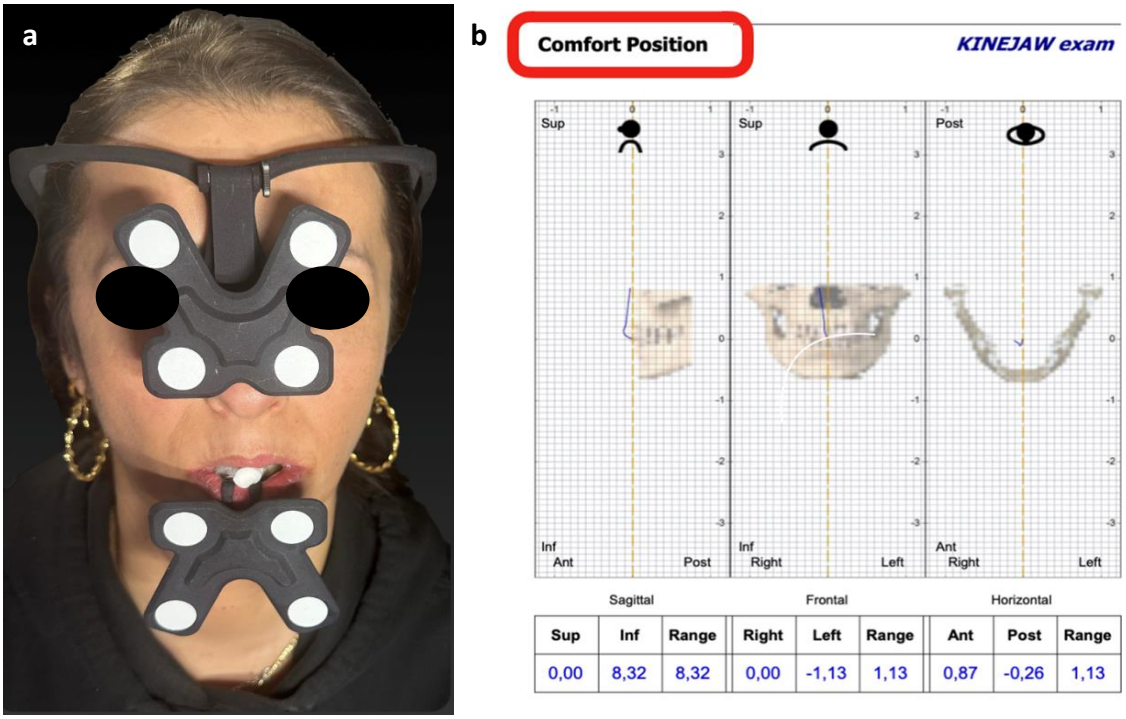


Fig. 4. *Various steps of a face scan acquisition through MetiSmile's software.*



Sup	Inf	Range	Right	Left	Range	Ant	Post	Range
0,00	8,32	8,32	0,00	-1,13	1,13	0,87	-0,26	1,13

Fig. 5. *ITAKA Kinematic jaw exam execution (**a**) and related report on the comfort position (**b**).*

The authors advocate for an extemporary fabrication of a Lucia Jig, employed as a muscle de-programmer, in tandem with a digital capture of the mandibular range of motion. This approach enables a precise determination of the patient's comfort zone, wherein the centric relation is established. This process considers the VDO required to meet aesthetic and functional requisites, thereby defining a neurofunctional position that extends beyond mere anatomical considerations, usually defining centric relation.

Virtual planning phase

The dental laboratory was equipped with a detailed collection of diagnostic information, encompassing extraoral and intraoral pictures, digital models of both arches, a digital bite record, a facial scan, and a digital evaluation of the lower jaw's movements. This comprehensive dataset eliminates the necessity for conventional facebow registration by utilizing the facial scan as a critical reference point. This scan is used to accurately align the digital upper jaw model with

the patient's cranial base, advocating for a facially driven approach in the planning and executing full arch implant-supported rehabilitations. Initially focusing on facial aesthetics ensures the restorative work is tailored to enhance the patient's overall appearance, subsequently guiding the prosthetic and surgical phases of treatment.

The provided data requirements to be matched for creating a virtual patient. The software of choice in the author's daily practice is Exocad (DentalCAD version 3.2) since it can handle all the planning and designing phases in a complete suite. 3D Standard Tessellation Language (.STL) files are uploaded and mutually registered using a dedicated wizard, including lower jaw kinematics. The next crucial step involves the integration of In-CAD Smile Design through the Smile Creator feature within Exocad. This tool transforms patient photographs into three-dimensional models, which can later be aligned with the 3D dental scan. This step serves as a double-check measure because any error in the data acquisition would be reflected in an incorrect 2D-3D matching and as a guide during the provisional fabrication.

Indeed, the next step is for the dental technician to start the fabrication of the first provisional, which won't be delivered before surgery but will be adapted when the post-operatory impression is sent so it can be delivered as fast as possible. This includes calculating the prosthetic space, derived by subtracting the freeway space from the VDO and determining the aesthetic space. A systematic review reports that 75%-100% of the upper front teeth are exposed during smiling (15). In contrast, another systematic review identified laypersons' preference for a slight coverage of front teeth crowns (16), placing the aesthetic space in the upper region at around 80% of the prosthetic space. The aesthetic space is crucial as it delineates the restoration segment visible during a smile and can be identified by the sustained pronunciation of the phoneme 'I'. However, this metric may vary and be tailored to accommodate the unique dental exposure observed in the patient pre-operatively.

In this specific patient, the dental lab digitally extracted residual hopeless teeth (used as index before) using the dedicated tool and proceeded with digital wax-up teeth positioning based on the aesthetic needs (Fig 6); once the distribution is accommodated on aesthetic, a simple tool can make slight changes to consider the previously acquired data on lower jaw movements to implement dynamic occlusion onto the newly created occlusal schema (Fig. 7). The result is a digital wax-up, that is confirmed by both the patient and the clinician.

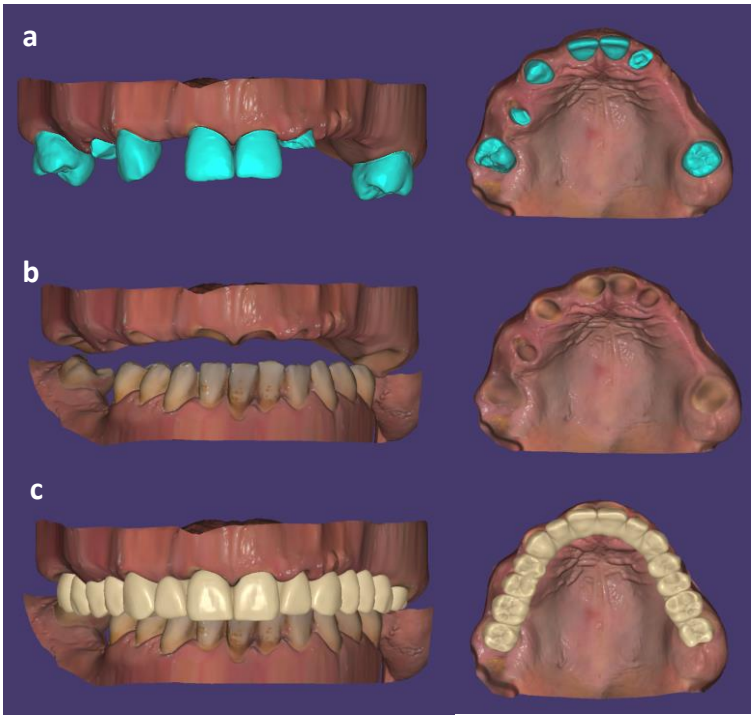


Fig. 6. *Hopeless teeth are marked (**a**) and virtually extracted (**b**). Aesthetic and static occlusion guide the initial positioning of denture teeth (**c**).*

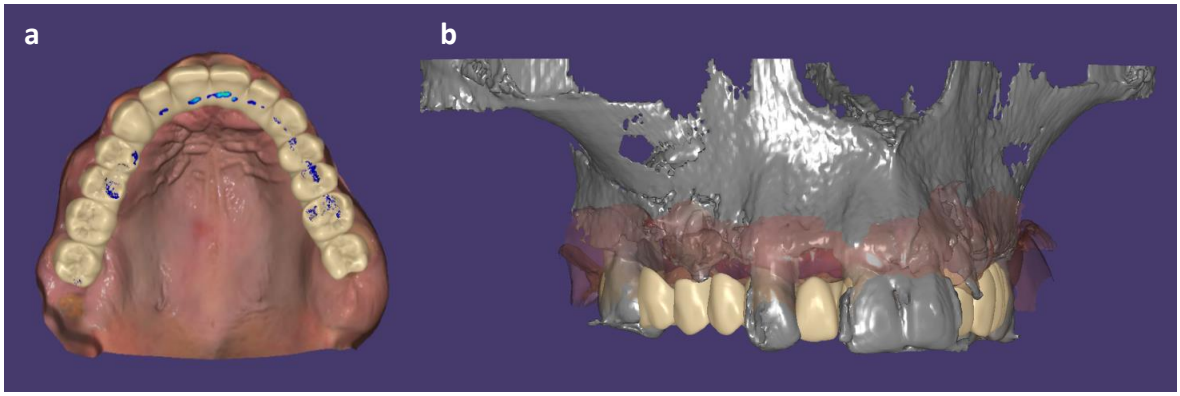


Fig 7. *Teeth are adjusted to dynamic occlusion (**a**), and the provisional project is finalized (**b**).*

The concluding steps of the pre-surgical process are timed. Ideally, all preparatory procedures, specifically the finalization of the digital wax-up, are completed one week before the scheduled surgery. This timeframe is crucial as it allows for necessary adjustments based on patient or clinician feedback. In the final week leading up to the surgery, attention turns to the design and fabrication of a customized prosthetic-surgical guide. This stent is peculiar in its design approach. Following the virtual extraction of the deemed hopeless teeth, save for the most distal ones, it is crafted to replicate the soft-tissue contours accurately.

The design is informed by the previously finalized provisional, supported by the palatine wrinkles, with strategic perforations aligned over the crestal bone where each prosthetic tooth, not implant, is to be placed (Fig. 8). The primary function of this surgical stent is not to direct the implant drills physically but to serve as a visual reference for the future dental prosthesis. This innovative approach allows the clinician to place implants with a prosthetically driven mindset, ensuring the implants' optimal position, the Low Profile Zimvie® abutments choice, and proper orientation for the planned restoration.

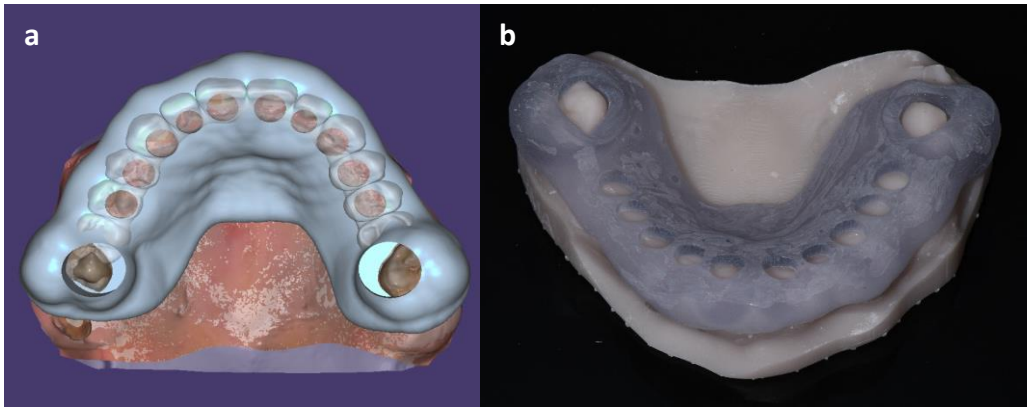


Fig. 8. *A prosthetic-surgical stent is designed according to the teeth's future position (**a**) and is 3D-printed for delivery on the day of surgery (**b**). Note the mucosal support given by the palatine wrinkles.*

In preparation for the surgery, a second template is crafted using digital design and 3D printing technologies - a custom individual impression tray tailored for easier data matching (Fig. 9). This template follows the previously outlined steps for the virtual extraction of hopeless teeth and the fabrication of a soft tissue-adapted stent, yet it introduces some additional feature. Firstly, the tray design incorporates an open top, allowing for the adequate placement of rigid impression materials, namely plaster. Additionally, the tray design extends over the palatine wrinkles since they are stable over time and unextensible, making it an ideal reference point for future data matching. Furthermore, a practical hand-hold is included, facilitating the device's manipulation and usage during the impression-taking step.

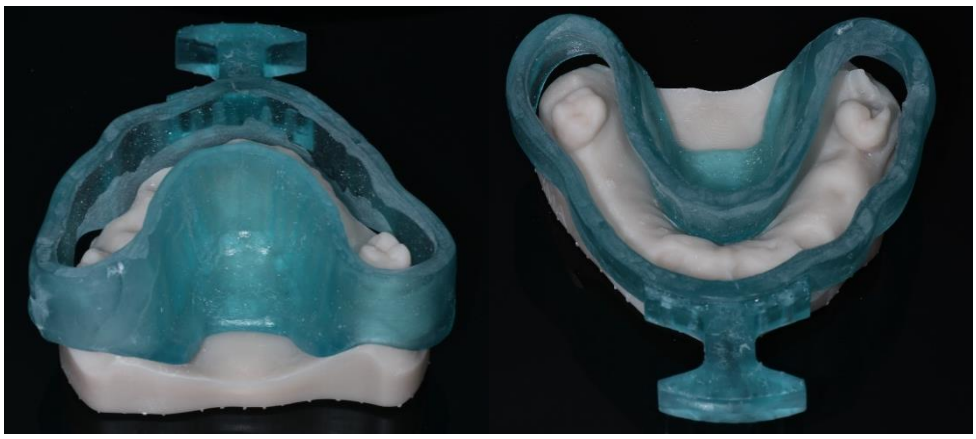


Fig. 9. *A digitally designed customized open-top impression tray extending over the palatine rugae.*

Implant surgery and provisional delivery

On the day of surgery, a full-thickness flap was elevated, with the initial crestal incision slightly decentred on the palatal side. The failing teeth, except for the distal ones, were extracted to allow the placement of the previously fabricated prosthetic-surgical stent (Fig. 10).

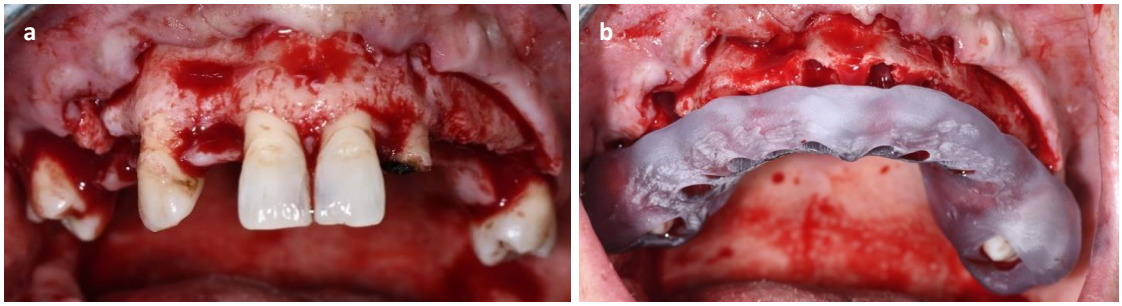


Fig. 10. *A full-thickness flap is raised (**a**), and the prosthetic-surgical glass-like template is placed after failing anterior teeth extraction (**b**).*

This template does not represent a static surgical guide but a pre-implant aesthetic guide. After that evaluation, tapered dental implant placement (T3® PRO, Zimvie Inc., Westminster, USA) in the premaxilla was possible, maximizing bone availability. Once the stent had fulfilled its role, it was removed, the distal teeth were extracted, and two tilted implants were positioned.

These posterior implants engaged the pterygoid lamina as part of the authors' usual implant positioning protocol for atrophic patients (17). Low-profile angled abutments were screwed in place, and grafting material (Endobon® Xenograft Granules, Zimvie Inc., Westminster, USA) was used to secure adequate marginal bone levels over time. Before suturing with single stitches using Vicryl® 3.0 (Vicryl® 3.0, Ethicon, Raritan, USA), healing abutments were secured in place.

As a final step, open-tray impression transfers were used in combination with plaster, polyvinylsiloxane, and the previously fabricated individual tray to obtain an immediate impression of the four anterior implants since the immediate load was not planned for the posterior pterygoid (Fig. 11).

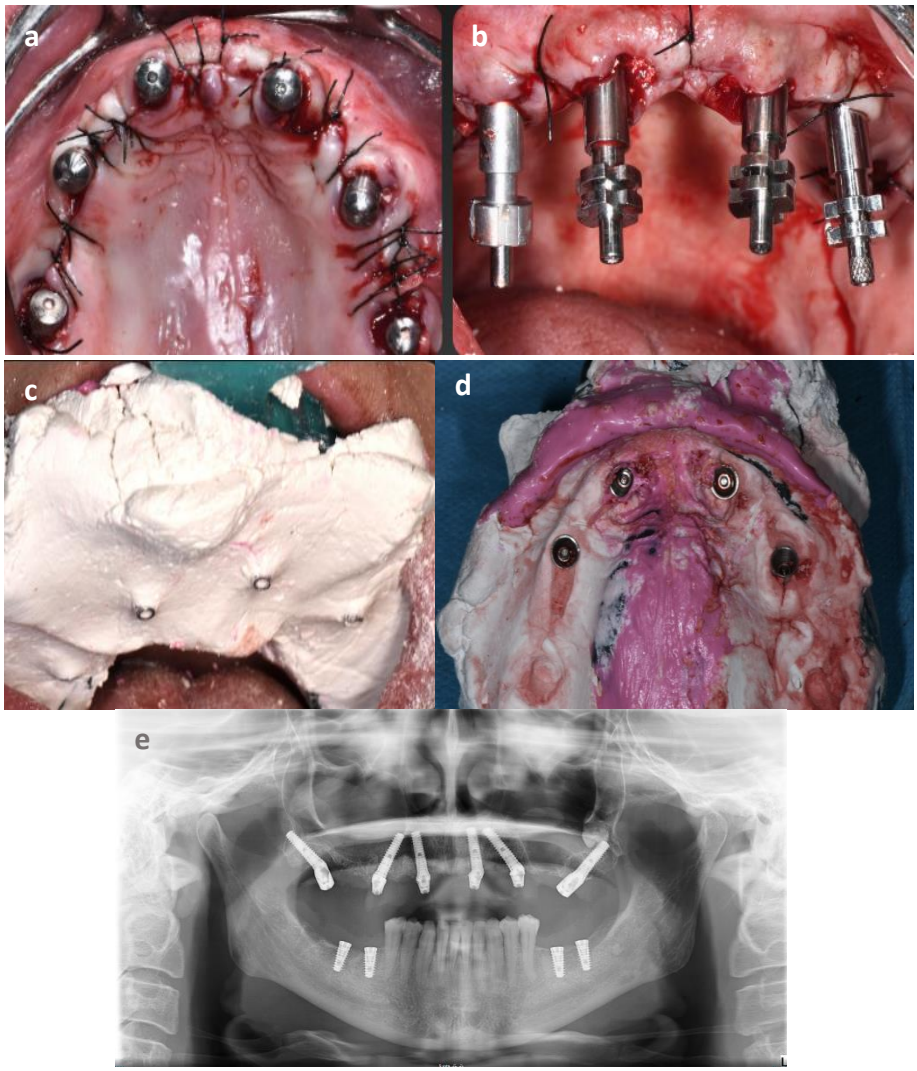


Fig. 11. *Implants and healing cups are placed, and sutures are positioned (**a**). A mixed plaster impression is taken with transfers positioned on the four anterior implants (**b**, c, and **d**) using a customized impression tray derived from the same aesthetic guide template and mucosal supported in the same palatine wrinkles reference area. The radiological Orthopantomography is scanned after the delivery of the milled Polymethyl Methacrylate (PMMA) provisional restoration screwed on 4 Low Profiles: let's note the radiolucent aspect depending on the absence of the armor (**e**).*

The patient is dismissed with post-operatory indications for a few hours. In the meantime, at the dental laboratory, the plaster impression cast is scanned using scan bodies, and the post-operatory data is aligned with the presurgical plan thanks to the palatine wrinkles, which are a stable reference point that allows for VDO maintenance (Fig 12).

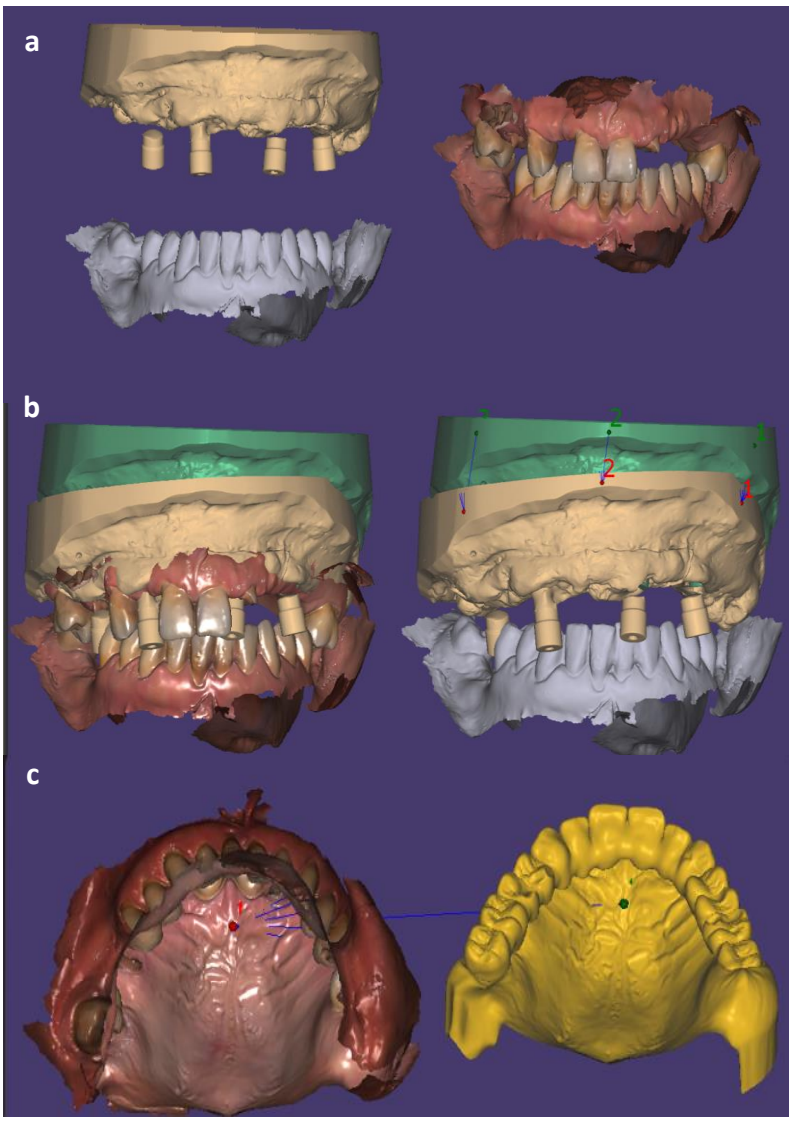


Fig. 12. *The immediate mixed impression is digitalized (**a**) using scan bodies and imported into the presurgical project (**b**). Palatine wrinkles allow for the data matching (**c**).*

Thanks to these newly gathered data, the dental technician matches the ScanBodies of the post-operative plaster cast digitalization with their digital correspondence. In the Authors' experience, using higher offset ScanBodies allows for a more precise matching. Specifically, scan bodies with 6 matching references at the coronal level were employed (ScanBody ProCam, Biaggini Medical Devices srl, Arcola, Italy). Once this step is accomplished, the previously designed provisional can be adapted according to the newly established implant positions to accommodate holes slightly larger than the abutments (Fig. 13). The abutments will be luted with anaerobic cement, allowing maximum passivity.

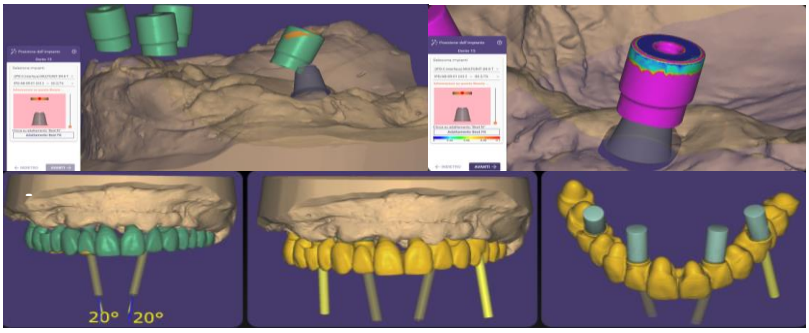


Fig. 13. *ScanBodies are precisely matched thanks to the coronal offset of the 6 reference points (**a**), and the previously confirmed digital mock-up is adapted (**b**).*

The resulting .STL file is sent to a 5-axis milling machine to obtain a long-lasting multilayer Polymethyl Methacrylate (PMMA) (Dentsply Sirona Inc., Charlotte, USA) provisional (Fig. 14); this material is chosen for its optimal mechanical properties, specifically an elasticity module greater than 2200 MPa and flexural strength greater than 80 MPa. The product is checked for passivity both digitally prior to the milling, thanks to a one-screw test, and on the original plaster cast. The provisional rehabilitation, loaded on four implants, is delivered within 24 hours, and minor occlusal corrections are made if necessary (Fig 15).

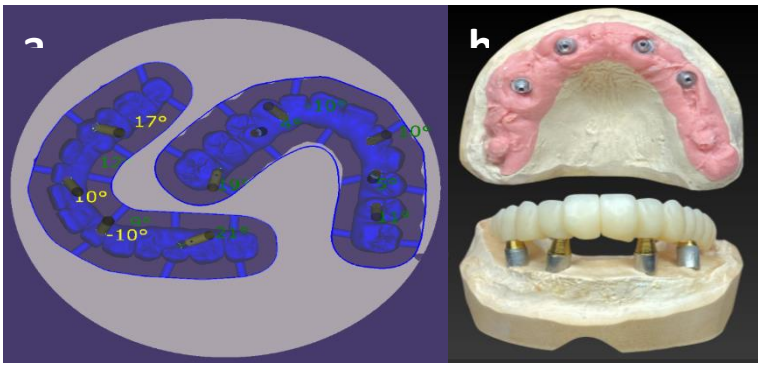


Fig. 14. *The provisional restoration project is sent to a milling machine (**a**), and the deriving product is checked for absolute passivity on the plaster cast (**b**).*

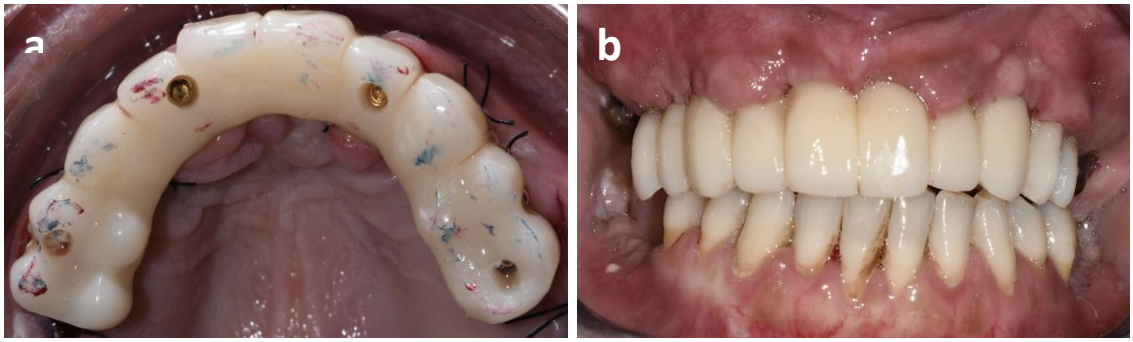


Fig. 15. *Contact points are refined intraorally (**a**), and the provisional is delivered within 24 hours of surgical intervention (**b**).*

Provisional re-evaluation

At the 3 months, the provisional needs to be re-evaluated, and further data must be acquired. While a detailed exposition of the fabrication process for a final full-arch implant-supported rehabilitation exceeds the scope of this document and has been comprehensively addressed in a recent publication by the authors (18), key steps will be outlined here to ensure a complete case presentation (Fig. 16).

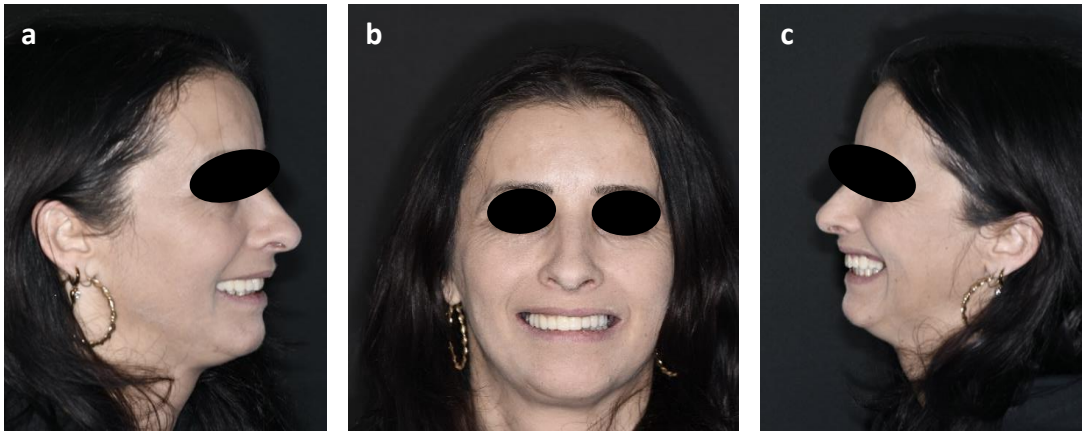


Fig. 16. *Front facing (**b**) and profile (**a**, **c**) smiling photos of the patient with the final restoration in situ.*

At this stage, the provisional is removed from the oral cavity, and intraoral ScanBodies (ScanBody ProCam, Biaggini Medical Devices Srl, Arcola, Italy) are positioned on the implants. The ScanBodies are interconnected using a pattern resin splint to ensure a highly accurate intraoral scan. This technique solidifies the ScanBodies as a single unit, stabilizing them to prevent any movement during scanning, which could compromise the precision of the data capture. Following the stabilization of the ScanBodies, a detailed intraoral scan is conducted. This scan captures comprehensive data on the soft tissues surrounding the implants and the solidarized ScanBodies, providing a precise digital representation of the mouth's current state. This data is further enriched by an extraoral scan of the provisional and an extraoral scan of the patter resin jig (Fig. 17).

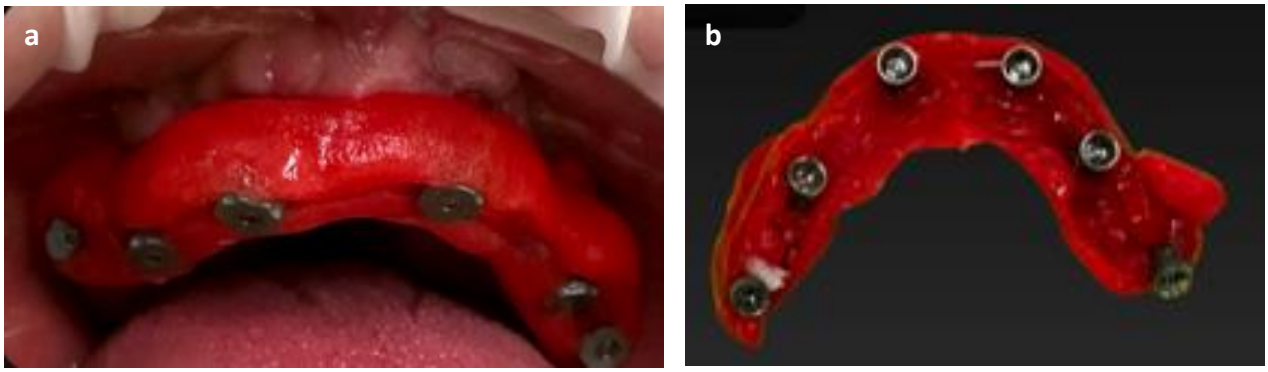


Fig. 17. *Thanks to pattern resin, ScanBodies are interconnected (**a**), and the jig is scanned intraorally and extraorally (**b**).*

A fundamental second step in this phase involves acquiring an extraoral scan of the worn provisional prosthesis and conducting a follow-up surface electromyography (Teethan®, Teethan S.p.A, Milan, Italy). This approach enables, after import in the CAD software, a detailed assessment of the functional wear on the provisional by comparing the.STL file from the scan with the initial CAD project. Such comparison aids in identifying any deviations or wear patterns that may have occurred during the provisional functionalization timeframe. Meanwhile, surface electromyography serves a dual purpose. It confirms the achievement of a balanced occlusion in the absence of prior pathological indicators. It assesses the impact of the rehabilitation process, especially if there were initial complaints or symptoms. Thanks to this data, the clinician and the dental technician can proceed with the final restoration fabrication.

DISCUSSION

In the conventional framework of implant dentistry, particularly when addressing full arch implant-supported restorations in failing or absent dentitions, a series of critical steps are indispensable for ensuring the success of the treatment. Among these, the accurate determination of the VDO stands out as a foundational requirement. This process, essential for both aesthetic outcomes and functional efficiency, varies depending on the presence of any remaining natural teeth. In cases where residual dentition persists, the assessment typically commences with measurements of the existing VDO. However, in scenarios where posterior dental contacts are missing, a meticulous registration of centric relation (CR) is performed to establish a base from which a new VDO can be evaluated.

This traditional method often necessitates the fabrication of an intermediate removable denture. While critical for assessing a suitable new VDO, this step introduces several challenges to the treatment timeline and patient experience. Firstly, it significantly prolongs the overall duration of treatment. Each phase, from the initial evaluation to the final loading of implants, is extended due to the additional steps required to fabricate and adjust the removable denture. Furthermore, this approach incurs higher costs attributed to the materials and labor involved in creating the denture and the extended clinical and laboratory work duration. Most notably, from the patient's perspective, this process mandates using a removable device from the moment of teeth extraction up until the placement and loading of implants. While necessary for determining the correct VDO, this interim solution may compromise the patient's comfort, aesthetics, and overall satisfaction with the treatment process. The necessity to adapt to a removable denture, even temporarily, can be a significant inconvenience, impacting their daily life and confidence.

Despite the benefits of digital technologies facilitating immediate loading protocols in edentulous arches, transferring occlusal information, namely VDO, from the removable provisional denture to the fixed one remains challenging due to the lack of reference points in edentulous impressions (19). The emerging digital workflow addresses

these difficulties by minimizing the need for a physical interim denture for occlusal evaluation and exploiting digital techniques for data alignment and VDO transfer from initial assessment to post-operative restoration. In this context, hopeless teeth can be used as starting indexes for VDO assessment before extraction, thanks to the digital scans, if they still carry valuable information.

A notable advancement by Lorenzetti et al. (20) in 2021 introduced a method for fabricating an immediate load fixed implant-supported interim prosthesis for both arches without a removable denture, using palatine rugae as a reference point for the upper jaw. Lorenzetti's protocol still required analogic adjustments to the VDO and interocclusal relationship if necessary. At the same time, this proposed approach is based on fully digital evaluations, so no physical adjustment is required in the patient's mouth before taking the pre-operative impressions. A significant help in this direction is the implementation of both a face scan and a digital registration of the inferior jaw dynamics so that the most meaningful parameters are digitalized and joined into a single software. Palatine wrinkles are the chosen point of reference due to their inextensibility and stability over time, two mandatory features when identifying a fixed landmark; the data matching is indeed possible thanks to their presence both in the post-operative plaster impression and in the digital wax-up, eliminating reliance on mini-implants, which are poorly tolerated by patients and augment costs.

A second key element of the proposed approach is the retention of the most distal hopeless teeth during implant surgery. The specially designed stent can be accommodated with tooth support, which is much more precise than mucosal and less invasive than bone stabilization (21). This stent is defined as a prosthetic-surgical guide. Its focus is not to serve as a limiting guide to implant placement but rather to be a visual representation of the optimal teeth positioning, replacing the role of an interim denture with the benefits of no additional cost and little effort.

This workflow also highly emphasizes aesthetic considerations, starting from macroesthetic principles and extending to microesthetic considerations. The ability to create a virtual patient model by capturing a face scan and joining it with 2D photos in various settings makes it possible to analyze the dynamic aspects of facial expressions during social interactions within the dental laboratory. This analysis focuses on the proportions of the facial thirds, their alignment with the midline on the coronal plane, as well as the relationship of the maxilla to the skull base, and the VDO of occlusion on the sagittal plane. The virtual patient framework also facilitates the examination of the smile line and tooth proportions, enhancing the clinician's ability to communicate with the dental technician and the patient concerning the expected outcomes and aesthetic preferences, all without the need for creating a physical aesthetic try-in.

As the field evolves, the Authors anticipate an increasingly digital future for implant dentistry. Particularly for the discussed protocol and its variations, there's a push towards more accurate and streamlined digital scanning processes in full arch rehabilitations. Progress is evident with the introduction of dual-purpose impression abutments, designed to serve as transfer points for traditional plaster impressions and scan bodies for digital model casting. This innovation marks a significant step towards integrating and enhancing the precision of digital workflows in implant dentistry, bridging the gap between analogic and digital impression techniques.

CONCLUSIONS

This clinical report showed the efficacy of a mixed analogic and digital workflow in managing complex full-arch rehabilitation of the upper jaw. By employing a prosthetic-surgical guide and advanced preoperative digital planning, the proposed method facilitated the accurate transfer of crucial occlusal and aesthetic parameters from the initial assessment to the final restoration. Notably, this approach eliminated the need for traditional interim dentures to propagate the VDO of occlusion through different phases, exploiting the adequateness of digital scans in specific contexts and the traditional plaster impression, among others. This system significantly streamlined the treatment process, reducing treatment duration and costs without sacrificing the predictability of aesthetic and functional outcomes in complex cases.

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Evaluation Study

CLINICAL EFFICACY AND SAFETY OF NEOIAL HC (HYALURONIC ACID + COLLAGEN) FOR INTRA-ARTICULAR USE IN THE TREATMENT OF SEVERE KNEE OSTEOARTHRITIS

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ABSTRACT

Osteoarthritis (OA) is a common cause of pain and disability in adults, with at least 40% of individuals over 65 experiencing symptomatic OA of the hip or knee, according to the Osteoarthritis Research Society International (OARSI). Knee OA is the eleventh leading cause of years lived with disability, as reported by the World Health Organization. Current guidelines recommend using intra-articular injections of hyaluronic acid (HA) to treat OA, which can provide slow and prolonged pain relief for up to six months after the first injection. However, there is limited literature regarding the intra-articular use of isolated collagen or its combination with HA for treating knee OA. The present study (pre-market clinical trial) reports a clinically safe profile. It provides evidence of the efficacy of a viscosupplementation solution containing collagen type I, and HA obtained via bacterial fermentation (NEOIAL HC) in treating symptomatic knee OA. The primary endpoint was the safety and efficacy parameters of NEOIAL HC in intra-articular infiltration to treat severe knee osteoarthritis. The evaluation was conducted through subjective and objective clinical scores and reporting of adverse events. The secondary endpoint will be knee function 6 months after treatment. The preliminary findings suggest sustained benefits in pain and physical function from the cycle of collagen Type I and HA injections.

KEYWORDS: *hyaluronic acid, knee osteoarthritis, viscosupplementation, collagen*

INTRODUCTION

Osteoarthritis (OA) is a degenerative, chronic, and progressive joint disease with a multifactorial etiology and is most common in weight-bearing joints, such as knees (1). Currently, no treatment is available to stop OA progression, and joint replacement surgery is the only solution for severe cases. Non-operative treatment options include intra-articular drug injections into affected joints, which increase local bioavailability and reduce systemic exposure, adverse events (AEs), and costs compared with traditional pharmacologic therapies (2-4). Intra-articular injections of corticosteroids

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having anti-inflammatory properties (5) and of hyaluronic acid (HA), a viscosupplement with analgesic, anti-inflammatory, and potential disease-modifying properties (6, 7), have been widely used (2, 3).

In this context, a viscosupplementation solution containing collagen type I and HA obtained via bacterial fermentation (NEOIAL HC) was applied intraarticularly. Thanks to the interaction between collagen and HA, the local administration of the product into the joint space of patients with osteoarthritis is intended to restore articular cartilage homeostasis.

The medical device referred to in this work, called "Neoial HC (40 mg; HA sodium salt at 2% with two molecular weights 20% with pm at 400 kD and 80% between 1200 and 1500 kD t + collagen) contains HA, one of the most important structural polymers in the body. It is found as molecules on the cell surface and in the extracellular matrix of the skin, the vitreous body of the eye, joints, and muscles. HA is one of the body's most important structural and biological components and plays a fundamental role in viscosupplementation in cases of arthritic conditions. Hyaluronic acid is a biological polysaccharide (glycosaminoglycan) distributed in the extracellular matrix of most tissues; it is strongly hydrophilic and forms a viscous hydrated gel even at low concentrations. HA is a molecule that plays a key role in the joint; it is synthesized by the synovial cells and is responsible for the viscoelastic properties of the synovial fluid. It is one of the main components of the extracellular matrix. It also contributes to the lubrication mechanisms under load conditions and tries to protect the tissue from the penetration of inflammatory cells or lytic enzymes. In joints suffering from severe arthrosis, the inflammatory fluid is poor in elasticity and viscosity. Therefore, the intra-articular injection of HA, called viscosupplementation, restores the viscoelastic properties of the synovial fluid. The action of HA is anti-inflammatory and analgesic (8, 9).

In addition to HA, the alpha 1 R polypeptide chain of collagen reinforces the joint by providing structural strength to the cartilage matrix, deteriorated by the pathological processes in progress, whose scaffolding is formed by a dense interweaving of collagen fibers, thus acting as direct reinforcement of weakened and/or deteriorated collagen structures, improving mobility and helping to reduce painful symptoms affecting the joint. In the peri-articular route, collagen acts as a direct reinforcement to the damaged collagen framework of the peri-articular structures, such as tendons and / or ligaments, contributing to a reduction of pain and a faster functional recovery. Based on the preceding, it is possible to conclude that the main components of the medical device, hyaluronic acid with alpha 1 R polypeptide chain of collagen, exercise the expected mechanisms of action and that the medical device allows for the activities described. This gel presents a mechanical and rheological behavior close to the synovial fluid with both lubrication and shock damping effect, offering protection of the patient's cartilage. The first objective of this study was to determine the safety and efficacy parameters of NEOIAL HC (Hyaluronic acid (HA) + collagen) in the intra-articular infiltration for the treatment of severe knee osteoarthritis, which was evaluated through subjective and objective clinical evaluations while reporting the adverse events. The secondary endpoint is knee function at 6 and 12 months after treatment.

MATERIAL AND METHODS

This prospective monocentre, with open design, PMCF phase study, was conducted from November 2021 to March 2022. It was an open study where the patients were enrolled sequentially.

The study included 15 participants aged 50–80 who had been diagnosed with primary knee OA and met the inclusion criteria. Inclusion criteria required a diagnosis of knee OA with pain persisting for more than 3 months, BMI < 30, a VAS score greater than three based on the American College of Rheumatology Criteria, and Radiographic stage III and IV according to the Kellgren-Lawrence system as evidenced by recent x-ray, taken within the last six months (5). The exclusion criteria were: knee surgery, recent knee trauma, lower limb length discrepancy, BMI, intra-articular injection with steroids or HA, and/or current/regular treatments with steroids or non-steroidal anti-inflammatory drugs (NSAIDs) within the previous 3 months (acetaminophen was allowed), rheumatic pathologies (rheumatoid, psoriatic and reactive arthritis, arthritis associated with inflammatory bowel diseases, and spondylarthritis) endocrinopathies, malignancies and systemic diseases (renal, hepatic, cardiac, etc.).

Patients with severe knee osteoarthritis were enrolled in the clinical study and treated with 3 injections of 40 mg NEOIAL HC (HA sodium salt at 2% with two molecular weights 20% with pm at 400 kD and 80% between 1200 and 1500 kD t + collagen) at 1 week from each other, followed by a fourth infiltration of the same product at a distance of 1 month from the third. Patients underwent a baseline clinical evaluation and were monitored for adverse events after each single infiltration: follow-up evaluations were conducted at the end of treatment, 3- and 6-month post-treatment. Efficacy and safety were evaluated on the injection day and approximately 1 week, 1 month, and 3 and 6 months after follow-up. At each follow-up visit, a well-validated VAS score was used on which patients had to mark points on horizontal lines to represent their symptoms' perceptions (from no symptoms (0 mm) to extreme symptoms (100 mm)). The minimal

clinically significant difference (MCID) was defined as 20% or 10 mm of the baseline (10). The primary objective of the study was to evaluate the mean changes from baseline at Month 3 in the VAS Pain Subscale Score.

Moreover, the Knee Injury and Osteoarthritis Outcome Score (KOOS) will be used, and the changes in the functional index of Lequesne and the Womac score will be evaluated. (Timepoint: baseline, 3 months, 6 months). The KOOS is self-administered and assesses 5 domains: pain, symptoms, activities of daily living (ADL), sport and recreation function, and knee-related quality of life. This scale is used to evaluate knee function in terms of activities of daily living (ADL). The Lequesne index measures the severity of osteoarthritis for the knee (ISK). This can be used to assess the effectiveness of therapeutic interventions. Sections for index: (1) Pain or discomfort (2) Maximum distance walked (3) Activities of daily living. The index evaluates the overall assessment of the condition over the last four weeks.

Western Ontario McMaster Universities (WOMAC®) VA3.1 Osteoarthritis Scores allowed for a thorough evaluation of pain, stiffness, and knee function (24 questions through three subscales). The safety endpoints included the assessment of the occurrence of AEs and serious adverse events (SAEs) reported by patients' open questionnaires, related or not to the product or procedures, abnormal laboratory results in terms of hematology, serum chemistry, coagulation parameters, and clinically relevant findings at physical examination (including vital signs) during the entire study. All investigators assessed safety and efficacy data. The sample of patients was calculated considering both the investigators' clinical experiences and the statistical projection calculated on a clinical improvement in pain after administration of the product, which was estimated at 30%.

The statistical analysis examined the differences in mean changes from baseline in the VAS Pain Scale Score between the baseline and 3 and 6 months after the end of the treatment. Friedman's nonparametric test for paired samples determined differences, which were calculated using the exact method for small samples (a nonparametric test was preferred because the scores do not have a Gaussian distribution). In the case of significant results, a post hoc analysis for paired data with the correction for multiple comparisons was carried out.

Based on published data (10-13), the scenario of a mean baseline versus 3 months after treatment the difference of − 21 mm for the change in the VAS Pain scale from baseline at Month 3 with a standard deviation (SD) of 10.5 mm was assumed, which required 12 patients to reach a power of 80% to test the primary endpoint. With an estimated drop-out level of 10%, 15 patients were planned to be included.

The study was performed in accordance with the current version of the Declaration of Helsinki (Fortaleza, Brazil, October 2013) and the International Conference on Harmonization Good Clinical Practice Guideline. The study protocol, its amendments, and the patient information sheet were reviewed and approved by the appropriate independent Ethics Committees.

RESULTS

The participants enrolled were 15. In all 15 patients, and for all 4 administrations per patient performed, no adverse events were found due to the intra-articular infiltration of the product under study. The most often reported study treatment- or procedure-related AEs were mild and transient arthralgia and injection site pain. All the administrations performed had no pain or swelling during the infiltration procedure. The investigators concluded that there was no occurrence of serious AEs indicating safety concerns.

In the analysis, 14 patients were included to evaluate the efficacy. One patient was excluded due to an error in completing the personal data form, as he met an exclusion criterion (BMI >30). The mean age at enrolment was 71±7 years (range 54-80; median 73), and 12 of the patients were women (85.7%) and 2 male (14.3%). The mean BMI was 26.6±3.4 (range 21-30; median 28.5). Half of the patients were affected with knee OA Kellgren-Lawrence (K&L) grade II and half with K&L grade III.

The difference between baseline and control after 3 months and at the end of treatment in mean change from baseline in VAS Pain scale Score adjusted for baseline values was from 6.0±1.6 (6.0) to 4.4±1.7 (4.0) after 3 months and 3.6±1.2 (3.7) after 6 months, varying significantly (Overall p-value^ =0.002; Basal *vs* 3months p-value^ 0.047) (Table I, Fig. 1).

Table I. *Overall result at baseline and after 3 and 6 months.*

		Mean ±SD (Median)			Overall p-value^	Post hoc pairwise p-value*		
		bas	3m	6m		Bas *vs* 3m	Bas *vs* 6m	3m *vs* 6m
VAS		6.0±1.6 (6.0)	4.4±1.7 (4.0)	3.6±1.2 (3.7)	**0.002**	**0.047**	**0.001**	0.469
KOOS	Pain	57±13 (54)	71±23 (72)	76±15 (78)	**0.010**	0.267	**0.014**	0.771
	Symptoms	60±10 (63)	68±21 (68)	71±19 (67)	0.318			
	ADL	51±11 (54)	70±24 (76)	74±19 (83)	**0.011**	0.176	**0.010**	0.896
	Sport. Rec.	18±14 (15)	63±16 (65)	58±18 (58)	**<0.0005**	**<0.0005**	**<0.0005**	0.850
	QOL	31±8 (28)	61±17 (72)	66±16 (66)	**<0.0005**	**<0.0005**	**<0.0005**	0.896
WOMAC	A	9.4±2.3 (9.0)	4.9±4.6 (3.5)	4.6±4.3 (4.0)	**0.003**	**0.032**	**0.005**	0.978
	B	3.8±1.5 (4.0)	2.5±1.8 (2.0)	2.2±1.7 (2.0)	**0.004**	0.150	**0.018**	0.746
	C	34±10 (35)	19±14 (14)	16±13 (10)	**0.008**	0.176	**0.010**	0.851
LEQUESNE	1	4.7±1.6 (5.0)	3.1±2.6 (1.5)	2.1±1.7 (1.5)	**0.007**	0.108	**0.010**	0.558
	2	4.1±1.1 (4.0)	2.8±1.7 (2.5)	1.9±1.4 (2.0)	**<0.0005**	0.089	**0.001**	0.358
	3	5.1±1.1 (5.5)	2.8±2.1 (1.8)	2.1±1.4 (1.5)	**<0.0005**	0.054	**<0.0005**	0.392

^*Friedman nonparametric test* ***Bonferroni correction for multiple comparisons.***

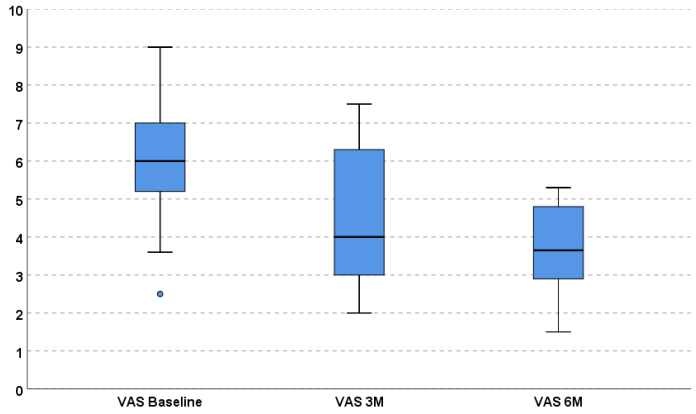

Fig. 1. *VAS score at baseline and after 3 and 6 months.*

The results of the KOOS questionnaire confirmed the data observed on the VAS scale. It is essential to consider that the score of the KOOS questionnaire related to pain (0-100 score) needs to be interpreted inversely to the score on the VAS scale (0-10 score). Indeed, the section's pain and physical function, sport, and free time correlate in a positive manner with VAS score, baseline 57±13 (median 54) *vs.* 3 months (71±23; median 72) and 6 months (76±15; median 78). Interestingly, the baseline values of the VAS scale, as well as the pain scale of the KOOS questionnaire (VAS score: 6.0±1.6 and KOOS pain score: 57±13), significantly correlate after six months of treatment (VAS score: 3.6±1.2 ($p>0.001$) and KOOS pain score: 76±15 ($p>0.014$). All other items of the KOOS questionnaire do not show significant changes after 3 and 6 months (Table I, Fig. 2).

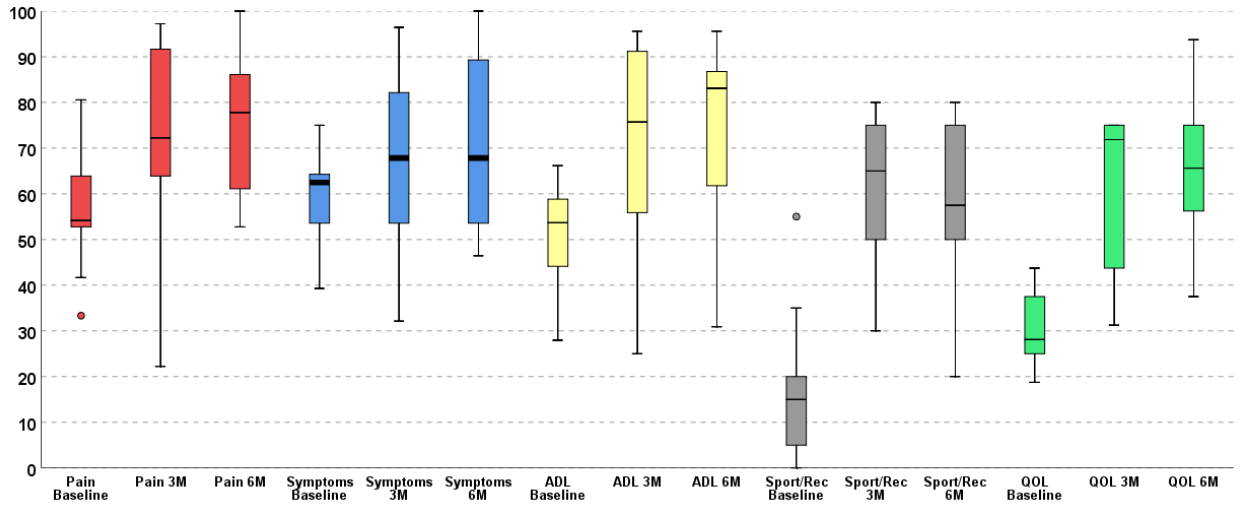

Fig. 2. *KOOS score items at baseline and after 3 and 6 months.*

The decrease in WOMAC pain subscale (A)at month 3 for the treatment group decreased from 9.4±2.3 (9.0) at baseline to 4.9±4.6 (3.5) after 3 months and 4.6±4.3 (4.0) at 6 months (Overall p-value^0.003; Basal *vs.* 3 months p=0.032; 3 months *vs.* 6 months p=0.005) (Tab.I, Fig. 3). The rigidity subscale (B) at months 3 for treatment group decreased from 3.8±1.5 (4.0) at baseline to 2.5±1.8 (2.0) after 3 months and 2.2±1.7 (2,0) at 6 months (Overall p-value^0.004; Basal *vs.* 3 months p=0.150; basal *vs* 6 months p=0.018) (Tab. I, Fig. 4). Daily living activity subscale (C)at months 3 for treatment group decreased from 34±10 (35) at baseline to 19±14 (14) after 3 months and 16±13 (10) at 6 months (Overall p-value^0.008; Basal *vs* 3 months p=0.176; basal *vs* 6 months p=0.010) (Tab. I, Fig. 5).

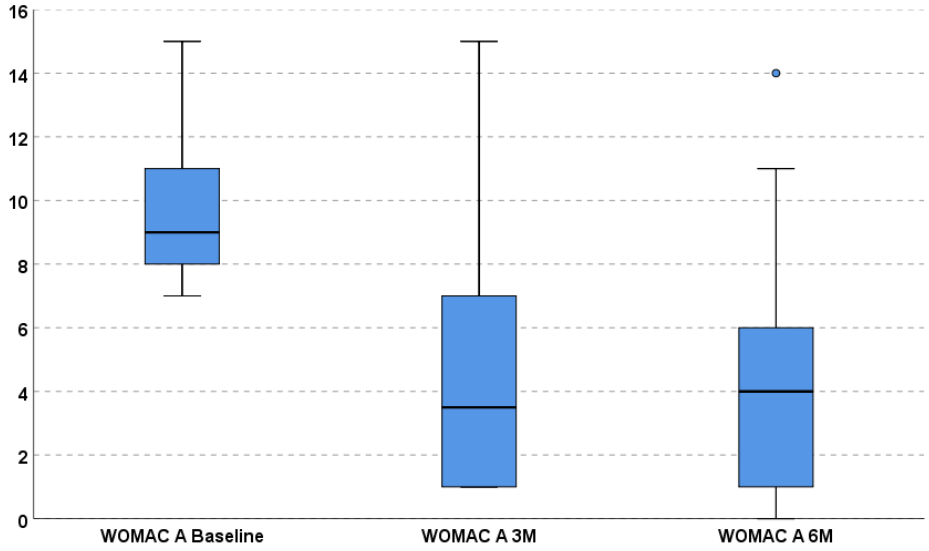

Fig. 3. *WOMAC subscore A items at baseline and after 3 and 6 months.*

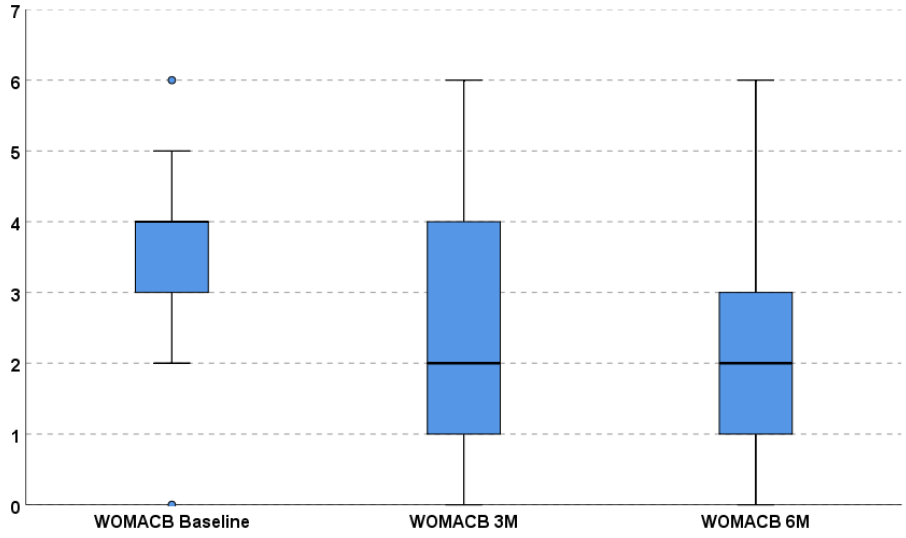

Fig. 4. *WOMAC subscore B items at baseline and after 3 and 6 months.*

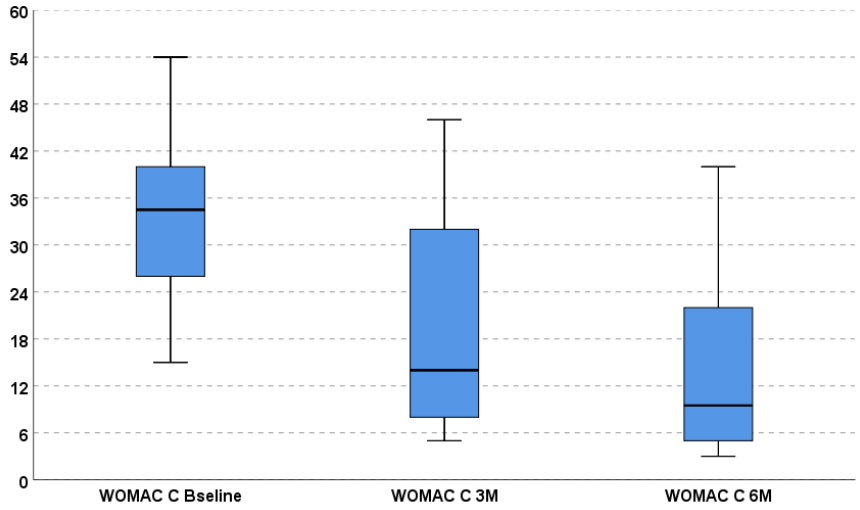

Fig. 5. *WOMAC subscore C items at baseline and after 3 and 6 months.*

The treated group experienced significant improvement over their baseline values in several domains of the Lequesne index (LI), predominantly belonging to physical functioning. LI is an objective tool to assess the study outcome of OA knee. LI contains parameters like Subscales of Pain and discomfort, Maximum Distance Walked Score, and Activity of Daily Life (ADL). This study-based findings of Lequesne parameters regarding subscales of Pain and discomfort, Activity of Daily Life (ADL) outcomes are highly significant. All subscales of LI decreased,

Pain and discomfort (Score 1) decreased from 4.7±1.6 (5.0) at baseline to 3.1±2.6 (1.5) after 3 months and 2.1±1.7 (1.5)at 6 months (Overall p-value^0.007; Basal *vs* 6 months p=0.010) (Tab. I, Fig. 6). Furthermore Maximum Distance Walked Score decreased from 4.1±1.1 (4.0) at baseline to 2.8±1.7 (2.5) after 3 months and 1.9±1.4 (2.0) at 6 months (Overall p-value^ <0.0005; Basal *vs* 6 months p=0.001) (Tab. I, Fig. 7).The Activity of Daily Life subscore (Score 3) decreased from 5.1±1.1 (5.5) at baseline to 2.8±2.1 (1.8) after 3 months and2.1±1.4 (1.5) at 6 months (Overall p-value^ <0.0005; Basal *vs* 6 months p=0.0005) (Tab. I, Fig. 8).

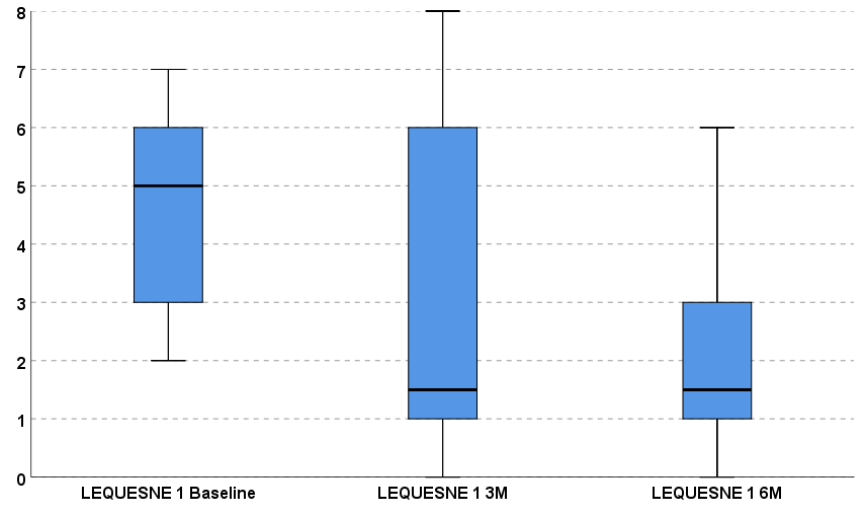

Fig. 6. *LEQUESNE subscore 1 items at baseline and after 3 and 6 months.*

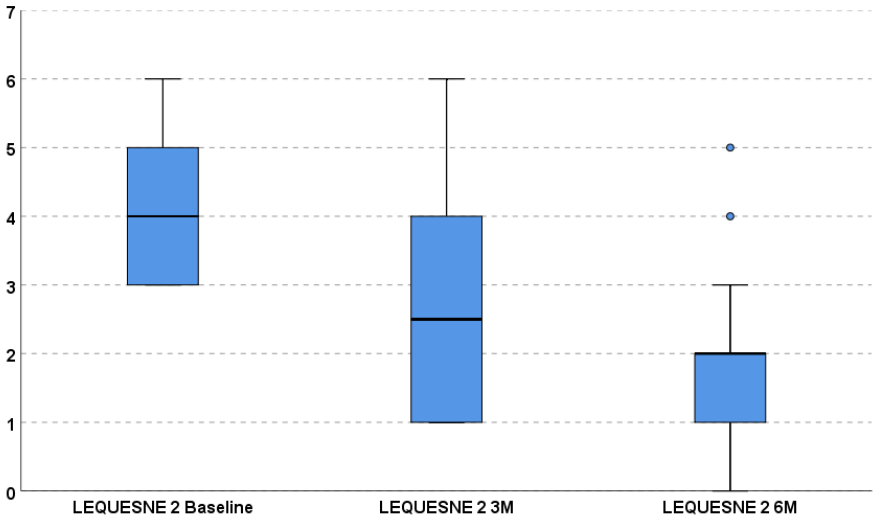

Fig. 7. *LEQUESNE subscore 2 items at baseline and after 3 and 6 months.*

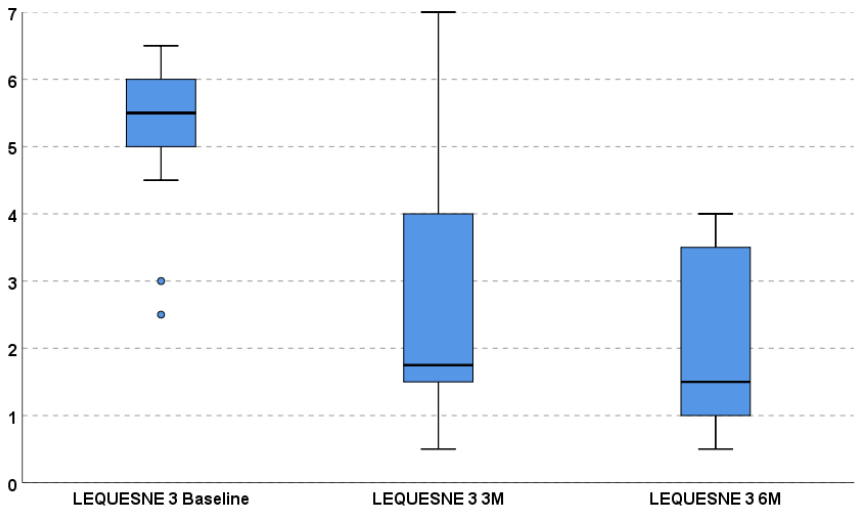

Fig. 8. *LEQUESNE subscore 3 items at baseline and after 3 and 6 months.*

No significant changes were recorded in the comparison data between baseline and 3 and between 3 months and 6 months in the subscores Maximum Distance Walked Score, Activity of Daily Life.

DISCUSSION

This study aimed to assess the safety and efficacy of NEOIAL HC for knee OA treatment over 6 months. Its statistical superiority over the baseline was observed, as demonstrated by the difference in adjusted mean changes in the VAS Pain Scale Score from baseline at 3 and 6 months post-injection, with a clinically relevant difference from baseline (>10mm, the MCID). Furthermore, the KOOS questionnaire showed a significant reduction in pain and physical function, sports, and free time items, which correlated with the VAS score results. Although this medical device induced more significant improvements than the reference in WOMAC Pain Subscale, Physical Function Subscale, and Total Scores at all time points, no differences met the statistical significance criteria.

Improvements in the WOMAC Physical Function Subscale from baseline were statistically more significant in the pooled patients who received the experimental product at 3 months post-injection. More specifically, age was found to directly correlate significantly with pain (Rho=0.808 $p<0.0005$) and inversely with WOMAC B (Rho=-0.582 p=0.029) and C (Rho=-0.558 p=0.038), LEQUESNE1 (Rho= -0.614 p=0.020) only in baseline values tendentially with LEQUESNE3.

BMI inversely correlated significantly with pain symptoms trending with ADL; directly correlated significantly with LEQUESNE1, tendentially with WOMAC A and C and LEQUESNE2, all only in baseline values. The influence of sex was not analyzable due to only 2 men, and there was no significant influence of KL or side on baseline or follow-up scores.

The more significant pain and function improvements observed with NEOIAL HC from baseline are encouraging since injections of HA-only were shown to result in pain relief, joint function, and quality of life improvements in knee OA patients, leading to the introduction of intra-articular HA injections in international recommendations. In our study, the potentially larger effect observed with NEOIAL HC from baseline may be explained by the fact that besides the natural HA polysaccharide obtained by bacterial fermentation, NEOIAL HC also contains active substances such as collagen type I with jellification and anti-inflammatory properties. This unique formulation has the potential to provide better lubrication and cartilage protection with a prolonged effect. Furthermore, the encouraging results observed in our study suggest that NEOIAL HC could be an effective treatment option for knee OA patients.

CONCLUSIONS

The present study showed a clinically good safety profile and provided preliminary evidence of NEOIAL HC's efficacy in treating symptomatic knee OA. The data analysis obtained at 3 months for the 14 patients enrolled in the study showed a significant improvement in the values in all 4 evaluation scales (VAS, KOOS Knee Survey, Womac Osteoarthritis Index, and Lequesne). This improvement was confirmed at 6 months, with a slight improvement noted for 4 out of 5 parameters on the KOOS evaluation board, 1 parameter of the WOMAC board, and all 3 parameters of the Lequesne index. The only figure that recorded a slight decrease was the "sports and recreational activities" parameter, which is not considered significant for the elderly sarcopenic patient population.

DECLARATIONS

Ethics approval and consent

This study was approved by the Ethics Committee “COMITATO ETICO DELLE PROVINCE DI CHIETI E PESCARA” (approval no. 12 of 06.05.2021). All participants provided written informed consent prior to enrolment in the study.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authors' contributions

The individual contributions of authors to the manuscript are specified below: R.B. and D.B. collected clinical data, and A. P. and D.D. were major contributors to writing the manuscript. All authors read and approved the final manuscript.

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Evaluation Study

DIODE LASER 980 NM: A GOOD MODALITY FOR EXPOSURE OF IMPACTED PERMANENT TEETH

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ABSTRACT

This study aims to demonstrate how laser technique could positively assist in exposing impacted teeth for orthodontic reasons. This study was comprised of 30 patients who were treated for impacted teeth exposed to a 980 nm diode laser for orthodontic reasons. Treatment was conducted from May 2013 to May 2016 in the University Dental Clinic in Tirana. The follow-up period was one week, two weeks, and six months for the evaluation of the results. The brackets were placed immediately after surgery due to the good coagulation. The intraoperative advantage of using a 980 nm diode laser was less chair-side time and the complete absence of bleeding, allowing immediate bonding of the bracket in dry enamel. None of the patients reported other post-surgical side effects, with no bleeding, pain, swelling, or discomfort one to two weeks after the treatment. Diode laser is effective and safe for soft tissue. In conclusion, a 980 nm diode laser is a promising modality for the exposure of impacted teeth for orthodontic reasons. This method provides good operative and postoperative results without any side effects.

KEYWORDS: *Diode laser 980nm, tooth exposure, wound healing*

INTRODUCTION

An impacted tooth has completed development and cannot and will not come out in its normal position for various reasons. Therefore, it needs observation or treatment (1, 2). The standard and essential reasons for delayed eruption are usually insufficient space, early loss of primary teeth, and some hormonal and metabolic disorders (3-10). The diagnosis may be obtained after a thorough clinical and radiographic examination. Impacted teeth have become the field of study and action in many specialties of dentistry. Various treatment modalities for the treatment of impacted teeth are available: surgical extraction, transplantation, prosthetic replacement, surgical exposure, and expectation of spontaneous eruption or surgical exposure, accompanied by orthodontic treatment (11, 12). Many studies have demonstrated that combined orthodontic surgical treatment can produce good results. Various treatment modalities have been proposed to avoid the complications associated with impacted canines, such as using a scalpel, caustic agents, electrocautery, and diode lasers. However, diode laser therapy is an effective and non-invasive treatment option for exposure of impacted teeth without bone covering the tooth. But in most cases, it first requires orthodontic preparation of

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the maxillary and mandibular arches to create adequate space before surgical exposure. Laser offers different wavelengths like 450nm/810nm or 980nm. 450nm can be used in non-contact/contact mode, whereas 810nm and 980nm are used in contact mode.

Diode laser therapy is a noninvasive treatment option for exposing impacted teeth (14-16). This study aims to demonstrate how laser technique could positively assist in exposing impacted teeth for orthodontic reasons.

MATERIAL AND METHOD

This study comprised 30 patients (12 males and 18 females) aged 10 to 24 who were treated for exposure of impacted teeth for orthodontic reasons with a diode laser 980 nm. Treatment was conducted from May 2016 to May 2019 at the University Dental Clinic in Tirana, Albania.

The diagnosis of teeth impaction was based on both clinical and radiographic examinations. The amount of space in the dental arch, morphology, position of the adjacent teeth, and contours of the bone were considered—the radiographic examinations including panoramic radiographs, CT, and the CBCT.

Informed consent was obtained from all subjects involved in the study. The treatments were performed under local anesthesia. The mucosa covering the teeth was excised with a diode laser 980 nm, CW, 3 w. The follow-up visits were scheduled for one week, two weeks, and six months after the treatment to evaluate early and long-term results. All teeth exposure was photographically documented at all stages of treatment and healing.

RESULTS

This study comprised 30 patients treated for impacted tooth exposure for orthodontic reasons. Impacted teeth were: 20 maxillary canines, 4 maxillary incisors, 3 mandibular canines, 3 mandibular premolars (Fig. 1a).

According to the protocol treatment, the teeth were exposed to a diode laser 980 nm, CW, 3 w under local anesthesia (Fig 1b). Immediately after diode treatment, the surgical fields were bloodless (Fig 1c). The intraoperative advantage of using a 980 nm diode laser was less chair-side time, reducing the fear and anxiety during surgical procedures. The impacted teeth were cleaned and scaled to permit bonding, and the orthodontic brackets were bonded to a position immediately in the same session after the surgical procedure. The absence of bleeding allowed immediate bonding of the bracket in dry enamel, preventing the possibility of detaching and reducing the risk of further re-intervention. None of the patients reported other post-surgical side effects, no bleeding, pain, swelling, or discomfort one to two weeks after the treatment (Fig. 1d, e). A fast and good healing process (Fig. 2a-c). Diode laser is effective and safe for soft tissue.

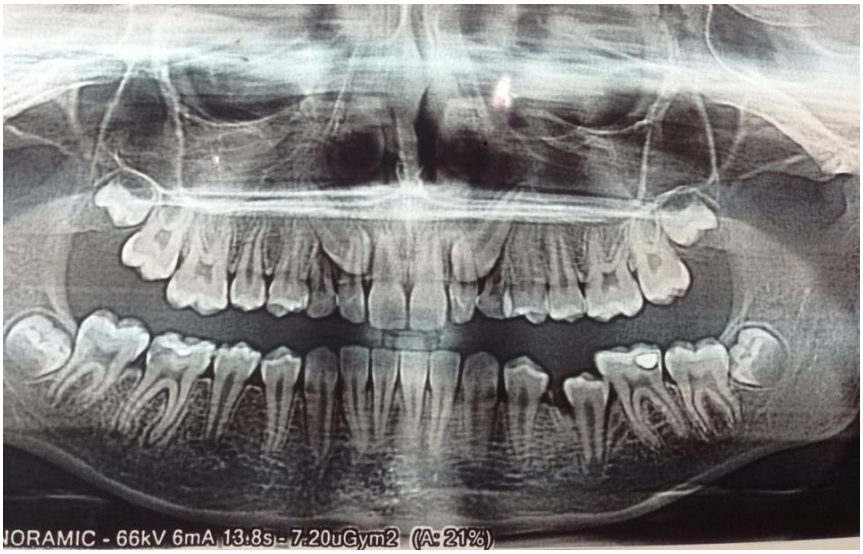

Fig. 1a. *Panoramic view of two impacted maxillary canines.*

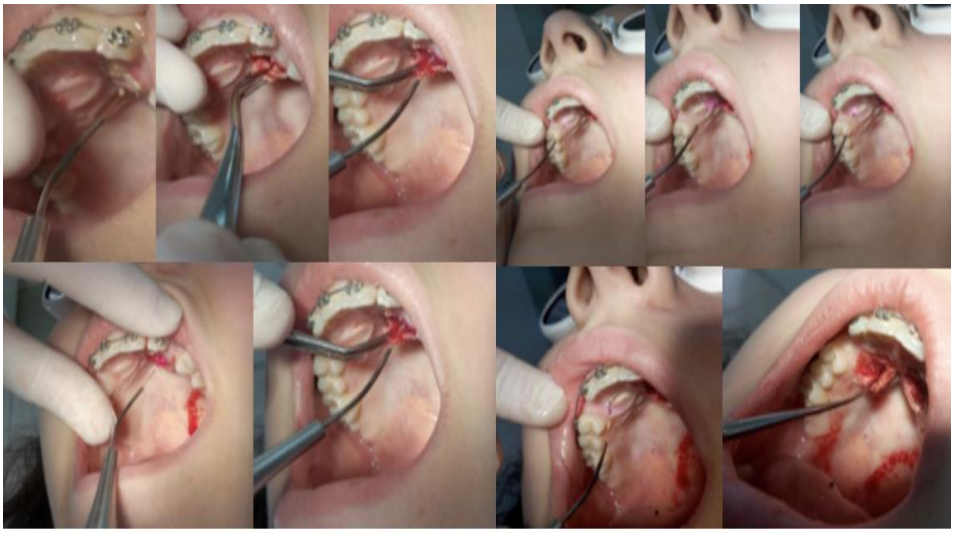

Fig. 1b. *During the surgical procedure. Exposure of the right and left impacted canines in the same session with diode laser 980 nm, CW, 3 w under local anesthesia.*

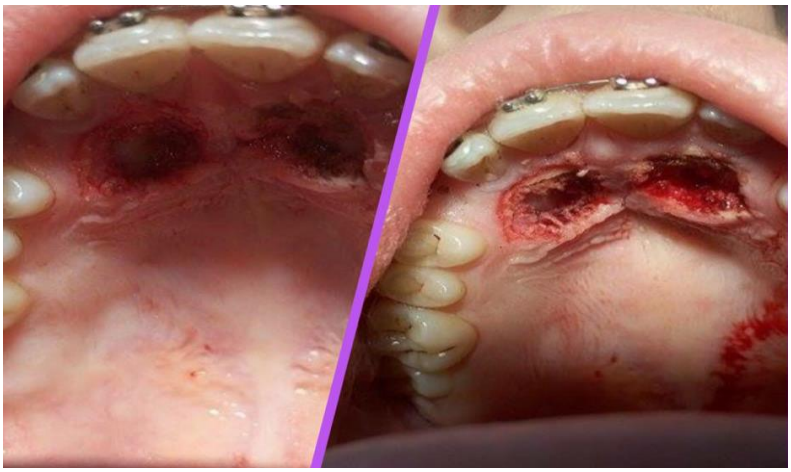

Fig. 1c. *Immediately after the treatment.*

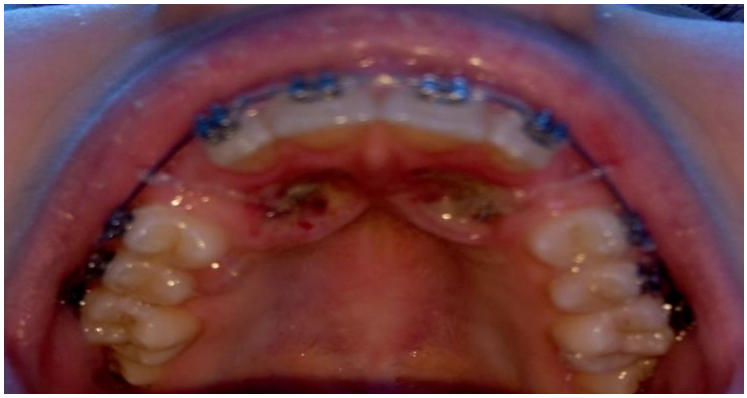

Fig. 1d. *Two days after the treatment.*

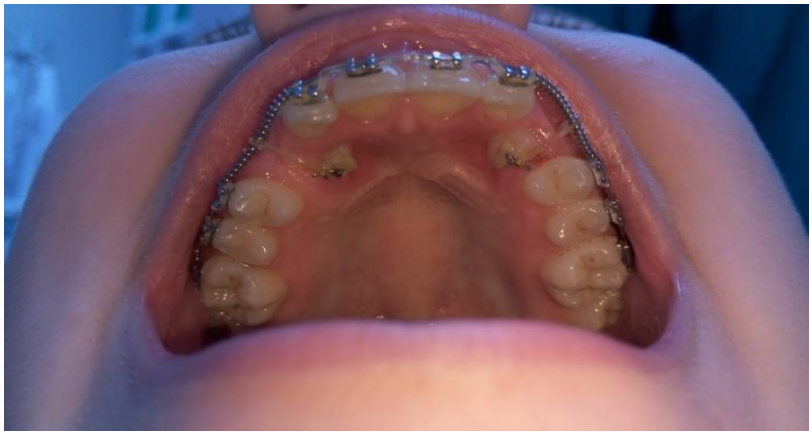

Fig. 1e. *Four weeks after treatment.*

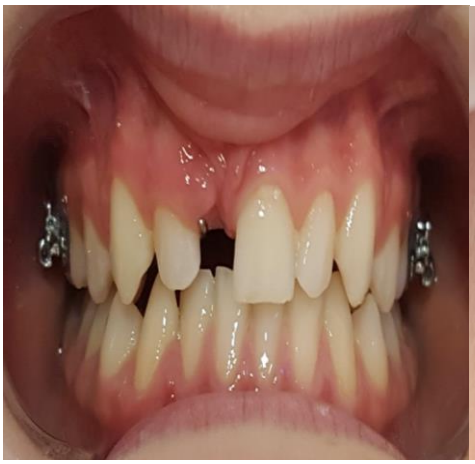

Fig. 2a. *Impacted maxillary incisor*

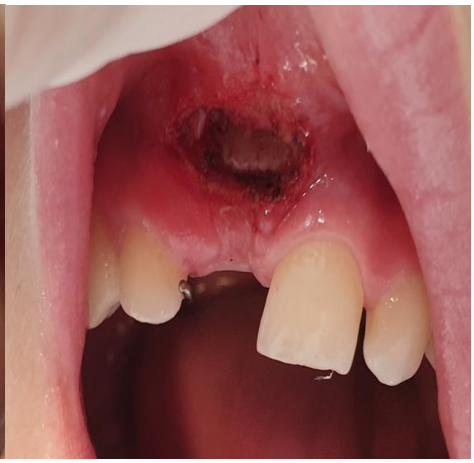

Fig. 2b. *Immediately after treatment.*

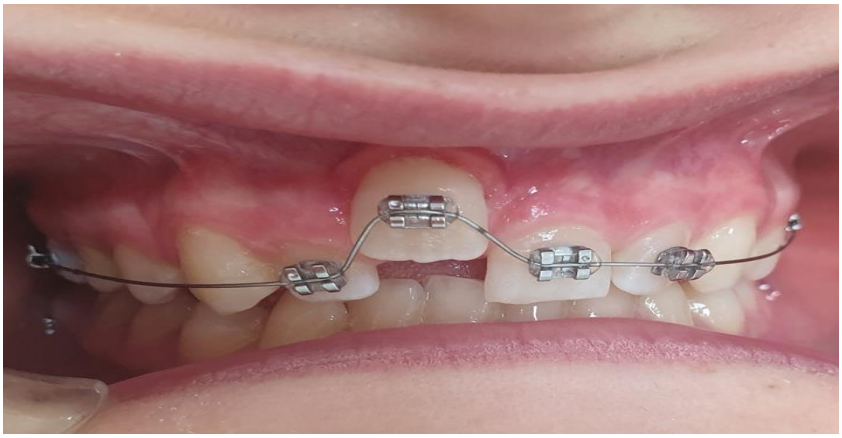

Fig. 2c. *Two months after surgical exposure.*

DISCUSSION

The diagnosis of tooth impaction is based on both clinical and radiographic examinations. The clinician must consider the amount of space in the dental arch, the morphology and position of the adjacent teeth, and the contours of the bone. The radiographic examinations include panoramic radiographs and the CBCT.

There are 3 main options in the management of impacted teeth: extraction of an impacted tooth, extraction of an adjacent tooth, or non-extraction treatment involving orthodontic space opening and surgical exposure (15, 16). When non-extraction treatment is performed, the orthodontic treatment is often initiated before the surgical exposure to align

the teeth, open the space for the impacted tooth, and enhance the natural eruption process (16-19). A diode laser is a promising modality for the surgical exposure of impacted teeth. Diode laser offers advantages like patient compliance, reduced pain and discomfort, a faster healing process, absence of bleeding, and less chair-side time (20). The most significant advantage is the complete absence of bleeding, which immediately allows bracket bonding in dry enamel.

Our postoperative no-pain and swelling results coincide with the authors' observations (21, 22). The surgical exposure of impacted teeth with a diode laser makes the placement of the brackets immediately after surgery possible due to good coagulation. These findings correspond with other reports (23-25).

CONCLUSIONS

Laser surgery for exposure of impacted teeth is a modality with beneficial effects and advantages. The intraoperative advantage is the perfect coagulation; the surgeon has a good visualization of the operative field, and the operative time is very short, making possible the minimization of fear and anxiety in the patient during the procedure. The postoperative period is without complications or discomfort. The use of lasers in orthodontics, particularly diode lasers, has made it possible for orthodontic clinicians to address the daily challenges faced in an orthodontic practice more efficiently.

Conflicts of Interest

There are no conflicts of interest or financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings.

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Case Report

LUMBAR SYNOVIAL CYST TREATED WITH OXYGEN-OZONE THERAPY: CASE REPORT

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ABSTRACT

The synovial cyst of the lumbar facet joints is commonly encountered in degenerative arthropathy. It can be symptomatic when its volume narrows the spinal canal or compresses a spinal nerve root. Many treatments have been proposed for treating symptomatic synovial cysts, from manual chiropractic therapy to systemic pharmacological therapy, from local infiltrations of corticosteroids to interventional radiology treatments with CT-guided needle fenestrations of the cyst to surgical removal. We report the results of an infiltration treatment of a cyst with the oxygen-ozone mixture in a 62-year-old patient suffering from left lumbosciatica resistant to pharmacological therapy for 4 months. Clinical and radiological findings showed a stenosis of the spinal canal caused by a synovial cyst in the left L4-L5. After the intracystic infiltrative treatment with an oxygen-ozone mixture, the patient had a reduction in radicular pain, which remained unchanged at the follow-up check-up**.**

KEYWORDS: *oxygen, ozone, therapy, synovial cyst, facet synovial cyst*

INTRODUCTION

The synovial cyst constitutes a common finding in the degenerative process of the spine, especially in the lumbar spine. It is typically associated with arthropathy of the facet joints, and it is most often constituted by a dilatation of the joint capsule of the lumbar vertebral joint, sometimes by a cystic dilatation of the yellow ligament, with gelatinous amber material inside. When projected into the vertebral canal, this dilatation causes a narrowing with consequent associated symptoms linked to the compression of the nervous structures in the vertebral canal.

From a histological point of view, fragments of *Ligamentum flavum*, synovial cells, myxoid mucinous material, fibrinoid, and calcium pyrophosphate deposits are present, with associated foreign body reaction giant cells surrounded by vascular, fibroblastic, and myofibroblastic proliferation (1-5).

The clinical presentation depends on the location, diameter, and relationships of the cyst with the nervous structures of the spinal canal. They are asymptomatic if they have a posterior, extracanal manifestation; however, when they develop inside the vertebral canal, they can cause lumbar pain, ipsilateral radicular irradiation, rarely a cauda syndrome, if they are associated with stenosis of the vertebral canal at the same level of development as the cyst.

On CT (Computerized Tomography), the internal density of the cyst can vary based on the composition of its contents: a simple fluid density is suggestive of a serous cyst, an increased density suggests hemorrhagic, hyperproteinic contents or with calcium deposits (6-7). Even on MRI, the appearance of the synovial cyst can vary based on its content: hyperintensity on T2 and hypo-isointensity on T1 suggest serious content. An increase in signal intensity in T1-weighted

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images highlights an increase in the protein or hemorrhagic content of the cyst. In contrast, a reduction in signal in all sequences reflects the presence of hemosiderin or calcifications.

The treatment of the synovial cyst can be conservative or surgical: among the former, we consider rest, physical therapy, acupuncture, the use of anti-inflammatories and painkillers, chirotherapy maneuvers, infiltration of the facet joints with steroids, aspiration of the cyst, CT-guided fenestration of the cyst wall (8-10). Surgical treatment via decompressive laminectomy followed by cautious dissection and removal of the lesion in its entirety is undoubtedly the most effective, with a lower risk of recurrence, even if it constitutes a more invasive approach, with the specific risk of increasing following the surgery, vertebral instability. For this reason, surgical treatment is limited to cases in which conservative treatments have not worked (11-14).

Among the most recently proposed conservative treatments is CT-guided intracystic infiltration of an oxygen-ozone mixture (15-23). The method adds the mechanical effect of fenestration/rupture of the cyst wall to the anti-inflammatory antioxidant effect of the oxygen-ozone mixture.

Case report

A 62-year-old woman with a silent remote pathological history who complained of left lumbosciatica pain resistant to pharmacological therapy with oral anti-inflammatories and corticosteroids, to infiltration with transforaminal and epidural corticosteroids and unresponsive to osteopathic and physiotherapeutic treatments (Tecar and Laser therapy).

The clinical evaluation, in addition to the neurological objective examination, used the Oswestry Disability Index (ODI) of the Visual Analogic Scale for the leg (VAS leg) and for the back (VAS LBP), were performed before treatment and in the follow-up after one and three months. The radiological investigations were based on magnetic resonance imaging without contrast medium in T1 and T2 sequences on the axial plane, T2 on the axial coronal and sagittal planes, and T2-STIR on the sagittal plane.

Technique

The patient was placed in a prone position, with support under the belly, to avoid excess lordosis. After careful skin disinfection and sterile field preparation, a CT scan of the lumbar region was performed. The synovial cyst was approached via an ipsilateral translaminar approach with a 22G Chiba needle. The needle was guided into position by performing further CT scans until it entered the cyst. After aspirating the cyst, approximately 5 cc of an oxygen-ozone mixture at a concentration of 27 mcg/ml was injected into the cyst. Finally, a final CT scan was performed to evaluate the rupture of the cyst and the leakage of gas into the epidural space and the facet joints (Fig. 1).

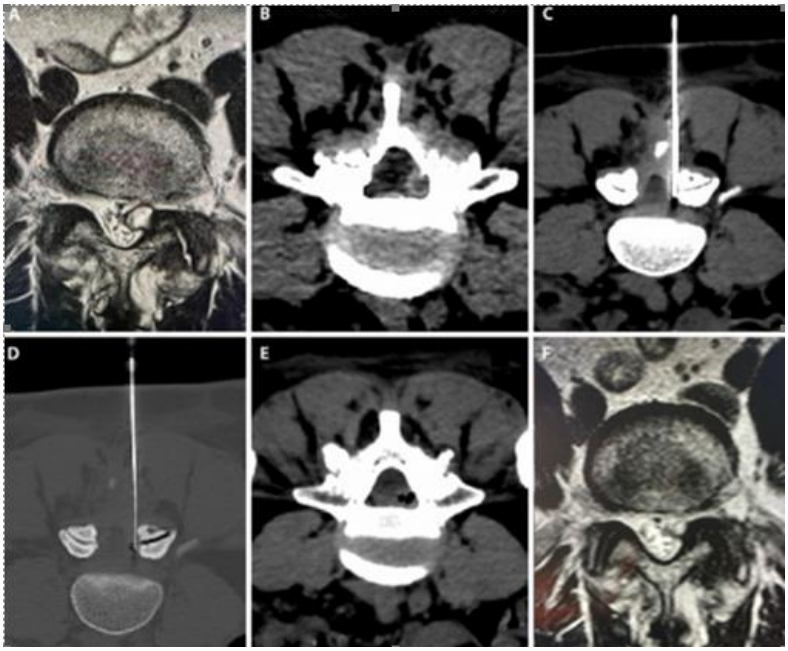

Fig. 1. ***A****): An axial T2W scan highlights a large synovial cyst of the left L4-L5 zygapophyseal joint;* ***B****): CT axial view of the same cyst with thickening of its walls;* ***C-D****): intraprocedural CT scan showing the correct positioning of a 22G Chiba needle inside the cyst;* ***E****): TC control after injection of the oxygen-ozone mixture; the presence of gas outside the cyst is evident.* ***F****): MRI scan highlights coarctation with a reduction in cyst volume.*

The patient was then discharged after two hours of observation with instructions for follow-up. The intracystic oxygen-ozone mixture injection procedure proceeded smoothly without adverse effects, and the patient was discharged two hours after the procedure. After the treatment, there was an immediate reduction in the painful sciatica symptoms with a reduction in the VAS, which remained reduced in the one and three-month checks (VAS Leg), without substantial changes in chronic lumbar pain between the pre-operative evaluation and the follow-up checks (VES LBP). In the follow-up checks one and three months later, the patient reported that she had maintained the improvement in painful symptoms perceived immediately after the procedure, and the ODI went from 74 before the treatment to 35 at the one-month check-up and to 37 that of three months (Fig. 2).

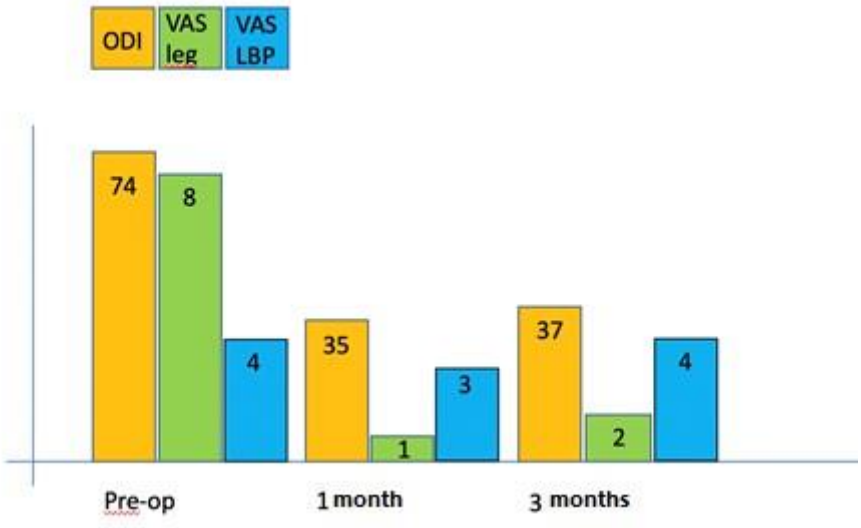

Fig. 2. ***ODI*** *went from 74 before the treatment to 35 at the one-month check-up and to 37 at three months; reduction in the* ***VAS****, which remained reduced in the one and three-month checks (****VAS Leg****); no substantial changes in chronic lumbar pain between the pre-operative evaluation and the follow-up checks (****VES LBP****).*

DISCUSSION

Treatment with the injection of an oxygen-ozone mixture is among the conservative methods commonly used in degenerative disc pathology to treat chronic lumbar pain and radicular pain through intradiscal nucleolysis, with transforaminal periradicular infiltration or within the paravertebral muscles (15-23).

Among the conservative treatments first proposed in the case of a symptomatic synovial cyst, there is the injection, under fluoroscopy guidance, of 1-3 cc of anesthetic, steroids, and contrast medium into the facet joints to try to obtain distension until rupture of the cyst wall (6-10). A good initial clinical response is followed by high relapse rates in the medium to long term.

A technique of direct puncture of the cyst, guided by CT scan, and infiltration of anesthetic and corticosteroids has also been described, with an increase in success in the immediate post-operative period, but also in this case followed by a high possibility of recurrence (10).

Shah et al. (12) describe the “fenestration technique,” which consists of repetitive movements of the needle back and forth within the cyst, followed by aspiration of the cyst, to create multiple holes in the wall of the lesion. Satisfactory long-term results have been reported (12, 13).

In the reported case, the infiltration of an oxygen-ozone mixture into the cyst immediately reduced the intensity of radicular pain, which was maintained in the follow-up checks one and three months later. This result is linked to the mechanical rupture of the cyst wall and the anti-inflammatory effects of ozone.

CONCLUSIONS

CT-guided infiltration of an oxygen-ozone mixture into the synovial cyst is a safe procedure with immediate effects because of the rupture of the cyst wall and the anti-inflammatory effects of ozone. Unlike surgical removal, it does

not pose the risk of causing future iatrogenic instabilities, although it should not be forgotten that these can still occur. The synovial cyst is an epiphenomenon of an initial segmental instability. However, to our knowledge, it would be important to increase the number of cases of this treatment modality and evaluate individual cases with adequately long follow-up exams to confirm the validity of a conservative treatment.

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Case Report

TREATMENT OF A DENTAL ELEMENT WITH ISOLATED PERIODONTITIS USING OXYGEN-OZONE THERAPY. A CASE REPORT

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ABSTRACT

The case of a patient with a single tooth suffering from periodontal disease, treated with oxygen-ozone infiltrations and root canal therapy with ozonated water, is reported. The patient, who in the past had already suffered from periodontitis with purulent exudate of the lower incisor group on the lingual side, was previously treated with antibiotic therapies associated with root planing techniques. In this case, the corpuscular and serous exudate gradually disappeared thanks to the treatment with oxygen-ozone therapy, and a good mucogingival seal was gradually reconstituted. The dental element completely lost its mobility; consequently, it was possible to proceed with the prosthesis of the element. The obtained stability of the tooth and the reformation of the ligament system with the maintenance of the mucogingival seal are evidence of recovery from periodontitis.

KEYWORDS: *periodontitis, oxygen, ozone, medical ozone, biofilm, gingivitis*

INTRODUCTION

The effectiveness of treatment with oxygen-ozone in cases of periodontitis has been known for several years, and numerous reports on this subject exist (1-10).

It has been documented that ozone therapy can be helpful in the effective treatment of periodontal lesions with narrow periodontal pockets in patients with aggressive periodontitis and a poor prognosis (11). Gingival and periodontal diseases are a significant dentistry concern (12-31). Most of the factors and causes that contribute to the etiology of these diseases are reduced or treated with ozone in all its forms of application, such as gas, water (32-33), and oil (34-35), which reduces the majority of and causes in the etiology of these diseases. The beneficial biological effects of ozone, its anti-microbial activity, oxidation of bio-molecules precursors and microbial toxins implicated in periodontal diseases, and its healing and tissue regeneration properties make the use of ozone well indicated in all stages of gingival and periodontal diseases.

In light of these considerations, we report the case of a patient who presented a single tooth suffering from periodontal disease, successfully treated with oxygen-ozone infiltrations and root canal therapy with ozonated water.

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CASE REPORT

G.L., male, born in 1956. He came to our attention with a compromised tooth number 24. There was spontaneous pain, pain on percussion, and inability to chew, alongside evident periodontal purulent budding with mobility of the element ranging between 2 and 3. The periodontal probing highlights a 4-walled pocket with a probing depth of 12 mm distal and palatal, 11 mm buccal and medial. An intraoral radiograph confirmed the situation of periodontal compromise (Fig. 1).

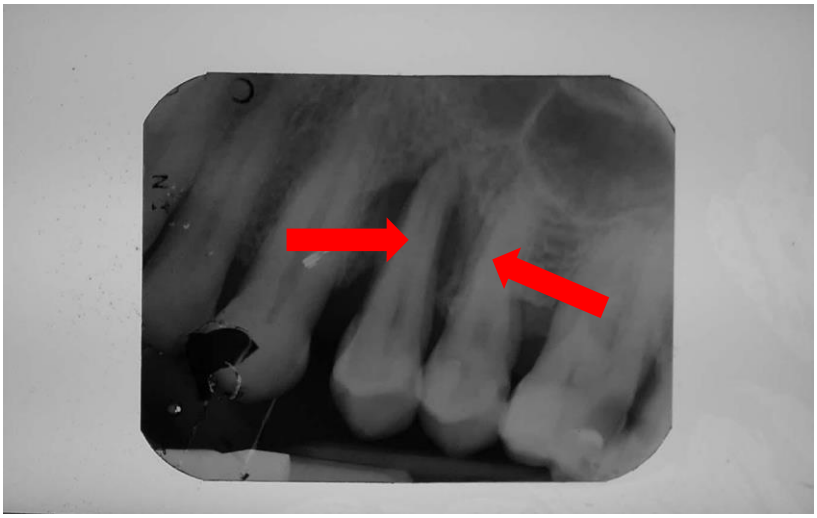

Fig 1. *Diagnostic evaluation radiograph at patient recruitment with periodontal compromise in tooth 24 (**arrows**).*

An initial dental hygiene session was conducted with antibiotics in order to remove any possible root tartar deposits. Subsequently, the pulp vitality of the element was verified with the C-Pulse tester. The vitality was found to be at the lower limits of the norm. Therefore, it was decided to devitalize the dental element to eliminate any possible bacterial focus. Intraoral X-ray control was carried out at the end of treatment and one year later. In the following paragraph, the therapeutic program of the sixteen sessions is described in depth.

Therapeutic Program

First session

Under topical anesthesia, the dental element was exposed to the pulp chamber, and the two roots, buccal and palatal, were probed. After the initial reaming of the canal with the removal of pulp residues, the roots and pulp chamber were irrigated with ozonated water for ten minutes.

Subsequently, after incomplete drying of the roots and pulp chamber, the cavity was filled with temporary enamel soft cement. A 30G needle connected to a syringe of oxygen-ozone mixture at 40 µg/ml was introduced, and the tooth was filled under pressure to make the gaseous mixture reach the collateral canaliculi. Leaving the gas in contact with the dentinal walls of the pulp chamber and canals for five minutes, the Enamel Soft plugging was removed by reciprocating it. During all root canal perfusion procedures with a gas mixture, the dental assistant maintained continuous suction near the tooth to prevent even the smallest amount of gas from inhaling by the patient and the operating staff. The walls of the root canals were reamed to remove the first layer of infected dentin and facilitate access of the various medications to all the accessory dentinal canaliculi. The tooth was rinsed in succession with sodium hypochlorite with water, and the excess water was removed; then, the canals were filled with calcium hydroxide and suitable temporary cement was placed to close the cavity.

The periodontal pockets surrounding the tooth were washed with recently produced ozonated water. The leakage of purulent exudate was evident. The area of adherent mucosa surrounding the dental element 24 on both the vestibular and palatal sides and the fornix were then infiltrated with 10 cc of oxygen-ozone gas mixture at 15 µg/ml.

The patient was advised to apply Ozoral gel at home, in the lesion area, 4 times a day for the entire duration of the outpatient treatment.

Second session

Under topical anesthesia, the temporary cement was removed from tooth 24, the calcium hydroxide was removed by rinsing, and the root canal was washed with ozonated water for ten minutes. The cavity was plugged again with Enamel Soft temporary cement, and the gaseous oxygen-ozone mixture at 40 μg/ml was introduced.

The Enamel Soft buffer was removed and rinsed in succession with 2.5% sodium hypochlorite and water. After partial drying, the pulp chamber and root canals were filled with calcium hydroxide, and the cavity was closed with temporary cement based on zinc oxide with a low shrinkage coefficient. The periodontal pockets were washed with ozonated water. Purulent exudate was still present. Adherent mucosa and fornix were infiltrated with 10 cc of oxygen-ozone gas mixture at 15 μg/ml.

Third session

The dental cavity was reopened under topical anesthesia. The calcium hydroxide was removed and irrigated for ten minutes with ozonated water. After drying, the cavity hole was plugged with Enamel Soft, and a suitable quantity of oxygen-ozone gas mixture at 40 μg/ml was injected into the cavity, changed several times. The elastic packing was removed, and the root canals were checked to ensure they could remain dry. Subsequently, the traditional maneuvers were performed to close the 2 root canals with root canal cement and gutta-percha cones and with the vertical condensation technique.

The periodontal pockets were washed with ozonated water. There was serous exudate, not macroscopically corpuscular. Adherent mucosa and fornix were infiltrated with 10 cc of oxygen-ozone gas mixture at 15 μg/ml.

Fourth session

Under topical anesthesia, the dental cavity was reopened and closed with a suitable permanent composite filling, taking care to keep the dental element in slight disclusion. The periodontal pockets were washed with ozonated water. There was a serious exudate that was not macroscopically corpuscular. At the end of irrigation, modest bleeding appeared. Adherent mucosa and fornix were infiltrated with 10 cc of oxygen-ozone gas mixture at 15 μg/ml.

Fifth session

Under topical anesthesia, the periodontal pockets were washed with ozonated water. Serous exudate was still present, followed by modest bleeding. Adherent mucosa and fornix were infiltrated with 10 cc of oxygen-ozone gas mixture at 15 μg/ml.

Sixth session

Under topical anesthesia, the periodontal pockets were washed with ozonated water. There was slight bleeding. Adherent mucosa and fornix were infiltrated with 10 cc of oxygen-ozone gas mixture at 15 μg/ml.

Seventh session

Under topical anesthesia, the periodontal pockets were washed with ozonated water. There was slight bleeding. Adherent mucosa and fornix were infiltrated with 10 cc of oxygen-ozone gas mixture at 15 μg/ml.

Eighth session

Under topical anesthesia, the periodontal pockets were washed with ozonated water. There was no evidence of serous exudate or bleeding. Adherent mucosa and fornix were infiltrated with 10 cc of oxygen-ozone gas mixture at 15 μg/ml.

Ninth session

Under topical anesthesia, the residual periodontal pockets were washed with ozonated water. Adherent mucosa and fornix were infiltrated with 10 cc of oxygen-ozone gas mixture at 15 μg/ml.

Tenth session

In topical anesthesia, it was verified that the gingival attachment reformed around the collar of the dental element. Therefore, it was preferable not to disturb the formation process, and washing with ozonated water was not performed. Adherent mucosa and fornix were infiltrated with 10 cc of oxygen-ozone gas mixture at 15 μg/ml.

Eleventh session

There was no probing along the entire dental circumference. Under topical anesthesia, the adherent mucosa and

fornix were infiltrated with 10 cc of an oxygen-ozone gas mixture at 15 µg/ml.

Twelfth session

The gum attack was reconstituted with no probing and no bleeding. Under topical anesthesia, the adherent mucosa and fornix were infiltrated with 10 cc of an oxygen-ozone gas mixture at 15 µg/ml. A control intraoral X-ray was performed (Fig. 2).

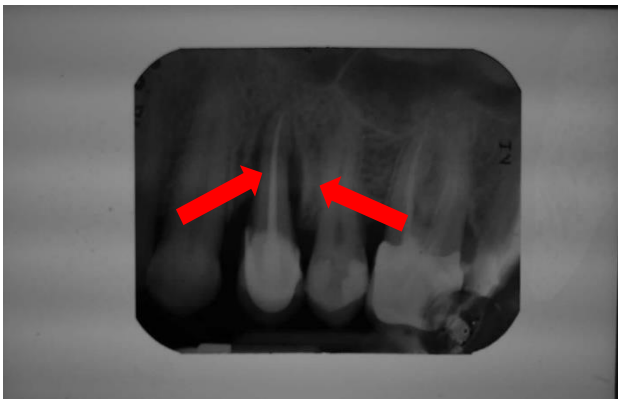

Fig. 2. *X-ray after the twelfth session: initial volumetric reduction of the radiolucent area (**arrows**) can be seen.*

Thirteenth session

Under topical anesthesia, the tooth was prepared according to the Loi technique with minimal invasion of the newly formed gingival sulcus. A temporary tooth was constructed according to Loi to protect the gum line. Adherent mucosa and fornix were infiltrated with 10 cc of oxygen-ozone gas mixture at 15 µg/ml.

Fourteenth session

An impression of the stump of tooth 24 was taken with precision material to prepare the zircoceramic crown, which would be the definitive covering of the tooth. Adherent mucosa and fornix were infiltrated with 10cc of oxygen-ozone gas mixture at 15 µg/ml.

Fifteenth session

After a test and careful control of the occlusal contacts, the zircoceramic prosthetic crown was cemented onto the abutment with a definitive cement. The excellence of the cement was carefully removed from the mucogingival sulcus. The possible presence of probing was checked, but no pathological value was found in the entire circumference of the dental collet with no exudation and no bleeding. Adherent mucosa and fornix were infiltrated with 10 cc of oxygen-ozone gas mixture at 15 µg/ml.

Sixteenth session

The treated tooth was checked, and the periodontal probing and bleeding were negative. Adherent mucosa and fornix were infiltrated with 10cc of oxygen-ozone gas mixture at 15 µg/ml (Fig. 3).

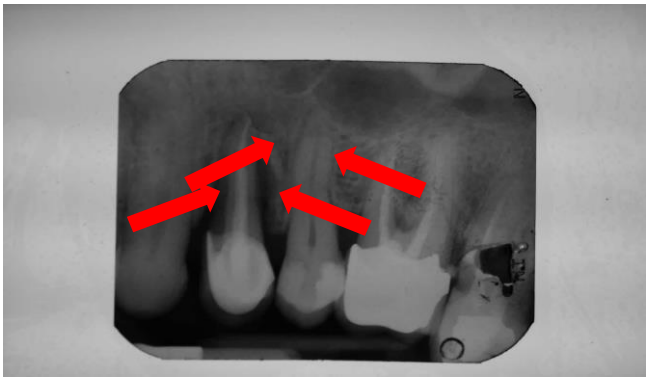

Fig. 3. *One-year follow-up X-ray: further bone regrowth and lengthening of the medial bony papilla (**arrows**) can be seen.*

DISCUSSION

Periodontal diseases are a group of pathologies involving the tooth and its supporting tissues. We can find anatomical and functional alterations at the gingival, ligament, vascular, bone, and dentinal levels. Often, the lesions caused by periodontal disease lead, among other things, to decreased tooth stability and, ultimately, to tooth loss.

The causes of periodontal disease are numerous: they include diabetes, malnutrition, alcoholism, smoking, hormonal changes, poor hygiene, occlusal trauma, and recurrent infections. Periodontal disease is a multifactorial syndrome that is not yet fully understood. The triggering causes may be periodontal and/or of endodontic origin. There is a genetic propensity to develop periodontal disease. There are also initially aseptic forms on a purely inflammatory basis, which often become super-infected, resulting in periodontitis (1-8).

The first sign of onset is usually gingivitis, which may go unnoticed by the patient (3-6). In this case, provoked bleeding may occur. There may be pain and the affected teeth may begin to show mobility. In manifest periodontitis, anaerobic bacterial morphologies are present to the detriment of cocci, which are predominantly aerobic and present in a more significant percentage in the mucous membranes with physiological trophism (5-12).

The patient presented in this article is healthy; he does not take drugs, he does not smoke, he has a marked propensity to produce tartar, he is a locksmith, and in 2008 he developed periodontitis on 4 lower incisors, lingual side, with purulent exudate and tooth mobility. He was treated with cycles of scaling and root planing associated with 3 cycles of antibiotic therapy. Healing occurred with a modest loss of mucogingival attachment. In 2020, the patient came to our attention for the annual dental hygiene recall with a 24 in a state of acute periodontitis, showing positive survey on the entire circumference of the tooth, purulent exudate, red and soft gums, pain on percussion and chewing and mobility of the element ranging between 2 and 3. At the beginning of treatment, the intraoral radiograph showed a loss of bone attachment covering more than two-thirds of the root with flattening of the bony peak of the mesial papilla. It was decided to start the first dental hygiene session with antibiotic prevention of endocarditis of 2 grams one hour before the treatment and 1 gram 6 hours after. This decision was dictated by observing the massive presence of pus in the pockets to be cured. At the end of the session, the pockets were irrigated with ozonated water until the bleeding stopped.

It was also decided to undertake the treatment of this periodontopathic dental element in a conservative, closed-air manner, making use of ozone considering its multiple properties, primarily antibacterial, antifungal, virustatic, anti-inflammatory, vasotrophic, normalizing of microcirculation and able to fragment the bacterial protective biofilm. In this way, we avoided using another multi-cycle antibiotic therapy.

Since the radiographic picture was not clear regarding the genesis of the pathology, it was decided to attribute a mixed periodontal and endodontic characteristic to the lesion even if, in the past, the patient had already shown similar pathology on other dental elements without endodontic compromise, recovering the state of eutrophism and maintaining the vitality of the elements involved. The decision was made after the pulp vitality test, which gave results at the lower limits of the normality range. The patient was advised of the therapy he would be subjected to. He was found suitable for using ozone for infiltration as he was free from G6PD enzymatic deficiency, thyroid pathology, and general pathology.

A specific consent form for using ozone as an alternative to antibiotic therapy was completed. The ozone therapy sessions were conducted under topical anesthesia for better patient compliance. The gaseous mixture of oxygen-ozone was used in the form of infiltrations both in the adherent mucosa surrounding the tooth and in the fornix of the second quadrant. Irrigations of instantaneous ozonated water were used in the periodontal pockets until a mucogingival seal was reformated. At an endodontic level, both forms of oxygen-ozone, water and gas were used, maintaining a long contact time with the endocanal dentin to sterilize the collateral canaliculi that were difficult to reach.

Due to organizational problems with the patient, carrying out more than one weekly session was impossible. The first eight sessions were, carried out on a weekly basis. After that, the patient was treated fortnightly. After the twelfth session, a control intraoral X-ray was performed. After the second oxygen-ozone therapy session, the patient's subjective symptoms disappeared, and the mobility of the tooth decreased.

Gradually, we witnessed the disappearance of the corpuscular exudate and the serous exudate; a good mucogingival seal was gradually reconstituted, and the dental element completely lost its mobility. It was possible to proceed with the prosthesis of the element by placing it in occlusion with its antagonist using a technique that was very respectful of the periodontium. The patient was then checked periodically and subjected to dental hygiene sessions, during which a periodontal survey of both arches was carried out with particular attention to tooth 24.

To date, the element appears to be healthy, not painful or mobile, with negative probing and pink, trophic, and non-bleeding mucous membranes. No gingival retraction occurred. A third control intraoral radiograph was performed, which showed an increase in the bone structure, the gradual reformation of the periradicular cortex, and an increase in the

mesial bone peak, which was flattened. It cannot be declared that there is an integral restitutio ad integrum to date, but it seems that bone healing is still taking place.

The stability of the tooth is related to the reformation of the ligament system, and the maintenance of the mucogingival seal with physiological probing is linked to the recovery from periodontitis.

CONCLUSIONS

The use of oxygen-ozone therapy in dentistry is an easily feasible method. Since the operation is generally performed on an anesthetized field, the patient feels no discomfort. In order to give due weight to the use of ozone in dentistry, it is essential to produce a large number of works that establish the boundaries within which to use this method.

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Case Report

MTG TECHNIQUE: A NOVEL MINIMALLY INVASIVE APPROACH FOR SOFT TISSUE AUGMENTATION BY MEAN A HIGH-DENSITY DERMAL MATRIX. A TECHNICAL NOTE

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ABSTRACT

In the following case report, the authors describe a case of single implant-prosthetic rehabilitation in the dilatory sector in which the high-density dermal matrix was successfully used with a specific technique (MTG) and had an excellent result in terms of increase in the peri-implant soft tissues both vertically and horizontally without the need to perform autologous tissue sampling or complex positioning of membranes (absorbable or non-absorbable).

KEYWORDS: *soft tissue augmentation, biomechanics, high consistency dermal matrix, scaffold-like structure, periodontal surgery, full-thickness flap, minimal invasiveness*

INTRODUCTION

In recent years, there has been a growing demand for aesthetic dental medicine among patients, leading to increased sensitivity in periodontics and implant prosthetics. This aspect includes the management of gum recession on natural teeth or restoration in not adequate supra crestal tissue height around dental implants. Periodontal surgery plays a crucial role in addressing periodontal defects and deficiencies, aiming to restore the health and function of periodontal tissues. Applying the connective tissue graft technique and a high-consistency dermal matrix presents an innovative approach for managing soft tissue defects and deficiencies in periodontal care (1, 2).

In this case report, the Authors present an innovative technique called Matrix Tissue Graft (MTG) for horizontal and vertical volumetric enhancement of crestal and supra-crestal soft tissues, which utilizes a high-consistency xenogenic dermal matrix (OsteoBiol® Derma 2mm, Tecnoss®, Giaveno, Italy). It differs from other techniques for tissue thickening using autologous tissue due to its reduced invasiveness and distinguishes itself from both the former and those involving the use of heterologous or synthetic tissue for two fundamental reasons: the matrix is positioned beneath a full-thickness muco-periosteal flap and in contact with the bony crest; the matrix is not secured with any fixation aid but is enveloped within the muco-periosteal flap. Periodontal surgery has witnessed significant progress in tissue augmentation and

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distraction techniques, along with the adoption of biomaterials. These developments have brought about a transformative impact on soft tissue implantation (3-6).

Soft tissue management plays a leading role in cosmetic and reconstructive surgeries, facilitating the restoration and improvement of tissue volume, contour, and function. Nonetheless, traditional approaches that rely on synthetic implants or autologous grafts can be linked to complications, restricted graft availability, or morbidity at the donor site. In place of traditional methods, the high-consistency OsteoBiol® Derma has come to the forefront, presenting the exciting potential for tissue augmentation and distraction in periodontal surgery (1, 2, 7, 8).

The high-consistency OsteoBiol® Derma exhibits numerous favorable characteristics for soft tissue implantation. Its scaffold-like structure offers a three-dimensional framework that stimulates cellular ingrowth and tissue regeneration, facilitating seamless integration with the surrounding tissues and leading to more natural and long-lasting results. Despite excellent results reported in *in vitro* and experimental studies, there is still limited availability of comprehensive multicentre clinical studies that assess its effectiveness, safety, and long-term results in tissue augmentation and distraction for soft tissue implantation in periodontal surgery (1, 2, 7-9).

The main goal of this article was to evaluate the efficacy of an innovative technique utilizing an OsteoBiol® Derma, attaining the most favorable results in soft tissue augmentation for periodontal and implant applications characterized by minimal invasiveness.

Moreover, the paper identifies potential areas for further research, providing valuable guidance for clinicians and researchers eager to utilize the high-density OsteoBiol® Derma for periodontal and implant surgical purposes.

MATERIALS AND METHODS

A 42-year-old male patient, non-smoker, with an ASA 1 classification, presented to our clinic seeking a solution for a single intercalated edentulism in the location of tooth 14. According to the patient's account, the tooth was removed about 4 years ago due to complications related to endodontic surgery. The patient needed a solution to address both the functional and aesthetic deficiencies, which involved the placement of a fixed prosthesis supported by an endo-osseous implant.

The residual alveolar ridge showed a marked transversal and vertical deficit also observable from the soft tissue morphology (Fig. 1). The consequent CBCT exam (essential for correct and safe implant planning) performed for diagnostic purposes to evaluate residual bone volumes showed a deficit comparable to that one detected by direct clinical observation of the lining soft tissues.

Fig. 1. *Pre-surgery patient's oral situation.* ***A****): Direct view showing lack of vertical keratinized tissue* ***B****): Occlusal view showing lack of thickness of keratinized tissue.*

Therefore, in addition to the CBCT exam, we performed an intraoral scan using a 3-shape trio scanner and included the patient in the control group for treatment with an OsteoBiol® Derma for soft tissue augmentation to improve the thickness of both peri-implant and supra-crestal soft tissues.

The overlap between the bone volumes of the CBCT and the soft tissues detected by the intraoral optical scan showed a thickness of the supra-crestal soft tissues of 1.8 mm; these data were subsequently confirmed by the direct intraoperative surgical control performed. The residual bone volumes were sufficient and suitable for a standard-sized implant insertion without further procedures. Hence the patient was offered a double treatment involving the insertion of an endo-osseous implant and the simultaneous thickening of the crestal and supra-crestal soft tissues, which were instead deficient for a suitable prosthetic rehabilitation from a functional and aesthetic point of view.

Once the informed consent was obtained and signed by the patient for the proposed treatment, he was provided with the hygiene and dietary instructions to follow before, during, and after the implant-prosthetic treatments. Moreover, the main periodontal indices were marked after the professional oral hygiene session. Once the absence of clinical signs attributable to periodontal disease was detected, the patient was prescribed antibiotic therapy using amoxicillin + clavulanic acid tablets of 1g to be taken every 12 hours (2 in a day) starting from the day before the operation and to be

taken for a further 5 days with the same frequency. Therapy with chlorhexidine 0,12% mouthwash was also administered once a day, to be performed 1 day before the operation and followed for a further 2 days.

The surgery involved the administration of loco-regional anesthesia with articaine 4% infiltration (adrenaline 1:100.000). Then, a full-thickness mucoperiosteal surgical flap was elevated using a 15c blade. The main incision extended from the center of the ridge, dividing the keratinized mucosa present into two equal portions, lingual and vestibular. The flap was then perfected through full-thickness medial and distal relief incisions from the primary ones with a divergent trend and without affecting the papillae of the adjacent elements reaching the muco-gingival line.

The osteotomy preparation with progressive drills was performed, and the implant was inserted with an implant micro-motor recording a peak torque of 55 N/cm2 (cone in 3p Devices Torino®). A trans-mucosal healing screw with a diameter of 3.8 mm was then positioned on the implant. The vestibular detachment of the full-thickness flap between the two relief incisions was stretched gently with anatomical forceps to check sufficient space for the matrix and make it suitable in terms of length and width for the consequent covering and stability.

The OsteoBiol® Derma 2 mm was separately stored in the greatest possible sterility, adequately shaped, and then positioned without any fixation aids. The flap was then sutured using a 4/0 PTFE thread and a 16 mm taper cut needle with simple detached stitches without placing other protective structures such as membranes or others (Fig. 2). No immediate prosthetic loading was performed.

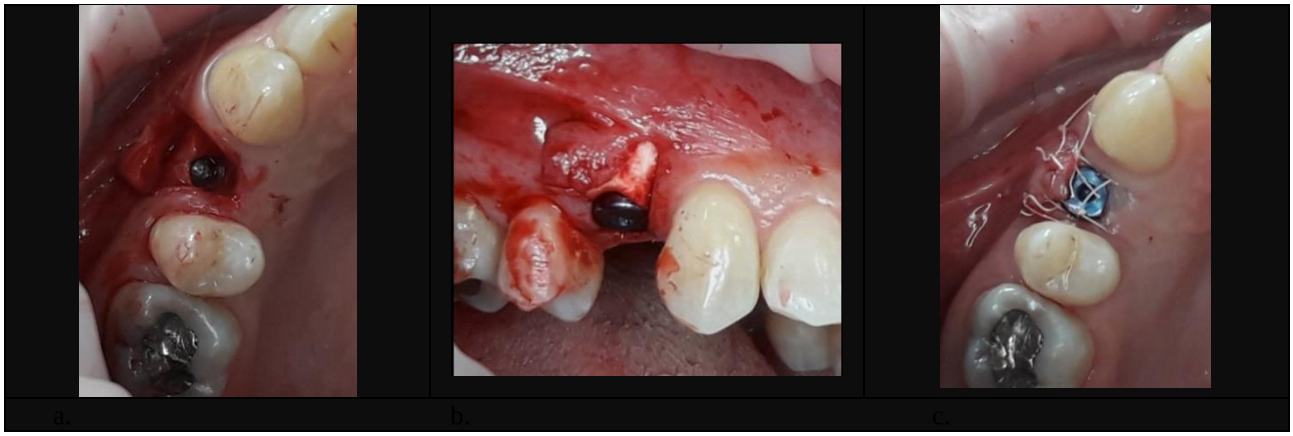

Fig. 2. ***A****): implant placement with the specific design of the flap;* ***B****): addition of OsteoBiol® Derma 2 mm without fixation aids;* ***C****): end of surgery with trans-mucosal healing, stitches, and primary closure.*

Once the tissues had fully matured, approximately after 3 months of healing time, we proceeded to create a temporary prosthesis for the implant. This temporary prosthesis utilized a PMMA temporary abutment for a single screw-retained prosthesis. Approximately 30 days later, we took an optical impression to reevaluate and gather precise measurements, and this information was used to fabricate the final prosthetic product. The definitive prosthesis was then placed 15 days after the optical impression was taken.

Almost complete maturation of the tissues with stabilization and tissue increase (both horizontal and vertical) is evident at the 6-month follow-up and 1-year follow-up with a definitive crown (Fig. 3-6). A further scan clinical control is expected in 2 years. The scans obtained will be compared using image superimposition software (Fig. 7, 8).

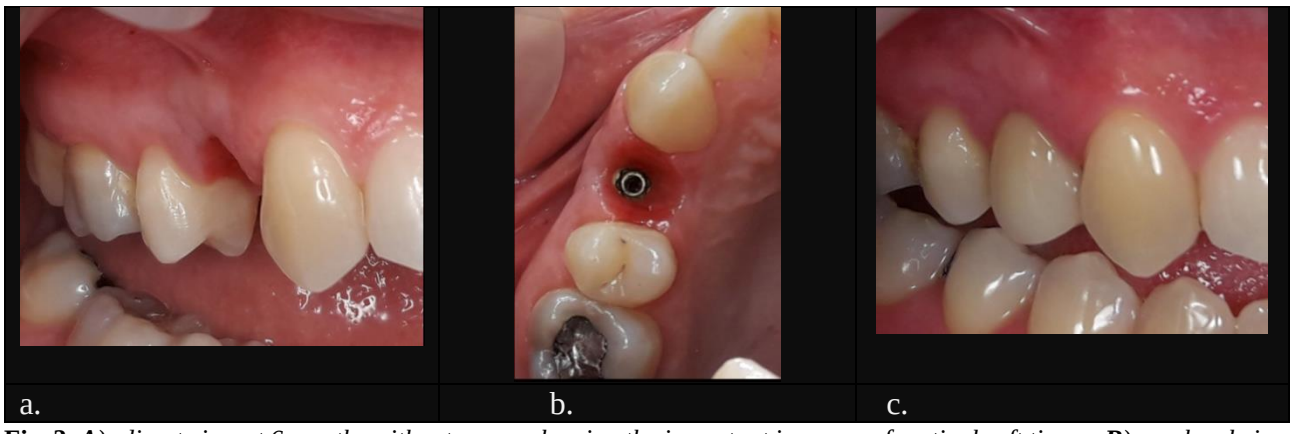

Fig. 3. ***A****): direct view at 6 months without crown showing the important increase of vertical soft tissue;* ***B****): occlusal view of implant's head with increase of thickness of soft tissue at 6 months;* ***C****): direct view at 12 months with the definitive crown.*

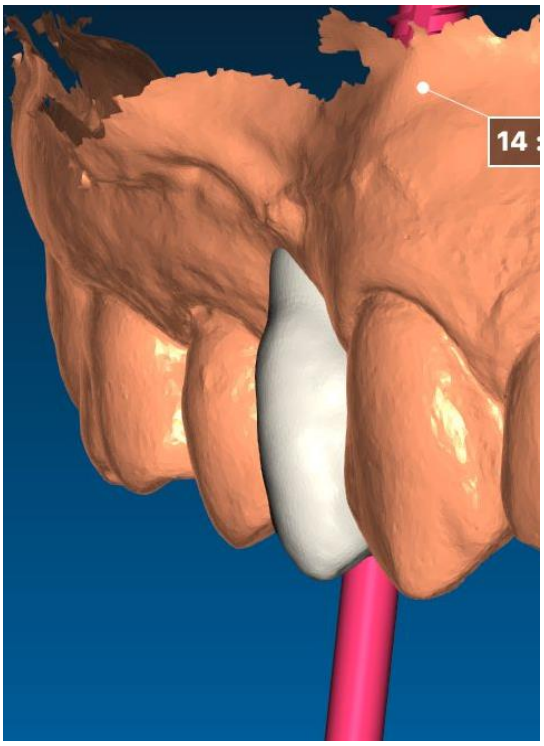

Fig. 4. *Digital planning of screw-retained implant-supported prosthesis.*

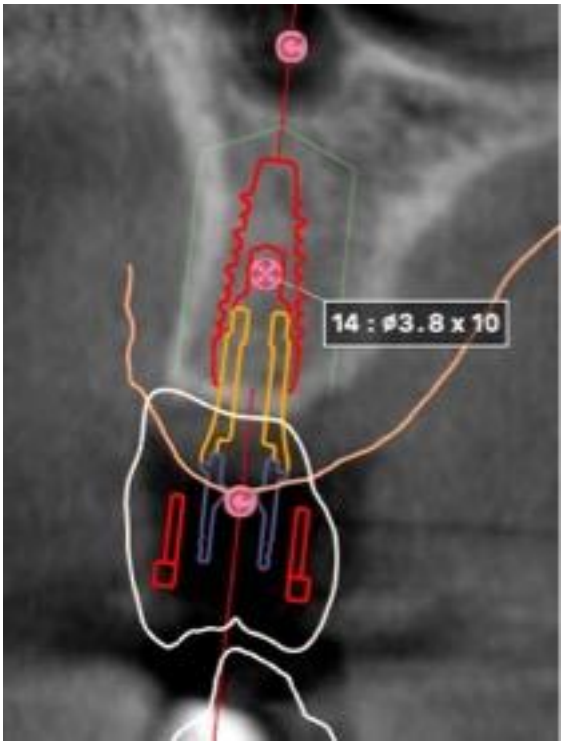

Fig. 5. *Digital surgical and prosthesis planning with superimposed file .stl*

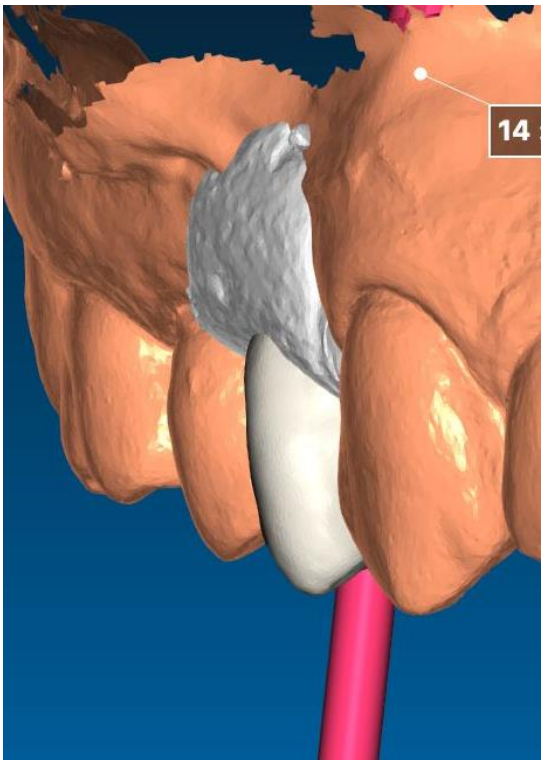

Fig. 6. *Digital planning of screw-retained supported prosthesis and super of scanned mtg graft in Stl file.*

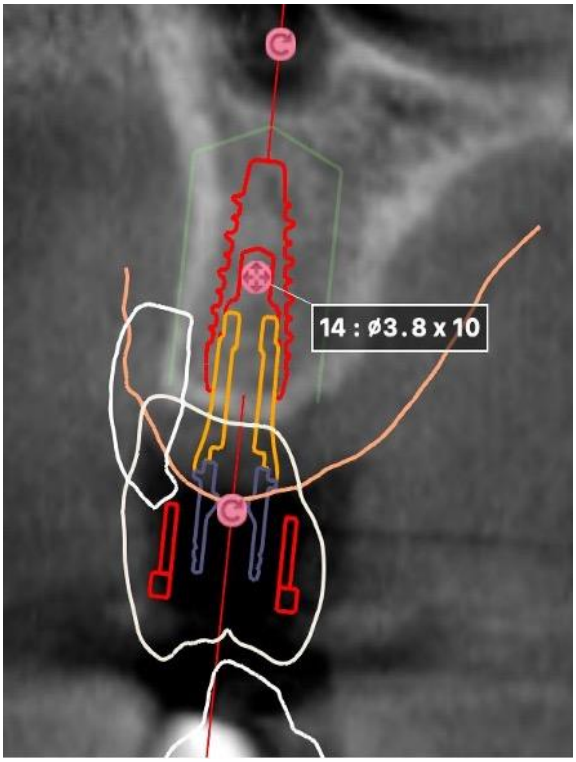

Fig. 7. *Cross section of the screw-retained implant. Implant-supported prosthesis planning imposition with superimposition of a double Stl. File (soft-tissue profile and derma graft upgraded from a Stl file Library).*

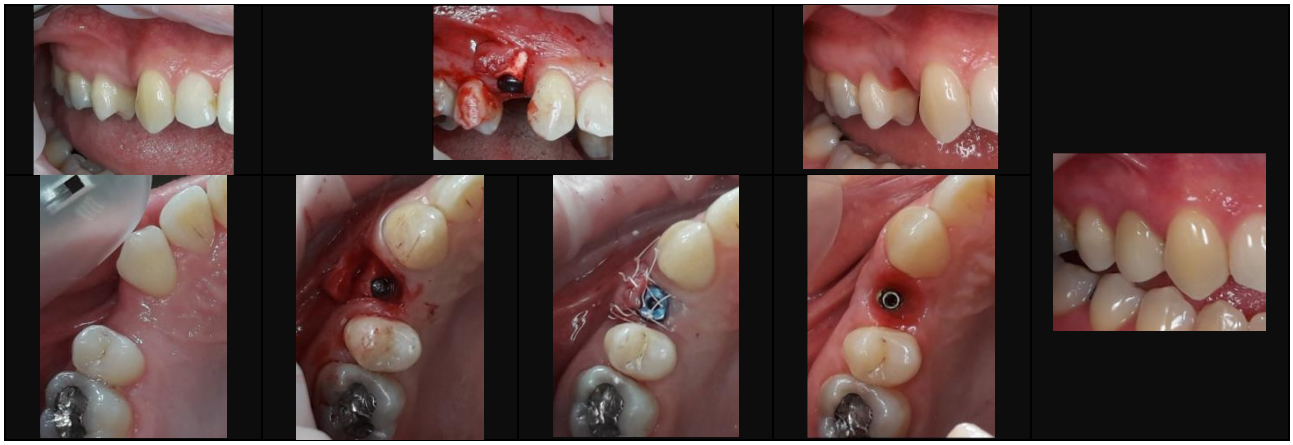

Fig. 8. *Summary of a composite of the technical note.*

DISCUSSION

MTG is a technique for enhancing the horizontal and vertical expansion of crestal and supra-crestal soft tissues. It involves the utilization of an OsteoBiol® Derma with a high level of consistency. It stands apart from conventional methods used for tissue thickening with autologous connective tissue due to its reduced invasiveness, eliminating the need for tissue sampling. Moreover, it differs from procedures that employ heterologous or synthetic tissue for two crucial reasons:

1. Reduced invasiveness: the matrix is positioned under a full-thickness periosteal mucus flap and in direct contact with the bone crest on one side and with the periosteal of the flap itself on the other;
2. Distinctive approach: the matrix is not stabilized with any fixation aid but placed in the correct position after careful preparation of the flap (10-14).

In this way, the morbidity of complex, multiple operations is significantly reduced, sampling is unnecessary, and all the additional inherent positioning and stabilization issues of membranes are avoided.

The OsteoBiol® Derma is characterized by a high consistency, which allows stable volumetric maintenance throughout the first surgical phase of soft tissue healing generated by the trauma of implant insertion. The thickening of the peri-implant soft tissues with site-specific biotype variation is the current focus in implant-prosthetic regeneration for medium and long-term maintenance and success. Normally, this thickening is performed with connective or epithelial-connective grafts, which still represent the gold standard but require a donor site, greater invasiveness and number of operations, and more excellent skills of the operating surgeon due to increased procedural difficulties (15). The application of the OsteoBiol® Dermatakes place immediately after implant positioning (taking into account both the prosthetic optimal orientation and the biology of tissues involved) precisely at 4 mm more apical than the free margin of the flap to prevent the demonstrated para-physiological peri-implant resorption in case the thickness of the soft tissues is 2 mm or less (16-20).

The significant distinction between a connective tissue graft and a dermal matrix graft is that, if executed correctly, the autologous graft quickly contributes to supra-crestal vascularization. In contrast, the dermal matrix becomes involved in vascularization only after full integration, typically around 4-5 months after placement. Hence, we cannot prevent the natural peri-implant bone resorption, which should be anticipated and proactively managed, as previously explained, by "sinking" the graft apically by 4 mm.

If the thickness exceeds 3 mm, the implant can be positioned in a juxta-crestal position. Another difference is that OsteoBiol® Derma is positioned below a full-thickness flap. If the inter-implant distance exceeds 10 mm, a trapezoidal flap can be used, thus obtaining the preservation of the papillae. If the distance is less than 10 mm, it is better also to involve the papillae of the adjacent entities within the flap, known as a "hockey stick" shape, trying in any case to preserve the lingual/palatal aspect of these papillae. The flap relief incisions must extend in the coronal-apical direction up to the muco-gingival line. In contrast, the crest incision will preserve the keratinized gingiva by dividing it into two portions: one lingual/palatal and one vestibular. The matrix must have a proper size so that it can be easily accommodated within this flap to stabilize it equally without any means of fixation.

The stability of the matrix is ensured not only by the flap but also by the employed sutures, which are applied with straightforward detached stitches. In specific situations where the muco-gingival line is situated more apically and the drains are in proximity, detached stitches can also be used on the mesial and distal drains to further secure the matrix.

The matrix can be positioned over the implant itself (overturned occlusally) in the case of a submerged fixture over a healing screw. The OsteoBiol® Derma can be shaped to be managed for trans-mucosal requirements creating two portions that "embrace" the healing screw medially and distally.

The sutures are removed in 14 days; the patient must be adequately informed about the behavior to maintain (especially when chewing food, reducing its consistency, or semi-liquid). Within 28-35 days, there is a complete epithelialization of any portions, even those left exposed (which defines another considerable advantage compared to the traditional matrix/membranes whose occurrences often mean complete failure of the entire operation). After 4 months, there is an integration of the matrix. In the meantime, you can still proceed with the temporary prosthesis phases starting from the second month.

The development of this technique was codified using STL superimposition. Through the application of dedicated software, we were able to superimpose intra-oral scans taken before and after treatment at intervals of 6 months, 12 months, and 2-3 years. This analysis revealed a consistent maintenance of tissue volume, accompanied by a favorable increase in tissue thickness and site-specific biotype after applying the matrix.

CONCLUSIONS

While it is essential to acknowledge that findings from a single case may not hold statistical significance, it remains valuable to emphasize the numerous benefits associated with using this material in conjunction with this technique for augmenting soft tissues, both horizontally and vertically.

The intrinsic simplicity of this procedure, primarily attributed to the absence of membranes or other structures required for protection, stabilization, and coverage, makes it more accessible and manageable even for less experienced surgeons compared to traditional techniques.

The MTG technique using high-consistency OsteoBiol® Derma 2mm has proven effective in thickening the specific peri-implant tissue biotype, increasing patient comfort, and recreating an implant emergence profile more suitable to the subsequently positioned prosthetic crown. In general terms, it can be deduced how survival and successful implant rate can be increased by stabilizing the surrounding tissues (quantity and quality) and reducing unwanted problems such as mucositis or peri-implantitis. Furthermore, this technique offers superior aesthetic results, allowing for a more accurate mimicry of ideal soft tissue, resulting in an improved overall appearance. Considering all the indications mentioned above, it can be argued that this procedure is more biologically sustainable and economically efficient for daily prosthetic implant rehabilitations.

The authors are hopeful that this initial endeavour can serve as an inspiration to many other colleagues and encourage a more comprehensive exploration of the material and technique. Even though it has shown remarkable effectiveness in just one case, there is potential for broader research and application in the field.

Conflict of interest statement

All the authors declare no conflict of interest.

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Case Series

JUVENILE OSSIFYING FIBROMA OF THE MANDIBLE A DIAGNOSTIC DILEMMA

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ABSTRACT

Juvenile ossifying fibroma (JOF) is classified as a benign fibro-osseous neoplasm characterized by the proliferation of mineralized osteo-fibrous tissue replacing normal bone. JOF are benign yet exhibit locally aggressive behavior with a strong tendency for recurrence. Juvenile ossifying fibroma is predominantly reported in the maxillary region, paranasal sinuses, orbit, and other bones related to paranasal sinuses. JOF is relatively rare in the mandible. In this current case series, we intend to report two cases of JOF in a child's mandible, diagnosis, surgical management, and follow-up. Pediatric dentists should know these entities of maxillofacial pathology so that appropriate diagnosis can be made and prompt treatment can be delivered.

KEYWORDS: *ossifying fibroma, fibro-osseous neoplasm, neoplasm*

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INTRODUCTION

Ossifying fibroma is a benign, fibro-osseous lesion with a similar presentation to Fibrous dysplasia (FD) but differs in the aspect that it is encapsulated; hence, it is more circumscribed and reported in third and fourth decade (1-3).

Juvenile ossifying fibroma (JOF) is a variant of the ossifying fibroma reported in younger children. Even though JOF is benign, it tends to exhibit locally aggressive behavior due to expansion and compression of adjacent tissue (4-8).

Juvenile trabecular ossifying fibroma (JTOF) and Juvenile Psammomatoid ossifying fibroma (JPOF) are two histological variants described in the literature (5). The psammmomatoid variant often presents as a painless growing mass, leading to asymmetry and compression of surrounding tissue (6). Radiographically, JPOF presents itself as an expansile radiographic lesion exhibiting varying degrees of calcification internally (7, 8).

Histopathologic appearance demonstrates a grainy texture that represents calcification and is often called Psammomatoid. Recurrence rates of JPOF vary from 10% to 19% based on the management protocol followed. Recurrence rate is higher when conservative treatment protocol is followed. Clinically, patients with JTOF are often asymptomatic, and early lesions are usually discovered as incidental radiographic findings. Displacement of teeth may be an early sign of this tumor process. JTOF may be aggressive in its growth potential, and as it matures, rapid growth may result in facial asymmetry and jaw deformity (5).

Radiographically, JTOF are usually unilateral, unilocular mixed radiolucent/radiopaque lesions (9). Computer tomographic imaging is required for larger lesions to determine the full extent of the lesion. JTOF tends to expand concentrically from a central point or epicenter outward in all directions, and this expansion may result in the displacement of teeth and the inferior alveolar nerve canal (10). The outer cortical plate remains intact despite significant expansion and thinning. Resorption of teeth is common, and JTOF maintains a well-defined corticated border (10). The primary histologic criterion for JTOF consists of a neoplasm predominantly composed of cellular fibroblastic tissue with thin trabeculae of immature bone, which may anastomose to form a lattice (11).

JTOF is usually well-demarcated but unencapsulated. Of note, there may be considerable variation in stromal cellularity. Plump osteoblastic rimming of bone is a standard feature. Clusters of osteoclastic multi-nucleated giant cells, areas of hemorrhage, and foci of pseudo cystic stromal degeneration may be observed (12). As the lesion proliferates, more aggressive behavior of JOF can be confirmed, usually due to incomplete initial removal or persistence of local irritants. It is seen that incomplete resection causes recurrence in aggressive tumors, and recurrence rates of 30% to 58% have been reported for juvenile trabecular ossifying fibromas.

The World Health Organization (WHO) classifies juvenile ossifying fibroma into two histologic variants: JTOF and JPOF (13). The former is usually seen in children and adolescents (mean age of presentation: 8.5-12 years), whereas the latter usually affects a more comprehensive patient age range (16–33 years). There is no gender preference for either entity. Both entities are relatively rare; however, JPOF is more commonly encountered than JTOF (14).

Localization differs for each subtype, with the maxilla being more common for JTOF and the paranasal sinuses more common for JPOF (15, 16). Here, we describe a case series of two cases with a trabecular variant in the mandible of two young children.

CASE REPORT AND RESULTS

Case 1

A 13-year-old female patient reported to the Department of Oral and Maxillofacial Surgery with a hard swelling on the left side of their face for 3 months. Upon clinical examination, diffuse swelling was on the left lower third of the face. Intraoral examination revealed bony hard expansion of the buccal and lingual cortical plates in the lower left premolar-molar region. The swelling was well-defined, measuring 4 × 3 centimeters and extending from the lower left lateral incisor to the first molar. The mucosa over the swelling looks normal in color and consistency, with no tenderness or visible pulsations (Fig. 1).

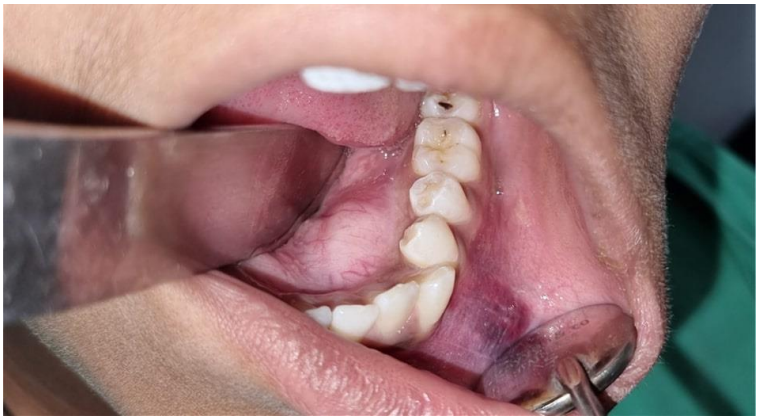

Fig. 1. *Clinical intra-oral picture of the expansile swelling.*

No draining sinuses were observed. Tooth mobility was present for the first and second premolars. Teeth vitality tests revealed no response for the first and second premolar and delayed response for the first molar. There was no complaint of paraesthesia or regional lymphadenopathy. Radiographic investigations and orthopantomography revealed a solitary, well-defined irregular radiolucency extending from the central incisor to the mesial root of the second molar. There was the displacement of the canine, first and second premolar, and resorption of the first, second premolar, and mesial root of the first molar. CBCT shows expansion and thinning of buccal and lingual cortical plates measuring 28.43mm buccolingually, 40.9mm anteroposteriorly, and 28.95 superior-inferiorly (Fig. 2).

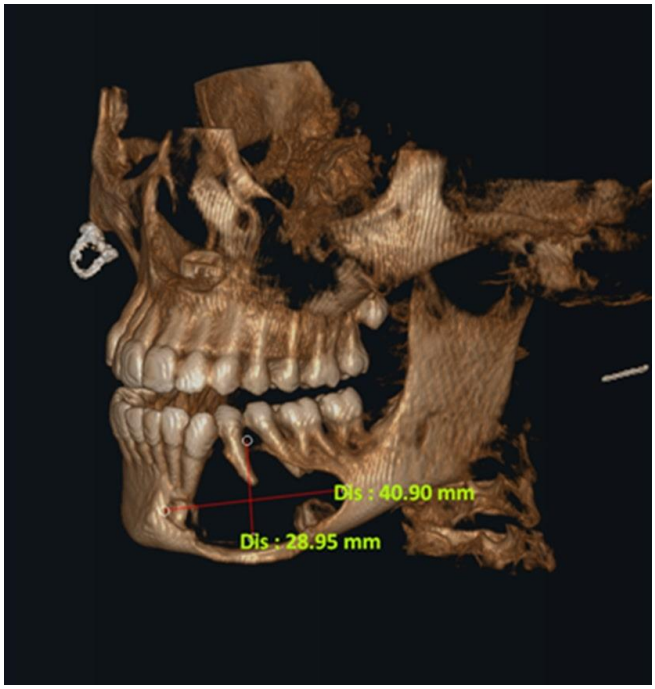

Fig. 2. *Pre-operative CBCT image of the lesion.*

The aspiration of the site was negative. Therefore, the cyst diagnosis was ruled out, and an incisional biopsy was done and sent for histopathological evaluation. Section revealed fibrous connective tissue with scattered bony trabeculae and multinucleated giant cells, confirming the diagnosis of JOF. Intentional root canal treatment for the central incisor, lateral incisor, canine, and first molar, followed by surgical enucleation and curettage of the tumor, was planned under general anesthesia.

Surgical management

Under strict aseptic conditions, general anesthesia was administered under naso-endotracheal intubation. First and second premolars were extracted, and enucleation was done through an intraoral crevicular incision extending from the lower right canine to the left second molar (Fig. 3).

Enucleation of the entire lesion and peripheral ostectomy of 1cm bone was done, followed by reinforcement with a titanium reconstruction plate and primary closure with 3-0 synthetic resorbable sutures (Fig. 4).

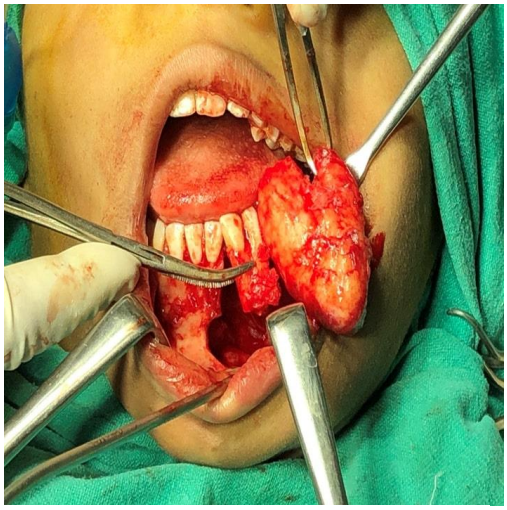

Fig. 3. *Surgical resection of the lesion.*

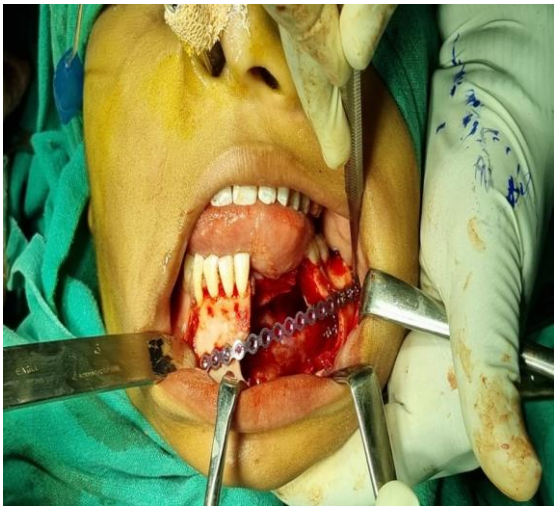

Fig. 4. *Post-resection stabilisation of the defect with a titanium mesh.*

The surgery was uneventful. The histopathological report confirmed the diagnosis of a trabecular variant of JOF. Postoperatively, the patient was put on Cefixime 1gm I.V. 12th hour, Metronidazole 500mg I.V. every 8th hour, and Diclofenac 75mg every 12th hour for 5 days. The healing was satisfactory. The patient has been followed up for 6 months. There are no complaints of swelling or paraesthesia, and gradual bone remodeling has occurred. Follow-up OPG showed reduced radiolucency and good amounts of bone regeneration (Fig. 5).

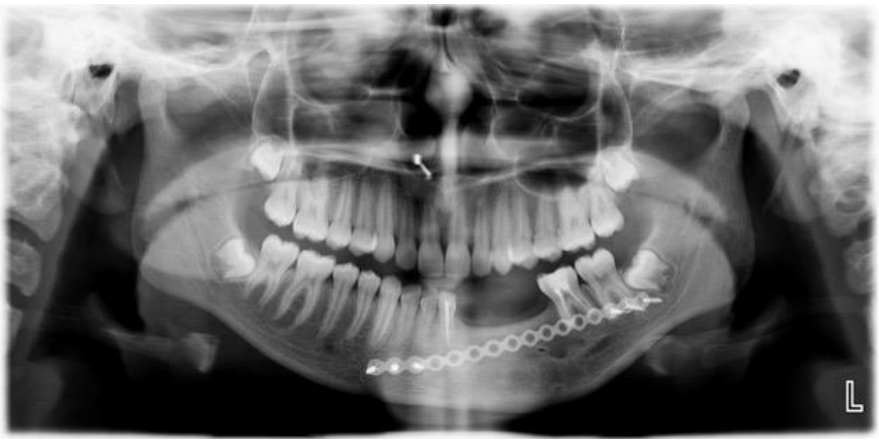

Fig. 5. *18 months follow-up visit.*

Case 2

A 5-year-old child reported to the Department of Oral and Maxillofacial Surgery with diffuse swelling in the left lower jaw for 10 months. The growth was rapidly increasing in size. On examination, an oval-shaped swelling measuring around 4x2 cm was seen. The swelling was well-defined; swelling extends from the deciduous canine to the second molar, causing expansion of buccal and lingual cortical plate expansion and obliteration of buccal vestibule concerning tooth numbers #74 and #75. The overlying attached gingiva and mucosa are normal. On palpation, the swelling was painless, hard in consistency, and without any pulsations or discharge. There was no paraesthesia over the lower lip or chin. Lymph

nodes were nonpalpable. Orthopantomography revealed a solitary, well-defined radiolucency surrounded by a radiopaque border (Fig. 6).

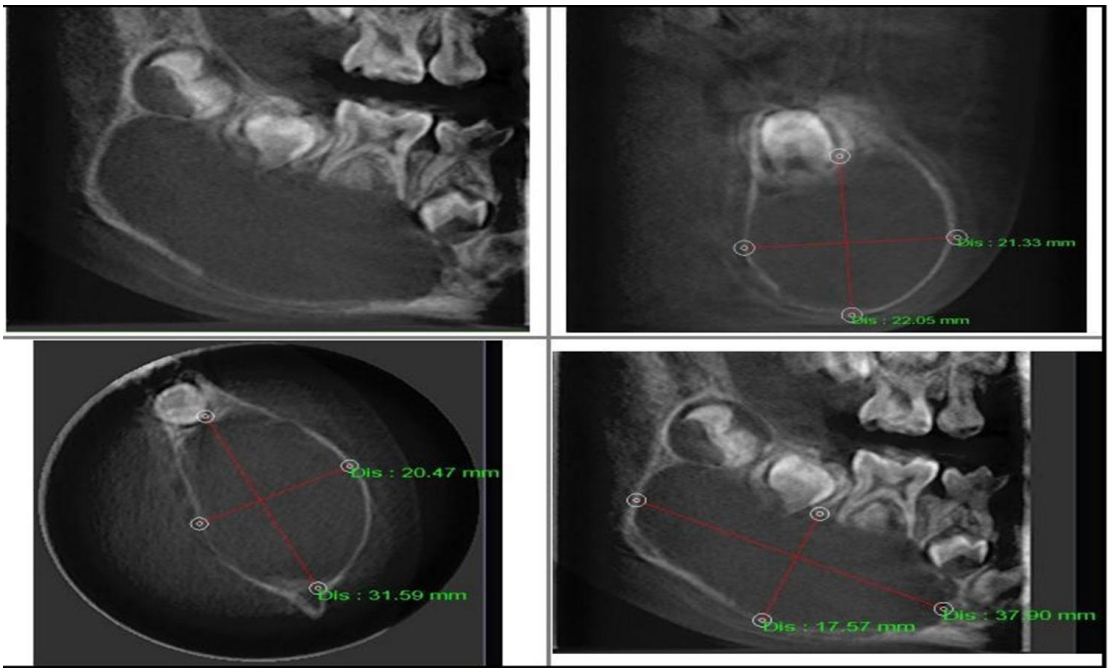

Fig. 6. *Pre-operative OPG of the lesion.*

Cone beam computed tomography showed expansion and thinning of buccal and lingual cortical plates measuring 21.33mm buccolingually, 37.9 mm anterior-posteriorly, and 17.52 mm superior-inferiorly. The inferior border was intact. The aspiration of the site was negative. An incisional biopsy was done and sent for histopathological evaluation. Section revealed fibroblastic stroma admixed with psammoma bodies.

Focal areas show mature bony trabeculae surrounded by fibrous stroma, confirming the diagnosis of JPOF. Considering factors like an intact inferior border, no involvement of adjacent structures, no paraesthesia of the lip, and the age of the patient, this case was planned for excision and curettage without resection.

Surgical management

The patient was operated under general anesthesia under naso-endotracheal intubation. The intraoral crevicular incision was given from the distal aspect of the deciduous canine to the first molar. Enucleation of the entire lesion along with peripheral ostectomy was done and sent for biopsy, followed by reinforcement with a titanium reconstruction plate, and primary closure was done with synthetic resorbable sutures (Fig. 7, 8).

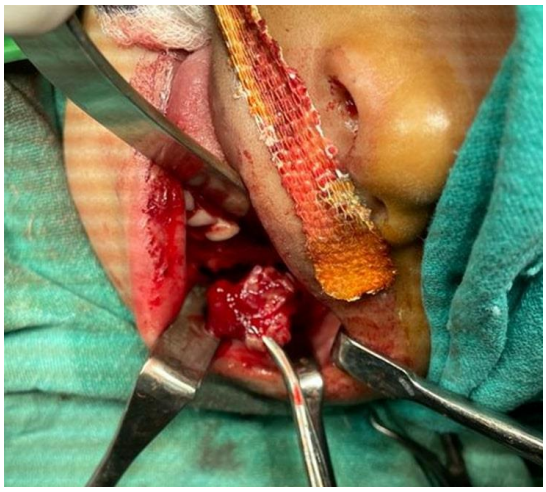

Fig. 7. *Surgical resection of the lesion.*

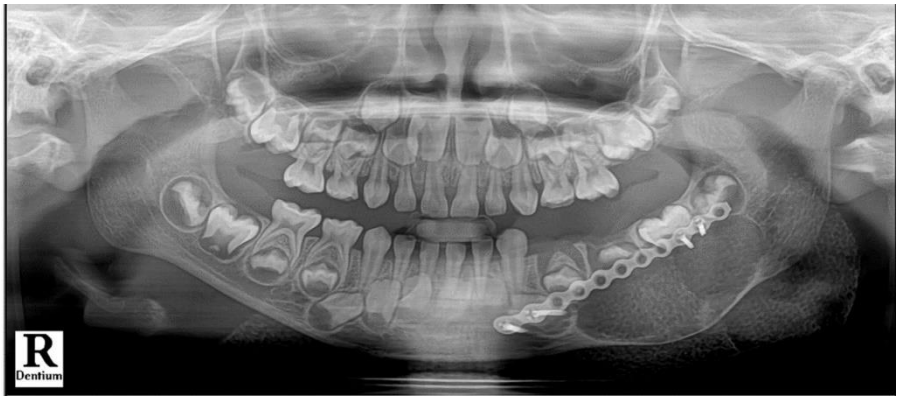

Fig. 8. *Post resection stabilization of the defect with a titanium mesh.*

The surgery was uneventful. The histopathological report confirmed the diagnosis of JPOF. A post-operative follow-up visit after 12 months showed a filling up of bone defect (Fig. 9).

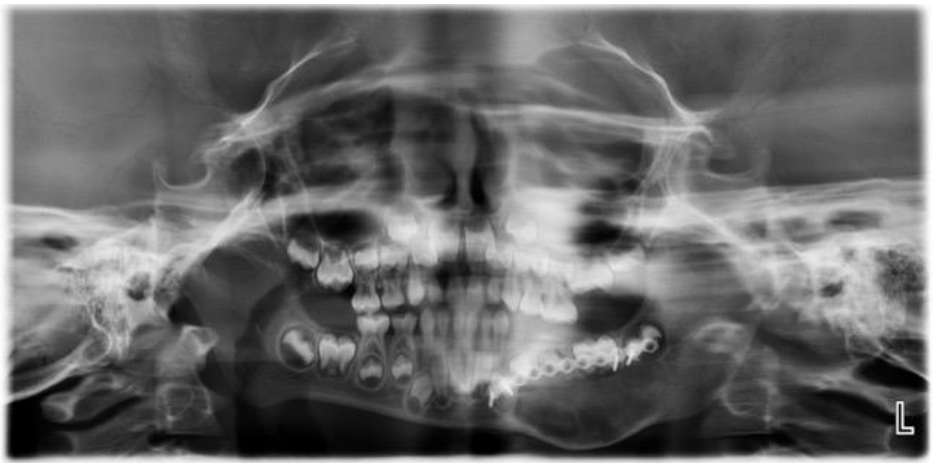

Fig. 9. *12-month follow-up visit.*

DISCUSSION

Previous literature has published multiple case reports on JTOF and JPOF (Table I). Most of the jaw's fibro-osseous lesions are benign, asymptomatic, and grow slowly. Ossifying fibromas fall within the group of benign fibro-osseous lesions. As previously believed, they are not of odontogenic origin but instead made of osteogenic calcified matrix.

Table I. *The table shows a list of previous case reports.*

Sno	Author	Type	Age/Gender	Variant	Location	Management
1	Adham et al 2023 (17).	Case report	12/Male	Psammomatoid	Maxilla: Left nasal bone, left paranasal sinus, left nasal cavity, nasal septum, and pushing the medial wall of the left eye.	Subtotal maxillectomy and reconstruction in one stage. Reconstruction surgery was made with titanium mesh and rib cartilage.

2	Kim et al. 2023 (18)	Case report	4/Male	Psammomatoid	Zygomaticomaxillary area on the left side	Excision
3	Nnko et al 2022 (19)	Case report	8/ Female	Trabecular	Right maxillary area	Hemi maxillectomy and reconstruction of maxilla with a rib
4	Arfaj et al. 2022 (20)	Case report	15/Female		Aggressive juvenile active ossifying fibroma of the ethmoid sinus with orbital and intracranial extension	endoscopic debulking of the lesion followed by lateral rhinotomy, and finally, frontal craniotomy with reconstruction
5.	Gotmare et al 2017 (21)	Case report	8/Male	Psammomatoid	Expansile lesion in the left ramus of the mandible.	enucleation and curettage with standard hemi-mandibulectomy along with the fixation of construction plate.
6.	Sarode et al 2018 (22)	Case report	10/Male	Psammomatoid	Anteriorly up to the right canine region, posteriorly up to the left side zygomatic bone, superiorly up to left infraorbital margin and inferiorly up to the alveolus	Excision with palatal prosthesis
7	Titinchi et al 2021 (23).	Retrospective study	3-31 years	Trabecular-10 Psammomoid-7	Different regions in the mandible and maxilla.	Enucleation for small well defined lesions in mandible Curettage with peripheral ostectomy for medium to large neoplasms Resection with reconstruction for large infiltrative recurrent neoplasms
8	Acosta et al 2023 (24)	Case Report	14/Male		Lesion involving the left nasal cavity, left maxillary ethmoid and sphenoid sinus, and left side of the nasopharynx	Multidisciplinary assessment and care were done by NS and ENT to debulk the base of the tumor via transnasal and sublabial access endoscopically
9	JamesI J Green et al 2023 (25)	Case Report	4/Male	Trabecular	Entire maxilla	Maxillary resection
10	Saad et al 2019 (26)	Case Report	9/Female	Trabecular	Right impacted molar area to the left first molar area causing perforations in the buccal and lingual cortical plates of mandible	Surgical excision
11	Sultan et al	Case Report	8/Male	Trabecular	Right mandibular	The tumor was

	2018 (27)				ramus.	enucleated, an ostectomy was performed, and the bone cavity heat-treated with electrosurgical coagulation
12	Aslan et al 2018 (28)	Case Report	13/Female	Psammomatoid	Maxillary sinus	Complete surgical resection
13	Solyman et al 2020 (29)	Case Report	4/Male	Psammomatoid	Left maxillary sinus and encroachment of left orbit	Debulking surgeries
14	Mouna Lyoubi et al 2021 (30)	Case Report	14/Female	Psammomatoid	polylobed mass filling the right nasal cavity,	Endoscopic transnasal approach with image-guided neuro-navigation system and complete surgical removal
15	Ashwan Paranthaman et al 2017 (31)	Case Report	13/Female	Trabecular	right side of the face, extending from right alar region to the infraorbital margin superiorly, and extending laterally to the right cheek region	Maxillary resection

Since they refer to the same thing, cementifying and cemento-ossifying fibroma are no longer used. Their epidemiology is poorly understood because they have long been mistaken for cemento-osseous dysplasia. Their distribution is primarily restricted to the craniofacial bones.

Ossifying fibroma is a rare fibro-osseous tumor composed of fibrous tissue and mature bone. It is subdivided into conventional and juvenile subtypes. JOF is an uncommon variant of ossifying fibroma that behaves in a more aggressive pattern than the conventional type (32).

Adults older than 30 to 40 years are typically affected with conventional form in their jaw. In 80% of cases, JOF develops in children and young adults before age 15. The JOF has been identified as a distinct histopathological entity among the fibro-osseous group of disorders because of its distinctive histological characteristics. Both variants exhibit distinct histopathological patterns, and hence, the diagnosis is more predictable. Age is an important factor in the diagnostic criteria of juvenile ossifying fibroma.

The clinical presentation of JOF is a slow-growing, asymptomatic, expansile, spherical or ovoid swelling, causing significant facial asymmetry, and depending upon the anatomical site of involvement, there can be nasal obstruction, epistaxis, exophthalmos, and proptosis. In most patients (85%), the tumors are located in the facial bones, but they also involve the calvaria (12%) and extracranial sites (4%). In the facial bones, 90% of the tumors arise from the

maxilla and paranasal sinuses, and the remaining 10% arise from the mandible (33). Rarely, pain and paraesthesia associated with the swelling are present. Root resorption and displacement of the involved teeth are observed. In the mandible, the angle and ramus are the most common sites of involvement (34).

Juvenile ossifying fibroma can be radiographically divided into 3 stages. Initial stage/Stage I: it appears as a well-defined radiolucent lesion. Mixed-stage/Stage II: radiolucent lesion with areas of internal calcification. Mature stage/Stage III-Completely radio-opaque mass. On CT, it appears as a well-demarcated lesion with a sclerotic rim and less dense fibrous central core. Three patterns have been described in CT. Pattern-1: Radiolucent central core with a thick outer mantle. Pattern-2: Ground glass mural nodule. Pattern-3: Homogeneous solid radio dense lesion (37).

Histologically, JOF is characterized by a cellular fibrous stroma, garland-like bony strands, and cement particles. A recent study by El-Mofty identified two histopathological variants: JTOF and Psammomatoid JOF (PJOF). The average age of occurrence of JTOF is considerably younger than JPOF, with the average being eight-and-a-half to twelve years compared to a 16- to 33-year range of PJOF (34).

CONCLUSIONS

Complete surgical excision is preferred to conservative curettage in both juvenile ossifying fibroma. Long-term follow-up is necessary because incomplete resection increases the risk of recurrence, which is more aggressive than primary and occurs 6 months to 19 years after surgery. For complete resection, an open surgical rather than an endoscopic approach may be required, depending on the degree of disease and invasion. Due to the tumor's radioresistance, high risk of malignant transformation, and late radiotherapy-related adverse effects in children, radiotherapy is not recommended. Juvenile ossifying fibroma should be managed as a locally aggressive neoplasm due to its high recurrence rate (30-50%) and aggressive nature.

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Case Report

AUTOMATIC SAGITTAL-TRANSVERSAL MAXILLARY EXPANSION: ORTHOGNATHODONTIC EVOLUTION

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ABSTRACT

The outcome of daily clinical practice in interceptive orthognathodontics is influenced by the severity of the pathology. It also heavily depends on the paediatric patient's ability to cooperate. The need to choose between dentoalveolar and skeletal expansion using fixed appliances arises from the necessity to achieve a predictable result in the shortest time possible and grant optimal patient growth, even in the absence of cooperation. However, the transposition of the typical three-way steel screw from removable appliances to fixed ones complicates expansion treatments, especially for the patient's parents, forcing the dental professional to perform frequent checks relative to expansion's activations. The introduction of an automatic one-way nickel-titanium expansion screw in the shape of a crossbow, to be intended as an evolution of the one-way steel screw present in traditional rapid expanders, has paved the way for a new interceptive orthognathodontics paradigm. Daily clinical practice makes skeletal transversal maxillary expansion substantially independent of patient cooperation. In this paper, a new device is presented, with the aim to further refine the concept of independence present in contemporary one-way crossbow-shaped expansion screw appliances, simply introducing three undersized crossbows made from nickel-titanium. This design can exert efficient expansion simultaneously in three directions, making maxillary expansion automatic both sagittally and transversally, minimizing the need for patient cooperation, and reducing parents' concerns.

KEYWORDS: *automatic, nickel-titanium, class III, expansion, simplicity, efficiency*

INTRODUCTION

In paediatric interceptive orthognathodontics, transversal skeletal maxillary expansion is one of the most frequent needs. The choice among the various expansion methods is primarily based on the skeletal and dental characteristics of the patient's malocclusion. Although vertical and horizontal skeletal growth components interact in shaping the final morphological framework of the dentoskeletal structures, the influence of transversal skeletal width is decisive. Morphological changes along the transversal plane of skeletal structures often induce skeletal modifications in

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the sagittal plane. In contrast, compensatory capacities in the sagittal plane are mainly expressed through dental alterations, as the dentition effectively absorbs any structural anomalies of skeletal growth (1).

Furthermore, the individual response to transversal expansion is determined by the patient's sutural activity: true sutural growth stimulation is possible only in patients who have not reached their pubertal growth peak (2). Moreover, a slight reduction in diameters at both molar and premolar levels is observed after transversal expansion, but the new occlusal relationships remain stable (3). Therefore, an early and accurate diagnostic evaluation is fundamental to classifying paediatric orthognathodontic patients based on age and type of malocclusion so that the most appropriate expansion protocol can be applied.

Malocclusion, resulting from skeletal deficit, may or may not involve the basal structure and thus present in dentoalveolar, skeletal, or more often mixed forms (4-6). The dentoalveolar deficit is often linked to problems in the eruptive sequence. It occurs mostly due to palatal inclination of the teeth in the upper arch and their alveolar processes in the absence of a transversal deficit in the upper jaw (4). The skeletal deficit consists of a reduction at the basal level of the maxilla, both at sagittally and transversally. It is associated with insufficient transversal development of the middle third of the face (4, 6, 7). The transversal skeletal deficit is thus characterized by a reduction in the width of the upper jaw, absolute or relative to the mandible, a reduction in the width of the nasal fossae, and, in most cases, overdevelopment of the lower third of the face in the presence of correct dental axes (8).

Therefore, based on the above considerations, for Class I and II malocclusions resulting from dentoalveolar, skeletal, or mixed maxillary deficits, transversal expansion combined with subsequent intra or extraoral appliances is appropriate to resolve imbalances. For Class III malocclusions, sagittal-transversal expansion combined with subsequent intra or extraoral appliances is necessary. Specifically, Class III malocclusion may be associated with either upper base retrusion, lower base protrusion, or a combination of the two anomalies. The upper jaw, when retrognathic, is often also characterized by a reduction in its transversal diameter (9). Therefore, careful evaluation of the transversal relationships between the arches and the maxillae is mandatory in the treatment planning of Class III malocclusion (10).

Finally, the favorable outcome of the chosen expansion for any malocclusion, even when selecting the most appropriate clinical protocol, depends on the cooperation of the child, which, paradoxically, is more difficult to achieve today despite well-known psychological approach techniques (11). This category of patients often has negative experiences due to an emergency intervention following trauma or some carelessness and/or lightness due to inexperience. These events generate a real phobia in the young patient, leading to a refusal of dental care and a tendency to reject any figure in the medical field, sometimes requiring pharmacological pretreatments as the only viable approach (11-15).

Having defined the theoretical concepts of interceptive orthognathodontic expansive treatment, resulting from more than a century of research, it is necessary to translate these considerations into orthognathodontic clinical practice. Such practice developed with the first interceptive orthognathodontic treatment of transversal skeletal maxillary expansion dating back to 1860 from an idea by Emerson C. Angel (16) through a prototype largely dependent on patient cooperation and operator skills. It was refined through Andrew J. Haas's work in 1961 (17), transforming the prototype into a Rapid Maxillary Expander (RME). It required almost a hundred years due to diverging opinions throughout the first half of the 20th century. Substantial modifications were not conceived until the end of the last century, despite the increasingly evident dependence of interceptive orthognathodontic treatment on patient cooperation, requiring frequent checks by the dental professional.

Since the 2000s, new ideas have emerged, among which tripartite expansion for fixed appliances, both transversally and sagittally, is perhaps the most interesting. However, this approach, realized through the welding of three steel screws expandable in three directions, entails complications in the treatment process, making its efficiency completely dependent on the dentist and the paediatric patient (17-19). In 2013, continuous technological progress and research produced a new clinically effective expander independent of patient cooperation, at least in terms of transversal expansion. This device, named the Leaf Expander (LE), was developed as a reactivatable expander equipped with a one-way steel screw combined with a Ni-Ti MEMORIA® crossbow spring. It allows for the expansion of the maxilla, predominantly through dentoalveolar remodeling, automatically without needing paediatric patient cooperation (20). The Leaf Expander (LE) has become the main expander in contemporary orthognathodontic clinical practice for treating transversal deficits, thanks to its high efficacy in the absence of cooperation, essentially making the therapy automatic. Building on the proven efficiency of the results found in the literature for this treatment protocol, the authors propose the use of the one-way steel screw combined with the Ni-Ti MEMORIA® crossbow spring in all three directions, automating the expansion both transversally and sagittally.

In this paper, a new device is presented through a pilot clinical case. This device emerges from the authors' desire to automate every scenario requiring expansive orthognathodontic treatment, both transversal and sagittal, simplifying the process of achieving high clinical efficacy without dependence on patient cooperation, excluding self-harm. This

appliance can be easily combined with any auxiliary third-class extra-oral orthopaedic traction, just like any Rapid Maxillary Expander (RME) or Leaf Expander (LE).

MATERIALS AND METHODS

Patients' case preparation involves traditional hygienic and health standards, conducting the initial visit, followed by the collection of initial photographic documentation, analogic and digital occlusal documentation, and radiographic exams (orthopantomography, lateral and postero-anterior teleradiographs). Subsequent digital measurements of the mandibular inter-canine distance (starting from the cusp apex) and inter-molar distance (starting from the buccal intercuspidal groove) are registered, combined with the digital measurement of the maxillary inter-incisive distance (starting from the distal margin of the lateral incisors) and inter-molar distance (starting from the palatal side of the mesiovestibular cusp), and are followed by the execution of a pre-treatment diagnostic cephalometry and a prognostic cephalometry according to a hypothetical post-treatment condition.

Data collection and processing allow for precise planning regarding dentoskeletal expansion needs in the sagittal and transversal directions, thereby drafting the fundamental diagnosis for an interceptive orthognathodontic treatment. Initially, authors adopted this prototype appliance on paediatric patients suffering from Class III malocclusions characterized simultaneously by bilateral crossbite and reverse bite. Subsequently, having observed good results, it was decided to expand the case studies to paediatric patients still suffering from Class III malocclusions but with unilateral crossbite and without reverse bite, treating 38 patients with this new orthognathodontic appliance.

This device consists of three one-way steel screws combined with a Ni-Ti MEMORIA® crossbow spring welded together: two are placed posteriorly in the transversal direction, and one is located anteriorly in the sagittal direction. For paediatric patients in the early age, two transversal screws of 450g each with an expansion capacity of 6mm are used, as they are associated with the possible compression of the nickel-titanium crossbow spring via the steel screw, and one sagittal screw with a force of 900g, also with an expansion capacity of 6mm. For paediatric patients in the prepuberal age, a force of 900g in all three directions with an expansion capacity of 6mm was chosen. The two posterior screws, welded together, are anchored distally to two steel bands placed on the first molars.

Palatally, expansion arms are welded to the same bands, while buccally, arms with hooks for potential third-class extraoral orthopaedic traction are attached. Finally, the anterior sagittal screw, welded to the two posterior ones, rests mesially on the palatal side of the incisors through a steel trapezoidal-like structure (Fig.1).

Fig. 1. *Construction of the new appliance.*

Therefore, based on the case studies conducted on the selected patients and the development of the new orthognathodontic appliance, a procedural protocol was planned, which includes:

- placement of the appliance (Time 0);
- first check after three weeks to verify the expansive efficiency of the Ni-Ti crossbow springs (Time 20 days);
- second check after one and a half months to assess the dentoskeletal expansive results achieved (Time 45 days);

- third check after three months to verify the result's stability, to observe the neuromuscular occlusal readjustment to the result, and to deliver the third-class extraoral traction associated with a reactivation of the expansion screws through the contraction of the Ni-Ti crossbow springs by 1mm (Time 90 days);
- fourth check after an additional three months to verify the efficiency of the third-class extraoral traction associated with a further reactivation of the expansion screws through the contraction of the Ni-Ti crossbow springs by another 1mm (Time 180 days);
- fifth check after another three months to assess the achieved result and subsequent removal of the appliance, followed by the creation of a rigid third-class myofunctional retention (Time 270 days).

RESULTS

Pilot case and case study

A 9-year-old paediatric patient characterized by prepubertal somatic, skeletal Class III malocclusion, dental Class III malocclusion, normodivergence, medium dentoalveolar discrepancy, mild hypomaxillia, medium hypermandibulia, bilateral crossbite, reverse bite, endoinclination of incisors, horizontal interincisal distance (-1.5mm), vertical interincisal distance (1mm), rectangular palate, concave profile, upper lip distance (1mm), lower lip distance (2mm), normal hourly growth, and phoniatric anomaly with mild sigmatism was enrolled (Fig. 2-12).

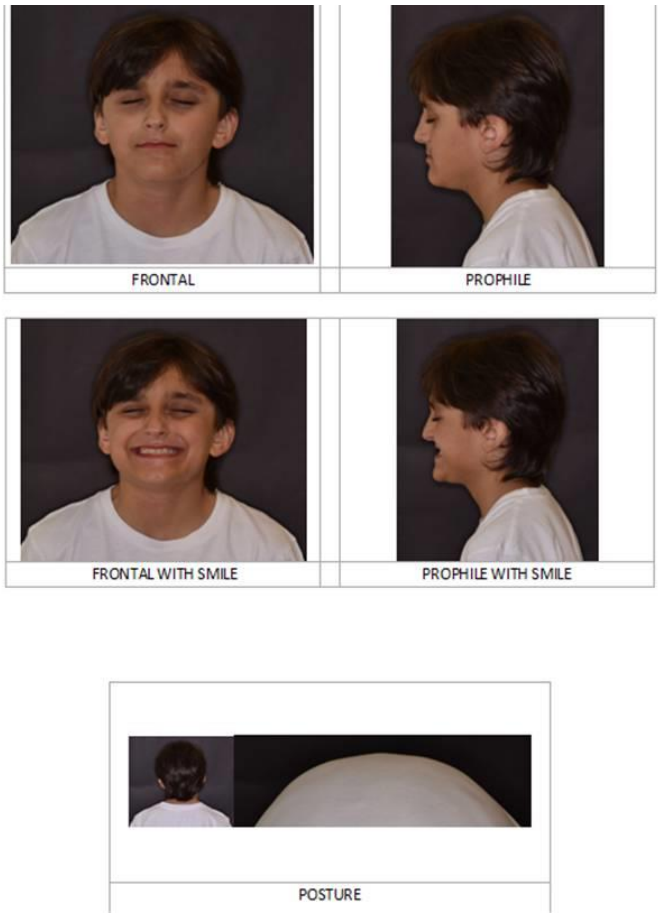


Fig. 2. *Extraoral photos.*

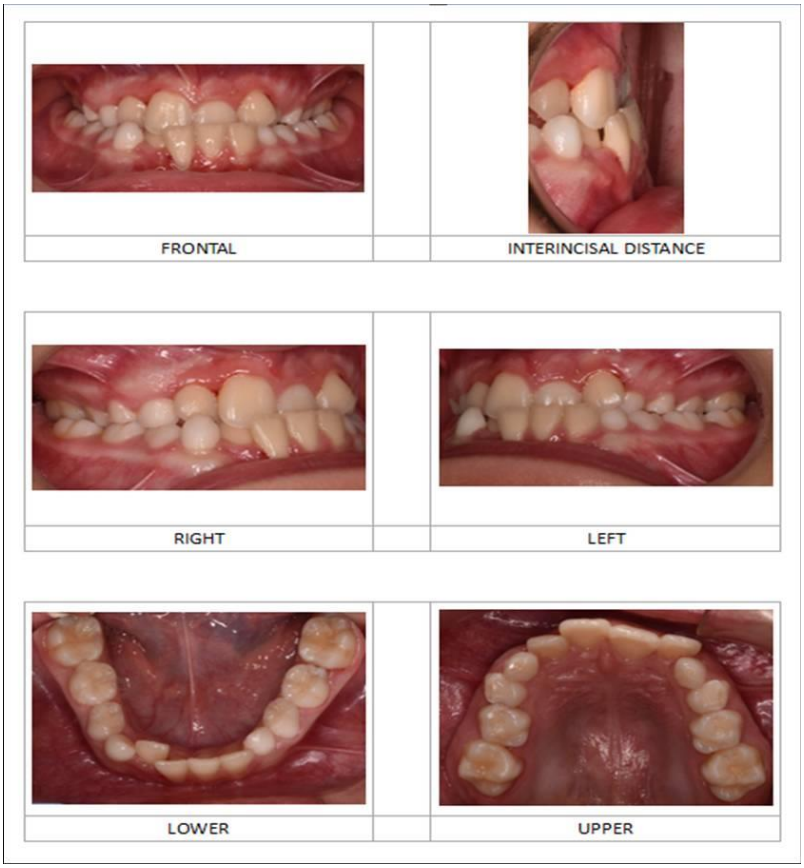
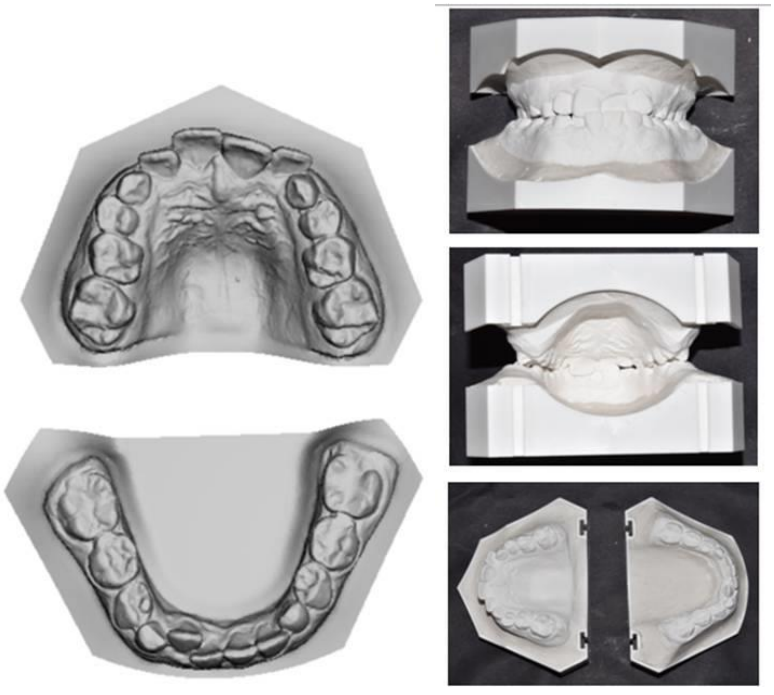


Fig. 3. *Intraoral photos.*



a. b.

Fig. 4. ***A****): digital models* ***B****): analog models.*

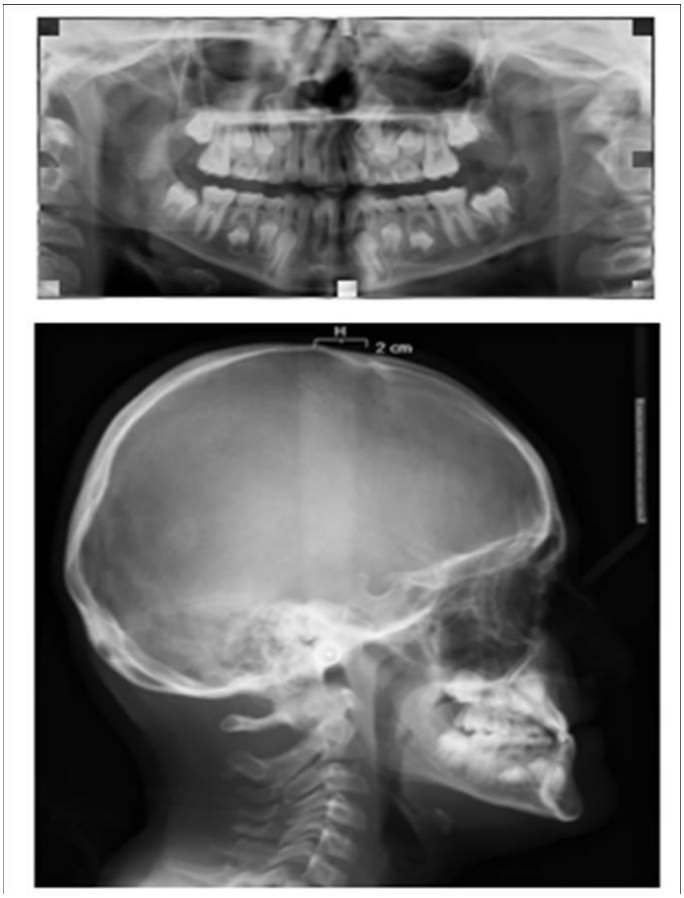


Fig. 5. *Orthopantomography and lateral teleradiograph.*

Sigla	Descrizione	Misura	U.M.	Normale	D.S.Sup.	D.S.Inf.	Int. di Tolleranza	Discrepanza	Valutazione
SNA	S-N-A	84,58	°	82,00	2,00	2,00	[80.00, 84.00]	+0,58	Protrusione del mascellare superiore
SNB	S-N-B	86,48	°	80,00	2,00	2,00	[78.00, 82.00]	+4,48	Prognazia o protrusione della mand.
ANB	A-N-B	-1,90		2,00	2,00	2,00	[0.00, 4.00]	-1,90	III classe scheletrica
CM	S-N ^ Gog-Me	26,40	°	32,00	3,00	3,00	[29.00, 35.00]	-2,60	soggetto ipodivergente
AJ	Sna-Snp ^ Gog-Me	24,03	°	26,00	1,00	1,00	[25.00, 27.00]	-0,97	angolo ipodivergente
OM	p.Occl ^ Gog-Me	15,56	°	16,00	1,00	0,00	[16.00, 17.00]	-0,44	angolo ipodivergente
II	Inc.sup. ^ Inc.inf	137,69	°	131,00	5,00	5,00	[126.00, 136.00]	+1,69	Endoinclinazione incisivi
SIS	Sna-Snp ^ Inc.sup.	113,81	°	109,00	5,00	5,00	[104.00, 114.00]		Normoinclinazione incisivi sup.
MII	Gog-Me ^ Inc.inf	84,48	°	90,00	5,00	5,00	[85.00, 95.00]	-0,52	Endoinclinazione incisivi inf.
GI	Gog-Me ^ Gog-N	69,84	°	73,00	2,00	2,00	[71.00, 75.00]	-1,16	tendenza anterotazione mand.
GS	Gog-N ^ Gog-Pc	55,42	°	53,00	2,00	2,00	[51.00, 55.00]	+0,42	tendenza anterotazione mand.
GO	Gog-Me ^ Gog-Pc	125,25	°	126,00	4,00	4,00	[122.00, 130.00]		tendenza normorotazione mand.
SGNC	S-Gn ^ S-N (asse Y)	59,40	°	67,00	1,00	1,00	[66.00, 68.00]	-6,60	crescita mand. preval. antero-post.
NBH	N-B ^ Ls-PgC (linea H)	174,77	°	8,00	1,00	1,00	[7.00, 9.00]	+165,77	profilo convesso
APgIi	A-Pg - Inc.inf	0,57	mm	1,00	2,00	2,00	[-1.00, 3.00]		normoposizione incisivi inf.
OB	Overbite	0,92		2,00	2,00	2,00	[0.00, 4.00]		morso coperto
OJ	Overjet	-1,39		2,00	2,00	2,00	[0.00, 4.00]	-1,39	III classe incisiva
SN	S - N	58,97	mm						
GogMe	Gog - Me	65,44	mm	57,22	0,00	0,00	[57.22, 57.22]	+8,22	
r1	(S-Gog) / (N-Me)	68,86	%	62,00	3,00	3,00	[59.00, 65.00]	+3,86	
SLS	Stiramento Ls	-11,05							
W	Indice di WITS	-5,16		0,00	2,00	2,00	[-2.00, 2.00]	-3,16	III classe scheletrica

Fig. 6 A1. *Pre-treatment cephalometric data and hypothetical post-treatment.*

Sigla	Descrizione	Misura	U.M.	Normale	D.S.Sup.	D.S.Inf.	Int. di Tolleranza	Discrepanza	Valutazione
SNA	S-N-A	88,71	°	82,00	2,00	2,00	[80.00,84.00]	+4,71	Protrusione del mascellare superiore
SNB	S-N-B	86,48	°	80,00	2,00	2,00	[78.00,82.00]	+4,48	Prognazia o protrusione della mand.
ANB	A-N-B	2,23		2,00	2,00	2,00	[0.00,4.00]		I classe scheletrica
CM	S-N ^ Gog-Me	26,40	°	32,00	3,00	3,00	[29.00,35.00]	-2,60	soggetto ipodivergente
AJ	Sna-Snp ^ Gog-Me	23,76	°	26,00	1,00	1,00	[25.00,27.00]	-1,24	angolo ipodivergente
OM	p.Occl ^ Gog-Me	15,56	°	16,00	1,00	0,00	[16.00,17.00]	-0,44	angolo ipodivergente
II	Inc.sup. ^ Inc.inf	137,69	°	131,00	5,00	5,00	[126.00,136.00]	+1,69	Endoinclinazione incisivi
SIS	Sna-Snp ^ Inc.sup.	114,07	°	109,00	5,00	5,00	[104.00,114.00]	+0,07	Esoinclinazione incisivi sup.
MII	Gog-Me ^ Inc.inf	84,48	°	90,00	5,00	5,00	[85.00,95.00]	-0,52	Endoinclinazione incisivi inf.
GI	Gog-Me ^ Gog-N	69,84	°	73,00	2,00	2,00	[71.00,75.00]	-1,16	tendenza anterotazione mand.
GS	Gog-N ^ Gog-Pc	55,42	°	53,00	2,00	2,00	[51.00,55.00]	+0,42	tendenza anterotazione mand.
GO	Gog-Me ^ Gog-Pc	125,25	°	126,00	4,00	4,00	[122.00,130.00]		tendenza normorotazione mand.
SGNC	S-Gn ^ S-N (asse Y)	59,40	°	67,00	1,00	1,00	[66.00,68.00]	-6,60	crescita mand. preval. antero-post.
NBH	N-B ^ Ls-PgC (linea H)	177,42	°	8,00	1,00	1,00	[7.00,9.00]	+168,42	profilo convesso
APgIi	A-Pg - Inc.inf	-0,93	mm	1,00	2,00	2,00	[-1.00,3.00]		normoposizione incisivi inf.
OB	Overbite	1,22		2,00	2,00	2,00	[0.00,4.00]		morso coperto
OJ	Overjet	3,94		2,00	2,00	2,00	[0.00,4.00]		I classe incisiva
SN	S - N	58,97	mm						
GogMe	Gog - Me	65,44	mm	57,22	0,00	0,00	[57.22,57.22]	+8,22	
r1	(S-Gog) / (N-Me)	68,86	%	62,00	3,00	3,00	[59.00,65.00]	+3,86	
SLS	Stiramento Ls	-6,32							
W	Indice di WITS	-1,89		0,00	2,00	2,00	[-2.00,2.00]		I classe scheletrica

Fig. 6 A2. *Pre-treatment cephalometries and hypothetical post-treatment.*

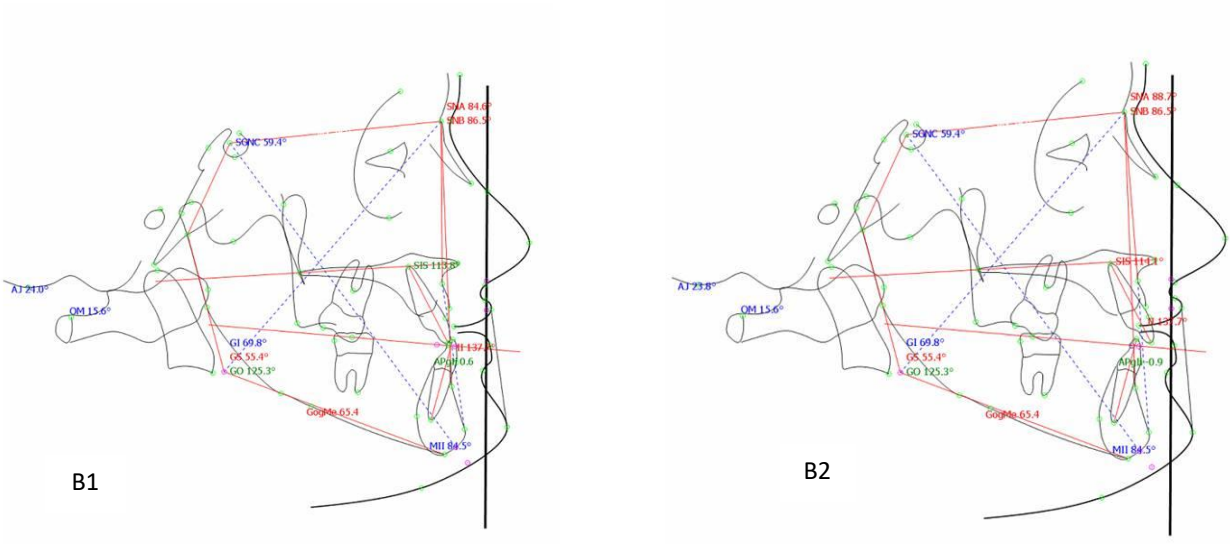


Fig. 6. B1, B2. *Pre-treatment cephalometries and hypothetical post-treatment*

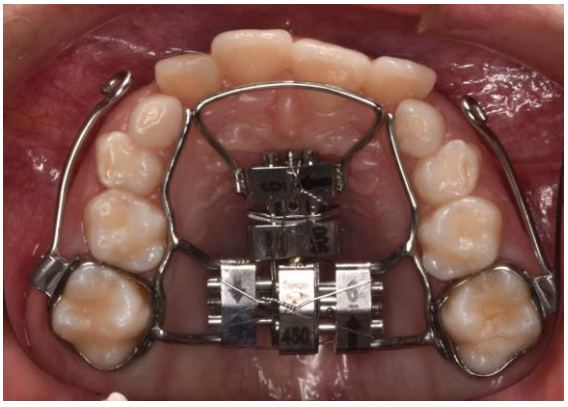


Fig. 7. *Time 0 with appliance.*

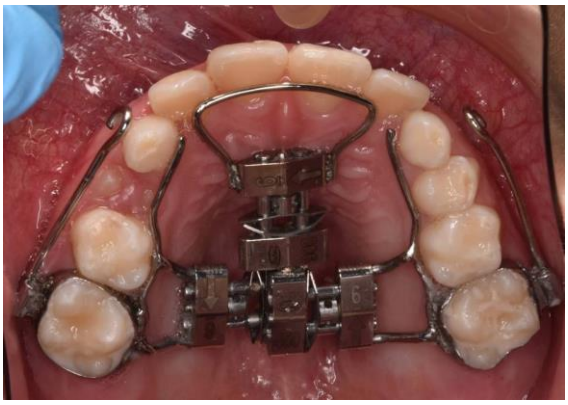


Fig. 8. *Time 45 days.*

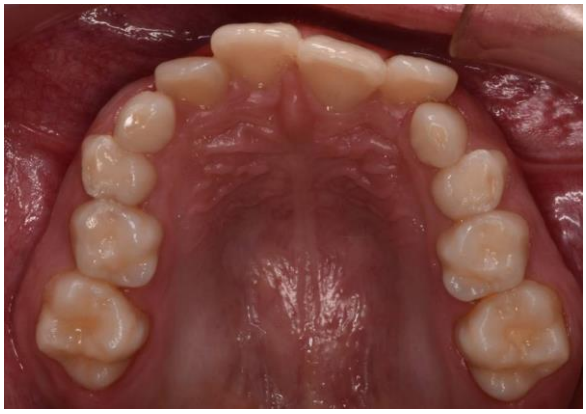


Fig. 9. *Time 0 without appliance.*

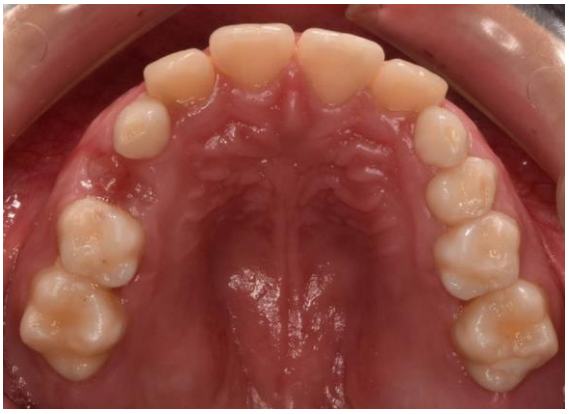


Fig. 10. *Time 90 days with no appliance.*

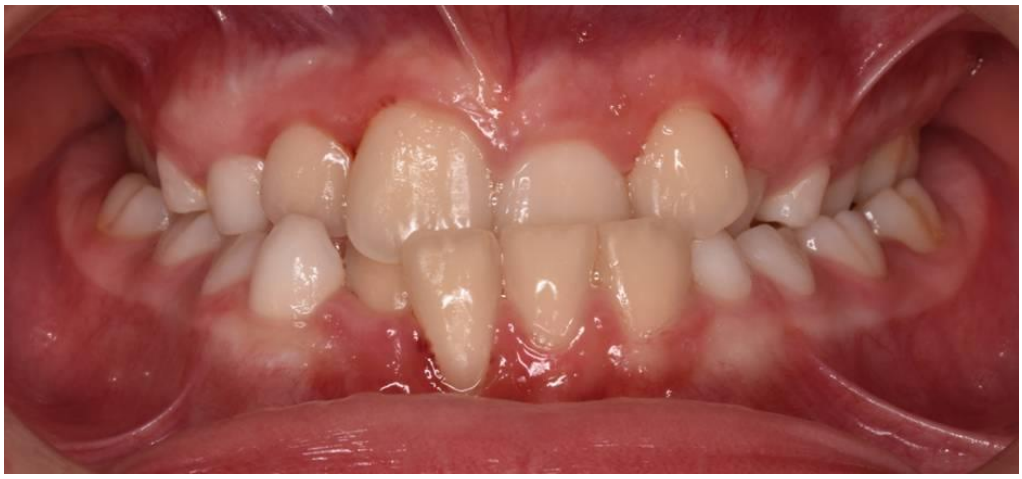


Fig. 11. *Time 0 reverse bite and bilateral crossbite.*

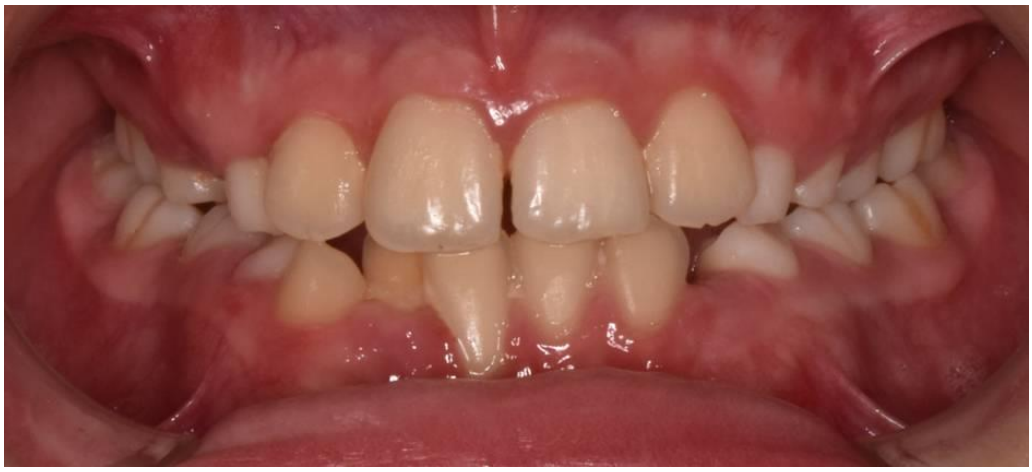


Fig. 12. *Time 90 days resolution of reverse bite and bilateral crossbite.*

DISCUSSION

Based on the achieved results, it is possible to highlight the extreme simplicity of such treatment compared to contemporary treatments with appliances consisting of non-automatic three-way steel screws, which are completely dependent on the collaboration between the doctor and the paediatric patient (16-18).

From the assembly of the appliance, nothing needs to be done by either the dentist or the parents during the first three months, as the treatment is efficiently automated. Thus, excluding self-harm, no patient cooperation is required. However, for the subsequent auxiliary third-class extraoral orthopaedic traction during the following semester, the new device encounters typical issues related to wear, patient oral hygiene, and patient cooperation. Therefore, while reiterating the extreme simplicity of treatment execution at least in the first three months and being aware of possible unforeseen issues during the subsequent semester, it is suggested to provide precise post-orthognathodontic instructions upon delivery of the appliance (for instance, avoiding hard foods to protect the Ni-Ti crossbow springs). At the end of the first three months, it is advised to disassemble and reassemble the appliance to check its integrity.

During the following semester, more frequent checks are recommended should any of the aforementioned issues arise (for example, poor patient cooperation in using extraoral elastic bands). Finally, it is recommended to construct the appliance directly with three welded one-way steel screws combined with a Ni-Ti MEMORIA® crossbow spring with a force of 900g and an expansion capacity of 6mm, both for paediatric patients in the early somatic stage and the pre-pubertal somatic stage, as the greater resistance of these screws guarantees higher efficiency to the appliance (21).

Additionally, the ability to fabricate increasingly personalized appliances by exploiting digital technology and making them more stable through absolute skeletal anchorage can further enhance their effectiveness and efficiency in the future.

CONCLUSIONS

Following a pragmatic clinical logic, just as the Leaf Expander (LE) revolutionized transversal maxillary orthognathodontics in 2013 by substantially automating it, the newly presented device aims to be its evolution. It completes the capacity for automatic transversal expansion with an automatic sagittal expansion, with the goal of becoming the appliance of choice for patients suffering from Class III malocclusion associated with the simultaneous presence of mono or bilateral crossbite and reverse bite.

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Review

HYALURONIC ACID INJECTIONS FOR TENNIS ELBOW: A SYSTEMATIC REVIEW

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ABSTRACT

Tennis elbow is a tendinopathy of the lateral elbow that causes pain and functional limitation. This systematic review investigates the effects of hyaluronic acid injections for treating tennis elbow. A systematic search of scientific electronic databases (CENTRAL, EMBASE, MEDLINE, PEDro, Web of Science, Scopus, PubMed, and CINAHL) was performed up to October 2023 with no restrictions of time and language. This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Inclusion criteria were articles that reported clinical outcomes about the use of hyaluronic acid for tennis elbow alone or in comparison with other injectable drugs. Outcome measures were the Visual Analogue Scale, handgrip strength, and the Quick-Disabilities of the Arm, Shoulder, and Hand score. Two independent authors performed the search and evaluated the articles. The inter-rater reliability in the quality assessment was evaluated using Cohen's kappa coefficient. The Modified Coleman Methodology Score was used to evaluate the methodological quality of the articles included in this systematic review. A total of seven articles were included with the overall quality of the included articles being evaluated as fair. Despite using different kinds of hyaluronic acid and injection protocols, and different scores applied, each included study showed clinically relevant improvements. Hyaluronic acid injections resulted in being superior to placebo but inferior in the short-term compared to other injections. Given the high heterogeneity of the included studies, we cannot conclude which kind of hyaluronic acid and injection protocol is the best for treating tennis elbow. Hyaluronic acid injections for treating tennis elbow seem safe and effective in reducing pain, improving function, and allowing a faster return to pain-free sports activities especially in the long term. High-quality and prospective long-term follow-up studies are needed to confirm the articles' outcomes in this systematic review.

KEYWORDS: *tennis elbow, TE, lateral epicondylitis, epicondylitis, hyaluronic acid, HA, injections*

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INTRODUCTION

Tennis elbow (TE), also defined as lateral elbow tendinopathy (1, 2), is a widespread painful and non-inflammatory condition that affects the tendon insertion or myotendinous junction of wrist muscle extensors (3). It causes subacute and chronic symptoms of pain at the lateral epicondyle and elbow disability and sometimes of the entire upper limb (4, 5).

TE occurs in a range of 1% and 3% of the general population and typically affects subjects between 30 and 60 years without gender difference (3). TE is usually considered a self-limiting condition, with most patients recovering in 6–24 months (6), even if symptom recurrence persists for many years in approximately 20% of cases (4, 7). Despite the classic relationship to the practice of tennis, only 5% to 10% of total cases of this disease affect practitioners of this sport (8), especially those who practice tennis at an amateur level, who often practice tennis without athletic and technical preparation, or with inadequate sports equipment (9).

The main clinical manifestation of TE is hyperalgesia during elbow active range of motion and during palpation of the lateral epicondyle area, which is exacerbated by prono-supination of the forearm (10). Specific tests for TE, such as Cozen's and Mill's tests, are also usually performed to reproduce the pain experienced by the patient (11).
Moreover, patients affected by TE complain of painful handgrip with consequent functional limitation, disability in activities of daily living, time lost at work, and poor quality of life (12, 13). Ultrasound (US) evaluation and, eventually, magnetic resonance imaging (MRI) are usually performed as an adjunct to the physical examination (14-16).

Different conservative treatments have been proposed for TE, such as pharmacological therapy, systemic and/or local treatments (corticosteroid injections, botulinum toxin, hyaluronic acid, autologous blood, and platelet-rich plasma) (4, 17, 18), manual therapy (19-21), therapeutic exercise (22), physical modalities (such as laser therapy) (23, 24), elbow braces, dry needling (25), acupuncture, and watchful waiting (12). Surgery is usually recommended for those patients with persistent pain and disability after a course of conservative therapy (26, 27). However, no consensus about the best treatment for improving pain and function in people with TE has been reached (5). Among conservative treatments, injection therapy is widely used for the treatment of patients with TE (28-30), with hyaluronic acid (HA) peritendinous injections representing an emerging treatment option that, anyway, lacks strong evidence to support its use.

HA was shown to regulate the tendinopathic tissue repair process through several pathways modulating the main phases of tendon healing (i.e., inflammation, cellular migration, and angiogenesis) (31-36). All these properties supported HA as a conservative treatment for tendinopathies (29, 34, 37-40).

Several studies evaluated the effects of peritendinous injections of HA for TE (41-44), showing promising results in pain control and functional improvement (5).

The aim of the present study was to systematically review the effects of HA injections for treating TE in athletic and non-athletic populations, alone or in combination with other management modalities, in short- and mid-term follow-up, and comparison, with other kinds of injections. We hypothesized that HA injections may improve clinical and functional conditions in patients affected by TE.

METHODS

Study design

The present systematic review and related procedures were organized and conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (45-47). The PRISMA flow chart can be retrieved in Fig. 1, while the PRISMA checklist can be retrieved from Appendix A. The research protocol has been registered in the International Prospective Register of Systematic Reviews (PROSPERO), registration number CRD42023457108.

Eligibility criteria

This review included randomized clinical trials, prospective studies, and case-series studies, with at least a 4-week follow-up. Articles such as editorials, technical notes, letters to authors, narrative reviews, systematic reviews, case reports, and animal or cadaveric studies that did not report clinical outcomes about the use of HA for TE were excluded.

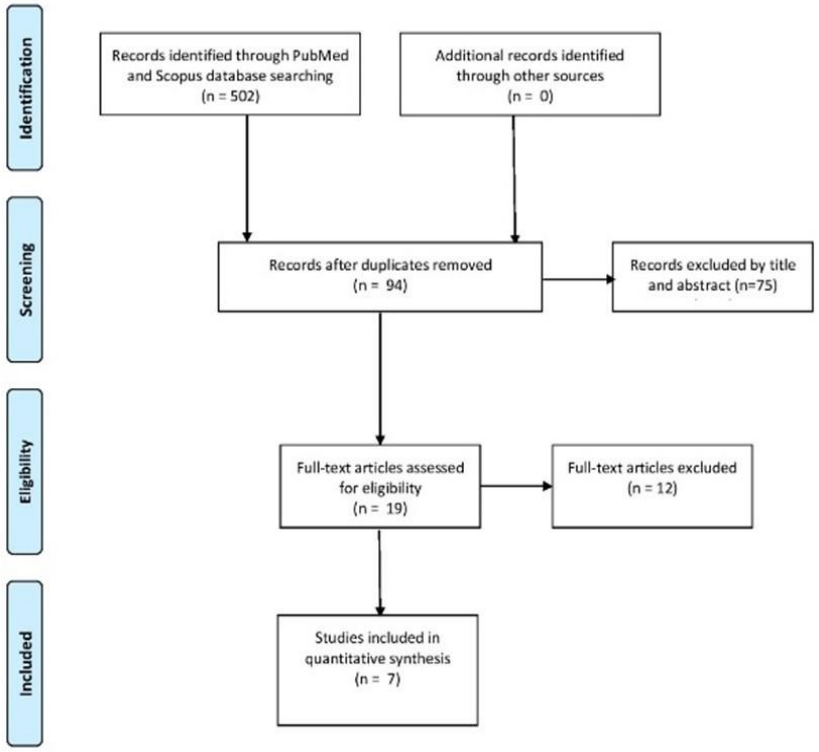

Fig. 1. *PRISMA flowchart.*

Information sources

Potential studies were identified by searching electronic databases, including Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE, MEDLINE, PEDro, Web of Science, Scopus, PubMed, and CINAHL. A systematic search of all databases was performed from their inception to September 2023, with no language limitations. Reference lists of relevant studies were also screened for additional possible studies.

Search strategy

The strategy had two components, including terms for HA and TE. Keywords for the population were "Tennis Elbow" [MeSH] OR "Elbow Tendinopathy" [MeSH] OR lateral epicondyle*[all fields] OR epicondylitis*[all fields]; keywords for the intervention were "Hyaluronic acid" [MeSH] OR sodium hyaluronate [all fields] OR hyaluronan [all fields].

Types of participants

This study included participants diagnosed with TE, defined as pain during palpation of the lateral epicondyle area exacerbated by prono-supination of the forearm or gripping and with or without confirmatory hypoechoic lesions on ultrasonography (48).

Types of interventions

For inclusion, HA had to be administered to at least one group in the RCTs. Studies in which the effects of HA alone could not be evaluated (such as a mixture of HA and another drug compared with HA alone or another drug) would not be included.

Types of comparison controls

Comparison groups were classified into active and inactive controls according to the Cochrane Handbook for Systematic Reviews of Interventions (49). Inactive control was defined as no treatment, standard care, or waiting list control, including watchful waiting, bracing, and usual care (50). Active control was defined as using different injection solutions such as corticosteroids (CS) (51), platelet-rich plasma injection 18, dextrose prolotherapy (DPT) (50, 52), and normal saline (53).

Outcome measures

The primary outcome of interest was pain reduction measured with the Visual Analogue Scale (VAS, 0-10). Secondary outcomes included the handgrip strength in kilograms and the Quick-Disabilities of the Arm, Shoulder, and Hand (Q-DASH) scores (where available). Other scores were evaluated case-by-case depending on the ones used in the included studies. The outcomes were evaluated at baseline, and final follow-up for each included study.

Study selection and data extraction

Two independent authors (D.T. and R.A.) performed the search and evaluated the articles. Experienced researchers in systematic reviews (D.T., R.P., F.S., B.C., C.R., R.A.) solved cases of doubt. Initially, investigators read article abstracts, selected the relevant ones according to inclusion and exclusion criteria, and then compared results with the other investigators. After two weeks, the same studies were read again to confirm the agreement. No disagreement was observed among the investigators.

One investigator (R.A.) extracted the data from the full-text articles to Excel (Microsoft, USA) spreadsheet structured tables to analyze each study in a descriptive fashion. The number of sample sizes, type of management, and HA used time of follow-up, clinical and functional outcome before and after treatment, adverse events, and complications were extracted from the retrieved articles and collected in Table I.

Table I. *A summary of the outcomes of the selected studies.*

Study name	Type of study	N. patient	Follow-up	Groups	HA used	Intervention	Scores at baseline	Scores at last follow-up	Adverse events
Apaydin et al. (2020)	RCT	32	6 and 12 weeks	HA (*n*=16) vs DPT (*n*=16)	30 mg/2 mL 1500 kDa	Single injection at baseline	**HA group** **VAS (rest):** 5.19 ± 1.1 **VAS (activity):** 7.25 ± 0.8 **VAS (night):** 6.08 ± 1.4 **Q-DASH:** 53.1 ± 12.5 **Grip strength:** 18.13 ± 8.6 **DPT group** **VAS (rest):** 4.94 ± 2.0 **VAS (activity):** 7.00 ± 1.5 **VAS (night):** 6.31 ± 2.3 **Q-DASH:** 53.2 ± 18.7 **Grip strength:** 19.87 ± 9.0	**HA group** **VAS (rest):** 2.44 ± 1.7** **VAS (activity):** 4.06 ± 2.3** **VAS (night):** 2.75 ± 2.0** **Q-DASH:** 24.7 ± 10.1** **Grip strength:** 22.94 ± 8.5** **DPT group** **VAS (rest):** 1.06 ± 0.8*,** **VAS (activity):** 2.19 ± 0.8*,** **VAS (night):** 1.19 ± 0.7*,** **Q-DASH:** 9.7 ± 6.4*,** **Grip strength:** 27.19 ± 9.6**	Injection site pain lasting 1-2 days (3 patients in the HA group, 4 patients in the DPT group)
							Significant improvement at last follow-up; DPT was favoured over HA for improvements for pain with activity, pain at night, and pain at rest. Q-DASH scores improved significantly more in the DPT group.		

Fogli et al. (2017)	PRS	26	1, 2, 8 weeks	HA (*n*=26)	20 mg/2 mL 500-730 kDa	3 injections (one a week for 3 weeks in a row)	**HA group** **VAS:** 8.19 ± 0.79	**HA group** **VAS:** 1.74 ± 2.17**	No complications
							Significant pain relief and reduction in tendon thickness and neovascularization in US evaluations at each follow-up.		
Petrella et al. (2010)	RCT	331	1, 2, 4, 12, 52 weeks	HA (*n*=165) vs placebo (*n*=166)	1% HA/1.2 cc	2 injections (one at baseline and one after one week)	**HA group** **VAS (rest):** 8.5 ± 11.1 **VAS (grip):** 9.8 ± 1.1 **PGS:** 0.3 ± 1.1 **PANF:** 1.1 ± 2.1 **PGA:** 1.1 ± 1.0 **Grip strength:** 49.2 ± 1.1 **Placebo (saline) group** **VAS (rest):** 8.4 ± 1.6 **VAS (grip):** 9.6 ± 0.4 **PGS:** 0.4 ± 1.1 **PANF:** 1.7 ± 2.2 **PGA:** 0.9 ± 1.2 **Grip strength:** 47.9 ± 0.4	**HA group** **VAS (rest):** 2.4 ± 1.4** **VAS (grip):** 2.9 ± 1.4** **PGS:** 4.8 ± 0.9** **PANF:** 4.6 ± 0.3** **PGA:** 4.7 ± 0.5** **Grip strength:** 65.7 ± 1.8** **Placebo (saline) group** **VAS (rest):** 7.7 ± 1.3*,** **VAS (grip):** 9.1 ± 1.1*,** **PGS:** 1.1 ± 1.8*,** **PANF:** 0.9 ± 1.9*,** **PGA:** 1.3 ± 0.7*,** **Grip strength:** 45.6 ± 1.3*,**	Pain during injection (3 patients in the HA group, 5 patients in the placebo group)
							Significant improvements in VAS and grip strength at each follow-up in the HA group. Statistically significant improvement in PGS, PANF and PGA were observed in the HA group.		
Stirma et al. (2020)	CSE	12	4 and 12 weeks	HA (*n*=12)	12 mg/1.2 mL	2 injections (one at baseline and one after one week)	**HA group** **VAS (rest):** 5.9 ± 2.6 **VAS (active):** 8.1 ± 1.6 **MEPS:** 61.3 ± 15.5 **Cozen's test:** 12 positives **Mill's test:** 12 positives	**HA group** **VAS (rest):** 2.1 ± 3.3** **VAS (active):** 3.6 ± 4.0** **MEPS:** 85.0 ± 21.2** **Cozen's test:** 5 positives **Mill's test:** 5 positives	No complications
							Significant improvement in VAS and MEPS at final follow-up.		
Khan et al. (2018)	CSE	45	4 weeks	HA (*n*=45)	1% HA/1 cc	2 injections (one at baseline and one after one week)	**HA group** **VAS:** 8.73 ± 1.07	**HA group** **VAS:** 6.42 ± 1.06**	Not reported
							Significant improvement in VAS at follow-up.		
Yalcin et al. (2022)	RCT	80	6 and 12 weeks	HA (*n*=40) vs CS (*n*=40)	30 mg/2 mL 2000 kDa	Single injection at baseline	**HA group** **VAS (rest):** 6.34 ± 0.73 **VAS (grip):** 7.2 ± 0.81 **Q-DASH:** 54.61 ± 8.11 **Grip strength:** 19.95 ± 4.46 **CS group** **VAS (rest):** 6.39 ± 0.8 **VAS (grip):** 7.54 ± 0.99 **Q-DASH:** 59.27 ± 9.03 **Grip strength:** 21.25 ± 3.43	**HA group** **VAS (rest):** 3.88±1 **VAS (grip):** 4.22±1.1 **Q-DASH:** 38.36±7.39 **Grip strength:** 37.1±2.54 **CS group** **VAS (rest):** 4.07±1.08 **VAS (grip):** 4.41±0.97 **Q-DASH:** 43.22±10.34 **Grip strength:** 38.82±3	Not reported
							Significant improvements in VAS, Q-DASH and grip strength were found in both group at six but not at 12 weeks, with changes being more prominent in the CS group. Within group comparison could not be performed due to the lack of data from the original article.		

Zinger et al. (2022)	PRS	18	12, 24, 52 weeks	HA (*n*=18)	16 mg/2 cc 800–1200 kDa	3 injections (one every two weeks)	**HA group** **VAS (rest):** 7.64 ± 1.21 **Q-DASH:** 53.7 ± 18.9 **PRTEE:** 67.0 ± 14.6	**HA group** **VAS (rest):** 1.43 ± 1.19** **Q-DASH:** 22.5 ± 17.1** **PRTEE:** 28.1 ± 15.8**	No complications
							Significant improvement in VAS, Q-DAH and PRTEE at final follow-up.		

P<0.05 (between groups**), **P<0.05 (**within group**). **HA**=hyaluronic acid; **DPT**=dextrose prolotherapy; **VAS**=visual analogue scale; **Q-DASH**=Quick-Disabilities of the Arm, Shoulder, and Hand (score between 0 and 100, with higher scores reflecting greater disability); **US**=ultrasound; **PGS**= patient global satisfaction using a 5 point categorical scale (0 = not satisfied, 5 = fully satisfied); **PANF**= patient assessment of normal function using a 5 point categorical scale (0 = no return to normal function, 5 = full return to normal function); **PGA**= physician's global assessment of elbow injury using a 5 point categorical scale (0 = poor patient elbow function and poor pain management, 5 = normal patient elbow function and normal pain management); **MEPS**=Mayo Elbow Performance Score (ranges from 0 to 100 with higher values indicating better results); **CS**= corticosteroid; **PRTEE**= Patient-Rated Tennis Elbow Evaluation (ranges from 0 meaning no pain and maximum function to 100 meaning maximum pain and minimum function); **RCT**=randomized clinical trial; **PRS**=prospective study; **CSE**=case series study.*

A second investigator (D.T.) independently double-checked the primary data extraction from all the articles. Doubts and inconsistencies were grouped and solved. All the authors participated in the drafting of the text.

All results compatible with each outcome domain in each study were sought. A *p*-value <0.05 was considered statistically significant. *P*-values are presented in Table I for a comparison of progression from baseline to the last follow-up within groups and a comparison of the between-group effects from baseline to the last follow-up.

The level of evidence analysis was determined using the Oxford Centre for Evidence-Based Medicine Levels of Evidence (54).

Quality assessment

The Modified Coleman Methodology Score (MCMS) was used to evaluate the methodological quality of the articles included in this systematic review (55). MCMS was used to assess the quality of the articles found in the present study, assessing methodology with 10 criteria, with a total score between 0 and 100 (which indicates that the study largely avoids chance, various biases, and confounding factors). Final score was categorized as excellent (85-100 points), good (70-84 points), fair (55-69 points), and poor (<55 points).

The MCMS criteria were modified to make them reproducible and relevant to the present systematic review. For example, we replaced the "description of surgical technique" criterion with "description of injection technique." Appendix B (56) reports more details about the MCMS (such as the definition for each criterion, the scoring system, etc.).

Two authors (D.T. and R.A.) independently applied the MCMS, and a final score was reached by consensus. The MCMS is calculated using ten different criteria (study size, follow-up, number of procedures, type of study, diagnostic certainty, description of the injection technique, rehabilitation and compliance, outcome criteria, outcome assessment, and selection process), with a maximum total possible score of 100 (55). Then, the agreement in the quality assessment between the two reviewers was evaluated using Cohen's kappa coefficient.

RESULTS

Eligible studies

After the initial literature search, 502 potentially relevant citations were retrieved. After the removal of duplicate records, 94 articles were identified. Then, following a first evaluation of titles and abstracts, 75 articles were not included since they did not investigate outcomes in the use of HA for TE. Finally, after further screening, other 12 articles were excluded as they did not conform to inclusion criteria, and a total of seven articles were included in the present systematic review (Fig. 1). Among the 12 excluded studies, one had only 1-week follow-up, so its outcomes could not be considered as reliable. Three articles were excluded because they combined HA with other drugs (such as chondroitin sulfate or CS) or physical therapy (such as laser therapy).

Quality of the included studies

The inter-rater (R.A. and D.T.) reliability in the quality assessment, evaluated using Cohen's K coefficient, was optimal (0.9). The raters were blinded to the other reviewer's ratings.

The results of the MCSMS are reported in Table II. There was a wide range of MCMS values, from 47 to 79, with a mean of 61.4±11.4 regarded as fair (55-69 points). Some of the selected studies presented some limits, therefore, a meta-analysis was not performed (Table II).

Table II. *Results of the Modified Coleman Methodology Score (MCMS) used to assess quality of the included.*

Article	Study size	Follow-up	N procedures	Type of study	Diagnostic certainty	Description of injection technique	Rehabilitation and compliance	Outcome criteria	Outcome assessment	Selection process	Total
Apaydin et al. 2020	4	0	7	15	5	10	0	10	12	5	68
Fogli et al. 2017	0	0	10	10	0	10	0	7	5	5	47
Petrella et al 2010	10	4	7	15	5	10	5	10	8	5	79
Stirma et al 2020	0	0	10	10	0	5	5	10	8	5	53
Khan et al 2018	4	0	10	10	0	10	0	7	5	5	51
Yalcin et al 2022	7	0	7	15	5	5	0	10	12	5	66
Zinger et al 2022	0	4	10	15	5	10	0	10	7	5	66
Maximum Score Possible	10	10	10	15	5	10	5	10	15	10	100
Mean ± Standard Deviation	3.6±3.9	1.1±1.95	8.7±1.6	12.85±2.7	2.85±2.7	8.6±2.4	1.4±2.4	9.1±1.5	8.1±2.9	5±0	61.4±11.4

Characteristics of the included studies

Detailed descriptions of the characteristics of the included studies are summarized in Table I. Of the seven articles retrieved, three were prospective and case series studies with no comparative group, reporting results after a different number of HA injections (two or three) (8, 57, 58). Three studies were RCTs, with one of them reporting outcomes comparing HA injections with saline (placebo) injections (43), one reporting outcomes comparing a single HA injection with a single dextrose prolotherapy injection (52), and one reporting outcomes comparing a single HA injection with a single CS injection (59).

One study was initially designed as an RCT comparing HA injections with saline (placebo) injections (4). Still, as the authors stated, they could not analyze the information from the saline-treated patients due to the high rate of loss to follow-up: for this reason, this study should be considered prospective.

The study period ranged from 58 to 52 weeks (4, 43). The total number of patients enrolled in the retrieved studies was 544, with a minimum of 12 patients 8 and a maximum of 331 patients (43).

A clinical diagnosis of pain from a minimum of three weeks 58 to a maximum of 12 months (8) at the lateral epicondyle during palpation and/or resisted wrist extension with the arm fully extended was also used in all the included studies (4, 8, 43, 52, 57-59).

When injections were performed using a US-guided approach, a US-based evaluation of the affected epicondyle was also performed (8, 57). Only in one study an MRI diagnosis of TE was performed (59). Only two studies reported using specific tests for clinical assessment of TE, such as Cozen's and Mill's tests (8, 59).

Adverse events

Adverse events with the use of HA were pain at the injection site pain lasting one to two days reported in the study by Apaydin et al. in which HA was compared to DPT (three patients in the HA group, four patients in the DPT group) (52), and pain during the injection reported study by Petrella et al. in which HA was compared to placebo (three patients in the HA group, five patients in the placebo group) (43).

Injection technique

Two studies used a US-guided injection technique (8, 57), while, in the other studies, the injections were delivered at the point of greatest tenderness (4, 43, 52, 58, 59) one centimeter distal to the lateral epicondyle (4, 43, 58) and with the affected arm flexed to 90° (8, 43, 58). In two studies, a single injection at baseline was performed (52, 59), while in the other studies, two (8, 43, 58) or three injections (4, 57) were administered.

Rehabilitation

Only one study mentioned the rehabilitation protocol followed after the injections, which consisted of standard home stretching and strengthening procedures guided by a physical therapist (8).

Primary and secondary outcomes evaluation

The initial assessment of patients was performed in all the included studies using the visual analog scale (a 0-score score means no pain and maximum function while a 10-score means maximum pain and minimum function), with including values going from 3/10 (52) to 7/10 (58).

In each study, VAS decreased at each follow-up more than the threshold for minimal clinically important difference (MCID) (60) compared to baseline. Interestingly, in four out of six studies with more than a single follow-up point (4, 8, 52, 57), the VAS decreased more in the long-term follow-ups than in the short-term follow-ups. Physical function was shown to be improved in all the secondary outcomes across all the included studies.

In the studies in which grip strength was assessed using a hand dynamometer (43, 52, 59), the scores increased at each follow-up compared to a baseline of more than the threshold for MCID (61, 62). In any case, only in one study (52) the grip strength constantly improved over time, while in the other two studies (43, 59), grip strength increased at the first follow-up (i.e., four weeks and six weeks, respectively) but then started to decrease until the last follow-up.

In three articles in which the Q-DASH was used (4, 52, 59), the scores decreased at each follow-up when compared to a baseline of more than the threshold for MCID (63), except at the 6-week follow-up in the study by Yalcin et al. (59) that did not reach the threshold. The Q-DASH constantly decreased over time. As for the VAS, Q-DASH scores decreased more in the long-term follow-ups than in the short-term follow-ups.

HA versus active controls

Studies by Apaydin et al. (52) and Yalcin et al. (59) showed that in their control groups (i.e. patients treated with injections of dextrose prolotherapy and CS, respectively) better outcomes in terms of pain and function were reached at 12 and six weeks, respectively.

In the study by Apaydin et al. (52) there were no significant differences between the groups at six weeks for pain ($p>0.05$). Each group demonstrated a substantial change in VAS score at six weeks. DPT was favored over HA for improvements from zero to 12 weeks for pain with activity ($p=0.04$), pain at night ($p=0.03$), and pain at rest ($p=0.04$). Q-DASH scores improved significantly from zero to 12 weeks in the DPT group ($p=0.04$). Each group significantly improved pain and Q-DASH over time ($p<0.001$).

In the study by Yalcin et al. (59) there were significant differences regarding pain at rest ($p=0.017$), pain with hand grip ($p=0.08$), Q-DASH ($p=0.001$), and grip strength ($p=0.004$) at the six-week follow-up favoring the CS group, but non-significant differences at the 12-week follow-up in the evaluated scores.

When HA injections were compared to placebo (saline injections) (43), pain at rest and after grip testing was significantly better using HA. These outcomes were also associated with significantly greater grip strength, patient global satisfaction, and assessment of normal elbow function in the HA group *versus* control. Physician global assessment of elbow injury was significantly better for the HA *versus* control. These differences persisted at each follow-up assessment. Time to return to pain-free and disability-free sport was 18 ± 11 days in the HA group, with this outcome not being achieved in any of the control group patients, meaning a faster return to pain-free sports activities compared to placebo.

DISCUSSION

The outcomes of the included studies highlighted the paucity of evidence on the effectiveness and safety of HA injections for TE. Despite the use of different types of HA and injection protocols, and different scores applied, each study evaluated in this systematic review showed that the administration of HA for the treatment of TE is safe and effective in reducing pain, improving function, and allowing a faster return to pain-free sports activities.

HA was shown to regulate the tissue repair process through several pathways modulating the main phases of tendon healing (i.e., inflammation, cellular migration, and angiogenesis) (31-36). All these properties supported HA as a conservative treatment for tendinopathies (29, 34, 37-40).

While the effectiveness of HA injections is well-established for treating osteoarthritis (OA) (64-67), its efficacy in managing tendinopathies is still debated (68).

A systematic review by Coombes et al. (51) about the use of peritendinous injections for tendinopathies showed that HA injections have moderate evidence of benefits in the short, medium, and long-term, while other kind of injectable drugs, such as CS, only give temporary relief. Another recent systematic review by Crimaldi et al. (32) about the use of HA for tendinopathies stated that although HA seems to be an effective therapeutic option for managing tendinopathies, further studies with a larger sample size are needed to confirm the available findings. Since few conservative treatments were proven effective for TE (4), HA injections may represent an effective and safe therapeutic option.

Despite the good outcomes reported by the studies included in this review, the use of HA alone for TE remains questionable, especially regarding its use for short-term pain relief. Apaydin et al. stated that the superiority of DPT injections over HA in the short term may be related to the fact that DPT is more effective in accelerating tendon healing and regeneration. In contrast, HA injection provides increasing tendon lubricity over a longer period of time (52).
For this reason, and given the lack of a hard scientific background, other treatments or combined treatments using HA and other drugs may be preferred.

One prospective RCT by Tosun et al. (69) evaluated the effects of a mixture of HA and chondroitin sulfate injections *versus* CS alone for the treatment of TE, reporting better pain and function scores at six months in the HA plus chondroitin sulfate group. Chondroitin sulfate has anti-inflammatory, viscoelastic, and hydration properties, which may contribute to the effectiveness of HA (70).

A prospective study by Saggini et al. (9) compared the effectiveness of injections of CS plus HA *versus* CS alone, showing that CS plus HA is more effective than CS alone in the long term (6 months). Mixing CS with HA may have the potential to undermine the accurate assessment of the effect of the HA for treating TE (71). Furthermore, the anti-inflammatory effects of CS may falsely exaggerate the beneficial effect of HA (44).

Recent evidence indicated that CS could have tenotoxic effects, increasing the risk of tendon or ligament rupture, increasing tenocyte necrosis, and decreasing cell viability (72-74). Furthermore, in a prospective, double-blind RCT by Lindenhovius et al. (75), steroid injections did not affect the self-limited course of lateral elbow pain.

These concerns lead to the use of other materials for injection therapies, such as platelet-rich plasma (PRP) (76) which has become popular despite insufficient scientific support since most of the literature on PRP contains low-quality studies (51, 77-79). Only one study, a double-blinded RCT (80), reported results comparing PRP to CS injection with a one-year follow-up for TE, finding a 73% success in the PRP group.

Three recent systematic reviews and meta-analyses discouraged the use of CS and PRP for the treatment of TE (81-83), while favoring the use of electrophysiotherapy (such as laser therapy, shock wave therapy, and microcurrent application) even over physical therapy (81, 84).

One retrospective cohort clinical study by Pellegrino et al. (5) compared the effectiveness of a combined approach based on high-intensity laser therapy (HILT) and HA injections to therapeutic exercise alone on pain, muscle strength, and disability in patients with painful TE. The authors stated that a combined HA plus HILT treatment might be more effective than therapeutic exercise for people suffering from TE in the short-medium term.

These findings showed that when HA is combined with other pharmacological or physical conservative treatments, such as CS or electrophysiotherapy, the outcomes are better than those of single therapies alone (5, 9, 69).

Study limitations

The present review is not free from limitations. First, only three included studies are level-II studies and the others are level-IV studies. For this reason, the reported outcomes (especially those from level-IV studies, including a single group of patients) need to be interpreted cautiously due to the substantial risks of bias. Furthermore, there was high heterogeneity in the type of HA used and the number of injections performed, and even when the same injection protocol was used, the type of HA administered was different.

In some studies, molecular weight and concentration of the HA were not specified, so we cannot conclude which HA and injection protocol is the best choice for the conservative treatment of TE.

Finally, the heterogeneity of the study population with the absence of a control group in many investigations is an important limitation.

CONCLUSIONS

The administration of HA for the conservative treatment of TE shows a trend toward benefits in pain and functional outcomes, with few and minor side effects. In each study, the scores evaluated improved significantly with good results andoutcomes, especially in the long term. However, five articles were level-IV studies, preventingdefinitive recommendations regarding the indicationfor the use of HA for TE. Furthermore, when HA was compared to DPT or CS, it appeared inferior regarding pain and functional improvements in the short term. Prospective long term follow-up studies and RCTs are needed to confirm the outcomes of the included articles.

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Appendix A. *PRISMA checklist.*

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pages 2-3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 4
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Pages 5-6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Pages 5-6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6-7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 6
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 6

Section and Topic	Item #	Checklist item	Location where item is reported
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Not applicable
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not applicable
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 6-7
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Not applicable
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 7
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 7
Study characteristics	17	Cite each included study and present its characteristics.	Table 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table 1
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Pages 8-11
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Not applicable
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 8
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 8
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Not applicable
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pages 11-13
	23b	Discuss any limitations of the evidence included in the review.	Page 13-14
	23c	Discuss any limitations of the review processes used.	Page 13-14
	23d	Discuss implications of the results for practice, policy, and future research.	Page 14
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Not applicable
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 14

Section and Topic	Item #	Checklist item	Location where item is reported
Competing interests	26	Declare any competing interests of review authors.	Page 14
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Not applicable

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Appendix B. *The Modified Coleman Methodology Score.*

Part 1: One score for each of the sections:

1.	Number of patients:	
	a. <30	0
	b. 30-50	4
	c. 51-10	7
	d. >100	10
2.	Mean follow-up	
	a. <12 months	0
	b. 12-36 months	4
	c. 37-60 months	7
	d. >61 months	10
3.	Surgical approach	
	a. Different approaches and outcome not reported separately	0
	b. Different approaches and outcome reported separately	7
	c. Single approach	10
4.	Type of study	
	a. Retrospective cohort study	0
	b. Prospective cohort study	10
	c. Randomized controlled trial	15
5.	Description of diagnosis	
	a. Described without percentage specified	0
	b. Described with percentage specified	5
6.	Description of surgical technique	
	a. Not stated/unclear – Inadequate	0
	b. Only stated – Fair	5
	c. Stated with details – Adequate	10
7.	Description of postoperative rehabilitation	
	a. Described	5
	b. Not described	0

Part 2: Scores can be assigned for each option of every section

1.	Outcome criteria	
	a. Outcome measures clearly specified	2
	b. Timing of outcome measures clear	2
	c. Outcome measures with reported reliability	3
	d. General health measure included	3
2.	Outcome assessment	
	a. Participants recruited	5
	b. Investigator independent of surgeon	4
	c. Written assessment	3
	d. Assessment completed by patients	3
3.	Description of participants selection process	
	a. Selection criteria reported and unbiased	5
	b. Recruitment rate reported (>90%)	5
	c. Recruitment rate reported (<90%)	0

The figure reporting the Modified Coleman Methodology Score was retrieved from the following article: Mancino, F.; Di Matteo, V.; Mocini, F.; Cacciola, G.; Malerba, G.; Perisano, C.; De Martino, I. Survivorship and Clinical Outcomes of Proximal Femoral Replacement in Non-Neoplastic Primary and Revision Total Hip Arthroplasty: A Systematic Review. BMC Musculoskelet. Disord. 2021, 22, 933, doi:10.1186/s12891-021-04711-w.

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Review

THE MOST FREQUENT ORAL MANIFESTATIONS IN THE COURSE OF DISEASES, SYNDROMES, AND PATHOLOGIES OF OTHER ORGANS AND SYSTEMS: AN OVERVIEW-PART 1

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ABSTRACT

Various pathological conditions manifest in the oral cavity and can be an epiphenomenon of systemic diseases, therapies, syndromes, or pathologies affecting other organs and systems. The recognition of oral lesions or manifestations related to systemic conditions is helpful for early diagnosis, leading to a better response to treatments and improved prognostic standards. Mucosal, osseous, articular, and glandular manifestations are described in the context of systemic diseases and therapies, categorized by organs, systems, and apparatuses.

KEYWORDS: *oral lesions, mucosal lesions, systemic diseases*

INTRODUCTION

The involvement of the oral cavity in pathologies and diseases affecting other organs or systems is fairly common. Clinicians must carefully observe early signs and record symptoms in the oral mucosa, teeth, salivary glands, or temporomandibular joint to guide or complete the diagnostic procedure. The inspection of the oral cavity holds significant importance as a crucial phase of the comprehensive objective examination, not only for dental patients but also for patients affected by seemingly unrelated pathologies (1, 2).

This article describes the most prevalent oral manifestations of diseases, syndromes, and pathologies of organs and systems different from the oral cavity (3). Also, the oral complications due to systemic therapies were treated. While not claiming to be exhaustive, we intend to draw the clinician's attention to the most common and typical pathological manifestations that affect the oral cavity, convinced that the oral cavity can be a privileged window for assessing an individual's overall health.

Neurological and psychiatric manifestations

Branches of several cranial nerves innervate the oral cavity, salivary glands, and temporomandibular joint, including a) the trigeminal nerve (V pair), b) the facial nerve (VII pair), c) the glossopharyngeal nerve (IX pair), and d)

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the hypoglossal nerve (XII pair) (4). Pathologies affecting the central and peripheral nervous systems can lead to motor and sensory impairments within the oral cavity (5).

One example is Huntington's disease, which presents a wide array of signs and symptoms. These can include dysphagia, dysarthria, difficulties with mastication, compromised oral health, and choreiform movements affecting the tongue and other orofacial muscles. In cases of stroke, motor and sensory disturbances related to oral motricity can also be observed, depending on the extent of hypoxic damage at the central level (6).

Multiple sclerosis often manifests with trigeminal neuralgia, trigeminal sensory neuropathy, and facial palsy as the three most common orofacial symptoms (7). Trigeminal neuralgia can even be the initial manifestation of the disease in 0.3% of cases (8). Chronic neurodegenerative diseases, such as Alzheimer's and dementia, are associated with cognitive decline, which often correlates with deterioration in oral health. Lower DMFT values characterize severe cases of these conditions, compromised chewing and swallowing disorders, and an increased risk of mortality, physical frailty, functional disability, hospitalization, falls, and decreased quality of life. Oral pain, specifically, is linked to physical frailty (9. 10).

Burning mouth syndrome (BMS) is frequently accompanied by depression and varying degrees of distress (11, 12). The presence of dynias in multiple mucosal sites (13), higher prevalence in females, and its occurrence during peri-postmenopausal ages suggest a peripheral neuropathy triggered by stress, hormonal changes, or emotional stimuli (14). Eating disorders, such as anorexia nervosa and bulimia, often exhibit oral features, including tooth erosion, dental caries, changes in salivary quantity and quality, xerostomia, gingival and periodontal diseases, and oral mucosal lesions such as palatal erythema and ulcers (15).

Oral manifestations in cardiovascular diseases

Cardiovascular diseases (CVDs), including conditions such as coronary artery disease, stroke, and heart failure, are significant causes of morbidity and mortality worldwide. In recent decades, emerging evidence has indicated a potential association between CVDs and oral health.

Focal infections within the oral cavity can potentially initiate endocarditis and myocarditis through the hematogenous dissemination of bacteria or their toxins. Necrotic roots, apical granulomas, cysts, dental caries, and periodontal pockets can act as reservoirs for cardiac infections or elicit an immune response that exhibits cross-reactivity with valvular and endocardial antigens (antigenic mimicry) (16-19). Furthermore, chronic inflammation resulting from periodontal diseases can contribute to systemic inflammation, leading to endothelial dysfunction, atherosclerosis, and an increased risk of cardiovascular adverse events (20).

Symptoms such as angina and myocardial infarction can manifest as referred oral pain or discomfort, emphasizing the importance of considering cardiovascular causes in patients experiencing such manifestations (21). The pharmacological treatment of hypertension, peripheral vascular disease, and angina pectoris may induce oral signs and symptoms. For example, the use of calcium channel blockers (CCBs) can lead to a condition known as Drug-Induced Gingival Overgrowth (DIGO) (22). The most prevalent CCB associated with DIGO is nifedipine, with a prevalence exceeding 20%. Other CCBs may also contribute to this condition, including diltiazem, felodipine, amlodipine, and isradipine (23). Gingival enlargement typically occurs within 1 to 3 months after starting treatment. Initially, it presents as a firm, nodular enlargement in the interdental papillae, gradually extending to the buccal and lingual margins. Anterior teeth are commonly affected, with the extension reaching the buccal aspect (24). Histologically, DIGO exhibits mixed inflammatory and fibrotic characteristics (25, 26).

Another consequence of cardiovascular treatment is Acquired Angioedema, which can arise from the use of angiotensin-converting enzyme (ACE) inhibitors. Clinically, it manifests as non-pitting, non-itching submucosal swelling, primarily affecting the oral cavity's extremities, such as the lips (27). Angioedema predominantly affects the tongue in women, individuals of African descent, and smokers. It typically manifests within the first month of initiating therapy in approximately 50% of cases (28).

A dry mouth, characterized by xerostomia (a symptom) and hyposalivation (a sign), is also a common side effect of various medications, including antihypertensives and diuretics (29). The prevalence of dry mouth increases with age due to atrophic glandular degeneration, affecting up to 30% of individuals over 65, particularly women (30). Polypharmacy, which is prevalent among older individuals, further contributes to the incidence of this condition (31). There is a therapeutic association between drugs used for cardiovascular diseases and over 400 classes of xerogenic drugs (32).

Oral manifestations in chronic renal failure

Oral manifestations are often observed in the advanced stages of Chronic Renal Failure (CRF), characterized by a significant reduction in glomerular filtration rate. Soft and hard tissue can be involved in the manifestation of CRF, presenting a wide range of clinical and symptomatic features. These manifestations can also be a consequence of the therapies the patients undergo. Moreover, changes in bacterial microflora are observed in these patients (33).

Regarding soft tissue involvement, Uremic Stomatitis is commonly observed and often localized on the lingual surface. It can present in four clinical variants: membranous-erythematosus, ulcerative, hemorrhagic, and hyperkeratotic. This condition is caused by an increase in serum nitrogenous waste products. The ulcerative variant is the most common, while the hyperkeratotic variant is the rarest.

Tissue Dystrophy, which is more prone to bacterial infection, can occur due to small bleeding events. Necrotic Pseudomembranous Gingivostomatitis may be observed in patients with unexpected increases in serum nitrogen levels. Xerostomia, characterized by reduced salivary flow, is present in 28-59% of patients with end-stage renal disease cases. Hyposalivation can lead to various sequelae, including a higher susceptibility to cervical caries, candidiasis, atrophic and chapped lips, and dry, pale labial mucosa. Spontaneous Gingival Bleeding may occur during CRF as a result of bacteremia. Bacterial toxins induce platelet dysfunction, exacerbated by renal anemia and anticoagulant therapies. Furthermore, endothelial dysfunction worsened by dyslipidemia leads to the development of Petechiae and Bruising in these patients (34, 35).

Regarding hard tissue involvement, Enamel Renal Syndrome (ERS) is a genetic condition characterized by enamel hypoplasia and nephrolithiasis. Both deciduous and permanent teeth can be affected, with tooth surfaces appearing rough or smooth and yellow-brown in color. Pulp stones may be present in the pulp chambers. Increased concentrations of volatile sulfur compounds due to microbiological degradation can lead to Halitosis, especially when blood urea levels exceed 55 mg/dl. There is also an increase in tartar levels. Another oral manifestation of CRF is the chronic kidney disease mineral and bone disorder syndrome (CKD-MBD), resulting from several metabolic disorders. Skeletal manifestations include osteitis fibrosa and osteomalacia, which show an excess of osteoid bone with a high risk of fractures, as well as adynamic and mixed bone disease. Expansive jaw lesions may appear radiographically as a radiolucent area due to the loss of bone trabeculae and reduction of the cortex. Other manifestations include temporomandibular joint defects, delayed eruption, and periodontal calcifications due to altered calcium-phosphorus products (36-38).

In kidney transplant (KT) recipients, DIGO can be induced by immunosuppressive drugs such as cyclosporine. Studies have shown that patients with severe DIGO may present this manifestation even before transplantation, and children and adolescents seem to be more predisposed than adults. Clinically, DIGO initially appears as soft and hyperemic nodules at the level of the papillae, extending buccally, lingually/palatal, and in a coronal direction. It appears pink, firm, and resistant to palpation, often covering up to ½ of the crown of the labial face of the upper and lower anterior teeth. Compared to cyclosporine, tacrolimus can induce partial or total regression of the lesion. Sporadically, GH may occur in patients who take cyclosporine from the beginning of therapy. Gingival hyperplasia is also associated with calcium channel blockers in patients undergoing dialysis or pre-dialysis (39).

Oral Candidiasis is present in kidney transplant recipients, with an incidence ranging from 4% to 43%. *Candida dubliniensis* and *Candida famata* have been found in many cases. Suburral Tongue can occur in 22% of KT recipients and presents as a yellowish-white superficial layer on the back of the tongue. Oral Hairy Leukoplakia (OHL) can be observed in transplant recipients in 8%-11% of cases. It is a painless, irregular white spot with prominent folds that cannot be scraped off. It usually appears on one or both lingual borders and sometimes on the posterior aspect of the tongue. This condition may be due to the reactivation of the Epstein-Barr virus following immunosuppression. Candida Albicans may also be associated with OHL. Finally, KT recipients following immunosuppression have a higher frequency of developing malignant lesions, with Kaposi's Sarcoma representing 5.7%-11% of cases. It is an angiogenic tumor of viral etiology caused by human herpes virus-8 (HHV8). Clinically, it can present as a macular, plaque, or nodular form, often localized on the palate or gingiva (40, 41).

Oral manifestations in hematological diseases

Hematological diseases, also known as blood disorders, encompass a wide range of conditions that affect the blood, blood-forming tissues, and the immune system. These diseases can significantly impact individual health and quality of life. Oral cavity involvement is frequent and, in some cases, the site of the first manifestations.

Iron deficiency anemia is the most common hematological disorder. It may manifest in the orofacial region as a burning sensation (in 76% of cases) and numbness of the oral mucosa, atrophic glossitis, taste dysfunction, recurrent aphthous ulcers, dry mouth, and oral lichen planus (in 33.3% of cases), as well as lingual varicosities. If the atrophy

extends to the mucous membranes of the upper aerodigestive tract, it predisposes individuals to develop squamous cell carcinomas, a condition known as Plummer-Vinson Syndrome (42, 43).

In patients affected by pernicious anemia, patients may present with Hunter's Glossitis (or Moeller-Hunter), characterized by atrophy of the filiform papillae with a smooth and erythematous appearance involving more than 50% of the dorsum of the tongue. Atrophic oral candidiasis, angular cheilitis, and recurrent aphthous ulcers may also be present. The symptomatology is characterized by glossodynia, burning, xerostomia, and lingual paresthesia. These signs often appear before symptomatic anemia, and one characteristic of this phase of pre-anemia is the so-called "magenta tongue" (44). During folate deficiency anemia, the same clinical manifestations are present in pernicious anemia without neurological implications (45).

In sickle cell anemia, the jaw bones are involved in most cases. This involvement is marked by an expansion of the marrow spaces due to compensatory hyperplasia of the marrow. Radiographically, there is a reduction in bone trabeculation, which leads to various sequelae. In less severe cases, there is an increase in mid-facial growth, potentially resulting in interincisal diastema and paresthesia or anesthesia of the mental nerve.

In more severe cases, complications can include osteomyelitis, osteosclerosis, ischemic infarction, or osteonecrosis of the mandibular bone. The mandible is more affected than the maxilla because it has less blood circulation. The only observable manifestation at the soft tissue level is pale or yellowish mucosa resulting from hemolytic jaundice (46).

In cases of Homozygous β-thalassemia (Cooley's Anemia), skeletal abnormalities are primarily evident in childhood. Patients often exhibit maxillary bone protrusion due to compensatory marrow hyperplasia, usually called the "squirrel face." The mandibular bone is less affected due to its thicker cortex, which resists marrow expansion. Patients may also present with anterior-superior diastemas, malocclusions, tooth discolorations, and tooth dislocations, which can have shorter roots and crowns (47). The oral mucosa frequently displays characteristic pallor.

In cases of cyclic neutropenia, recurrent aphthoid ulcers and rapidly progressive periodontal disease can be observed, especially in children and young adults. Neutropenic manifestations typically appear approximately every 21 days. Additionally, an atypical form of ulcerative gingivitis with gingival ecchymoses has been reported (48, 49).

Various signs may be observed in cases of qualitative and quantitative platelet deficits, including spontaneous petechiae (smaller than 3mm), purpura (3-10 mm), ecchymoses (larger than 3mm), hemorrhages, blood blisters that can spread to the oral mucosa, and excessive bleeding following trauma or extractions. Excessive gingival bleeding is also commonly reported after teeth brushing.

If the patient is affected by coagulation disorders, hemorrhages, and prolonged bleeding after routine dental procedures can also be observed. In Von Willebrand disease (the most common disorder), hemosiderin deposition can lead to the teeth appearing brown. In Hemophilia A and B, varying degrees of bleeding can occur following trauma, depending on the severity of the deficiency of factors VIII and IX, respectively.

Kaneda et al. identified gingiva as the site most commonly involved within the oral cavity, accounting for 64% of cases, followed by the pulp at 13%, tongue at 7.5%, lip at 7%, and palate at 2%. Rare instances of temporomandibular joint (TMJ) hemarthrosis and chronic hemophilic arthropathy have also been reported. Cases of gingival bleeding associated with swelling and ulceration in plasminogen deficiency have been documented, as well as the presence of fibrin pseudomembranes on the gums in cases of dysfunctional fibrinolysis (50).

Oral manifestations in genetic diseases

The tongue is the most frequently affected site in patients with lipoid proteinosis. However, many patients also experience involvement of multiple oral sites, including the floor of the mouth, lips, buccal mucosa, and palate. Oral lipoid proteinosis manifestations are caused by hyaline material deposits in the subepithelial connective tissue. Clinically, these manifestations appear as yellowish-white areas with thickening of the mucosa and a hard consistency resembling wood. Some patients may also exhibit a short lingual frenulum, restricting tongue movement. Additionally, gingival hyperplasia may occur more frequently in young individuals, while palatal involvement is typical in the elderly (51).

Dyskeratosis congenita presents a triad of symptoms: nail dystrophy, reticular skin hyperpigmentation, and oral leukoplakia, which shows a 35% risk of malignant transformation over 10-30 years. Recurrent blisters or aggregates may also be present, which, upon rupture, result in ulcerated and atrophic areas, particularly on the tongue and buccal mucosa (52).

In multiple hamartoma syndrome (Cowden's Syndrome), oral manifestations are present in approximately 80% of patients. Whitish or pink papules or nodules can be found on the gingiva, tongue, and buccal mucosa. These lesions can appear as isolated entities or fused, resembling a cobblestone-like appearance, typically on the gingiva. Other possible

oral manifestations include papillomatosis, fissuring, lobulations of the tongue, arched palate, caries, xerostomia, and periodontitis (53).

In patients with neurofibromatosis type 1, multiple or rarely isolated nodular neurofibromas can occur, particularly in children, affecting up to 72% of cases. These fibrous masses, located mainly on the tongue (26%), buccal mucosa (8%), labial mucosa (8%), oral floor, and palate (8%), appear as submucosal lesions without inflammation. Gingival localization (2%) can cause unilateral enlargement of the attached gingiva, extending to the interproximal area. This condition can lead to worsened periodontal health due to the impediment of oral hygiene. Some studies have reported macroglossia cases resulting from plexiform neurofibromas and enlarged fungiform papillae. These lesions have a 3%-5% risk of malignant degeneration. Deformities of the maxillary bones may also occur due to tumor localization in these areas or skeletal lesions caused by a generalized increase in osteoclast activity due to haploinsufficiency of the NF-1 gene (54).

Oral manifestations of Sturge-Weber syndrome can affect 38% of cases and result from facial capillary malformations. Angiomatous lesions are observed in the gingiva, tongue, palate, labial mucosa, and buccal mucosa. These lesions are usually unilateral and terminate abruptly at the midline. Gingival manifestations can range from slight hyperplasia to severe angiomatous proliferations, which blanch upon the application of pressure and may bleed following minor trauma. Furthermore, gingival enlargement can be attributed to the use of anticonvulsant drugs commonly prescribed for epileptic seizures in these patients. In some cases, macroglossia and maxillary bone hyperplasia have also been reported (55, 56).

In tuberous sclerosis (TSC) cases, oral manifestations often include fibromas. These fibromas are predominantly located in the anterior gingiva, with less frequent involvement of the labial mucosa, upper labial frenulum, palate, and tongue. Affected areas may exhibit confluent nodules smaller than 1 cm. Furthermore, enamel pits can be found on the labial surfaces of anterior teeth, including canines. This condition affects permanent dentition in 48-100% of cases, and some studies have also shown the involvement of deciduous dentition (57).

Patients with hereditary epidermolysis bullosa (EB) can exhibit various clinical manifestations depending on the specific form of the disease (simplex, junctional, dystrophic, Kindler). Blisters are commonly observed in patients with EB, often as a result of trauma, accompanied by erythema, atrophy, and ulcerations. Scarring can vary depending on the subtype and its variants. Microstomia, ankyloglossia, reduced gingival arches, and severe desquamative gingivitis are also commonly seen in these patients. Junctional EB can present various degrees of enamel abnormalities, ranging from pitting to generalized hypoplasia, which is not observed in the dystrophic variant (EDB). Recessive EDB is the most aggressive form of EB, as patients often struggle with oral hygiene, leading to high rates of dental caries. Malnutrition resulting from dysphagia can further contribute to reduced jaw growth, resulting in malocclusions and crowding. Periodontal disease is particularly prevalent in patients with EDB due to poor oral hygiene. Kindler syndrome, which involves a protein of the junctional epithelium, can also present with early-onset periodontitis (58, 59).

Focal palmoplantar and oral mucosa hyperkeratosis syndrome are characterized by focal painful hyperkeratosis primarily affecting the attached gingiva. This condition tends to occur in areas subjected to mechanical pressure or friction. At the gingival level, it often manifests as leukoplakia. Other sites in the oral cavity that can be involved include the palate, alveolar mucosa, lingual edges, retromolar mucosa, and buccal mucosa at the occlusal line. These areas are subject to mechanical stress during oral function (60).

Oral cavity and gastrointestinal diseases

The oral cavity serves as the initial segment of the gastrointestinal system, rendering it susceptible to involvement in gastrointestinal diseases. Crohn's disease, an inflammatory bowel disease of uncertain etiology, can affect any part of the gastrointestinal system, including the mouth (61). Oral manifestations of Crohn's disease may encompass aphthous stomatitis, mucosal tags, lip swelling, and pyostomatitis vegetans (62). Some studies have also reported additional oral changes in Crohn's patients, such as bilateral corrugated cobblestone changes in the buccal mucosa and erythematous gingival enlargement.

Ulcerative colitis, another form of inflammatory bowel disease, can also give rise to oral manifestations, with pyostomatitis vegetans being the most prominent. Pyostomatitis vegetans are elevated yellow-white circinate lesions that can affect multiple oral mucosal sites (63). Further oral abnormalities observed in ulcerative colitis include aphthous lesions, dental caries, and severe periodontitis (64). Gardner's syndrome, a genetic disorder characterized by intestinal polyps, multiple osteomas, and soft tissue tumors, can manifest in the oral cavity due to osteomas affecting various bones, including the jawbones (65). Celiac disease, a treatable gluten-induced condition, can exhibit oral manifestations, including recurrent aphthous stomatitis. It may also lead to enamel defects, delayed dental development, frequent caries, and lingual atrophy (66, 67).

Gastroesophageal reflux disease, resulting from the reflux of stomach contents into the esophagus or oral cavity, can cause oral alterations. Chronic exposure to acidic gastric content can result in irreversible dental erosion and irritation of the oral mucosa (68). Pseudo-lesions of the oral mucosa, such as hypertrophy of the lingual vallate papillae and lingual tonsils, may also occur due to chronic exposure to acidic gastric content (69).

Pediatric jaundice, characterized by elevated bilirubin levels in the circulation, can cause discoloration of the skin, eyes, and mucous membranes, including the oral mucosa. Neonatal jaundice is common, and although it often resolves, high serum bilirubin levels can become permanently trapped in dental hard tissues, leading to discoloration and structural alterations of enamel and dentin (70).

Peutz-Jeghers syndrome, a rare autosomal dominant disease often caused by a mutation in the serine/threonine kinase 11 gene, primarily affects the digestive system. It is associated with oral hyperpigmentation, which is considered a pseudo-lesion resulting from the hyperactivity of melanocytes, particularly involving the gums (71).

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Case Report

MANAGEMENT OF LOWER–THIRD OF THE FACE THROUGH UPPER DISTALIZATION IN PATIENT WITH CLASS II MALOCCLUSION: A CASE REPORT

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ABSTRACT

This case report presents the orthodontic management of the lower face through upper distalization in a 54-year-old male patient with Class II malocclusion. Class II malocclusion, characterized by misalignment of the upper and lower dental arches, poses unique challenges in mature patients, influencing both dental aesthetics and the lower third of the face. In this case, Spark Aligners were employed over an 8-month treatment period, comprising three appointments, to achieve controlled distalization of the upper arch. The successful restoration of incisors and improvements in facial aesthetics underscore the effectiveness of this targeted intervention. The use of aligners contributed to minimal patient discomfort and facilitated a streamlined treatment process. This case highlights the efficacy of upper distalization in adult patients with Class II malocclusion and emphasizes the importance of comprehensive aesthetic outcomes and tailored orthodontic approaches. The findings contribute to the evolving landscape of orthodontic care, offering valuable insights into managing complex malocclusions in older age groups. Further research and long-term studies will enhance our understanding of the stability and broader applicability of upper distalization using the "Malagón method" in adult orthodontic patients.

KEYWORDS: *orthodontics, aligners, class II malocclusion*

INTRODUCTION

Aging often changes dentofacial structures, impacting both function and aesthetics (1-2). This case report delves into the strategic orthodontic management of the lower face through upper distalization in a 54-year-old male patient with Class II malocclusion. Class II malocclusion, characterized by the misalignment of the upper and lower dental arches, can significantly impact facial aesthetics and functional harmony. In individuals of adult age, the repercussions of such malocclusions extend beyond the dental realm, influencing the lower third of the face, including the lips, chin, and surrounding soft tissues. Addressing these concerns becomes imperative for aesthetic reasons and overall oral health and well-being (2-4).

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The unique challenges posed by age-related changes in dentition and skeletal structures underscore the necessity for a tailored and nuanced orthodontic approach. In this context, the therapeutic choice of upper distalization emerges as a focal point in our case, representing a contemporary intervention aimed at achieving dental alignment and comprehensive facial harmony (5). By exploring the intricacies of this case, we aim to contribute valuable insights to the orthodontic literature, offering a deeper understanding of the management strategies tailored to the distinctive needs of adult patients with Class II malocclusion.

CASE REPORT

Patient history and examination

The 54-year-old male patient presented with a skeletal Class I and dental Class II malocclusion of maxillary origin. The primary concern was the restoration of incisors, which had undergone significant wear and misalignment over the years. In addition to the functional aspects, the patient expressed a desire for improved facial aesthetics.

A comprehensive examination revealed a decreased lower facial height and increased aging-related changes in the lower third of the face. The decision to employ the “Malagón method” focuses on upper distalization as the primary treatment modality aimed to address both the malocclusion and the patient's esthetic concerns. The patient had never had orthodontic treatment before.

Diagnostic assessment

A comprehensive diagnostic assessment was conducted, thoroughly examining dental and facial structures. The lower third of the face exhibited signs of aging, with reduced facial support and diminished chin projection.

Extraoral examination revealed an oval face, facial symmetry, adequate maxillary incisor exposure, and competent lips. Aesthetic Arnett analysis revealed a convex profile due to maxillary projection, a protruded upper lip, a slightly reduced nasolabial angle, and a chin in a retruded position.

An intra-oral examination revealed that the lower dental midline was shifted 1 mm to the left of the upper dental midline. There was a bilateral class II molar and canine relationship, an increased overbite and overjet, and upper and lower misalignment. The upper and lower arches were narrow, with a "V" shape (Fig. 1).

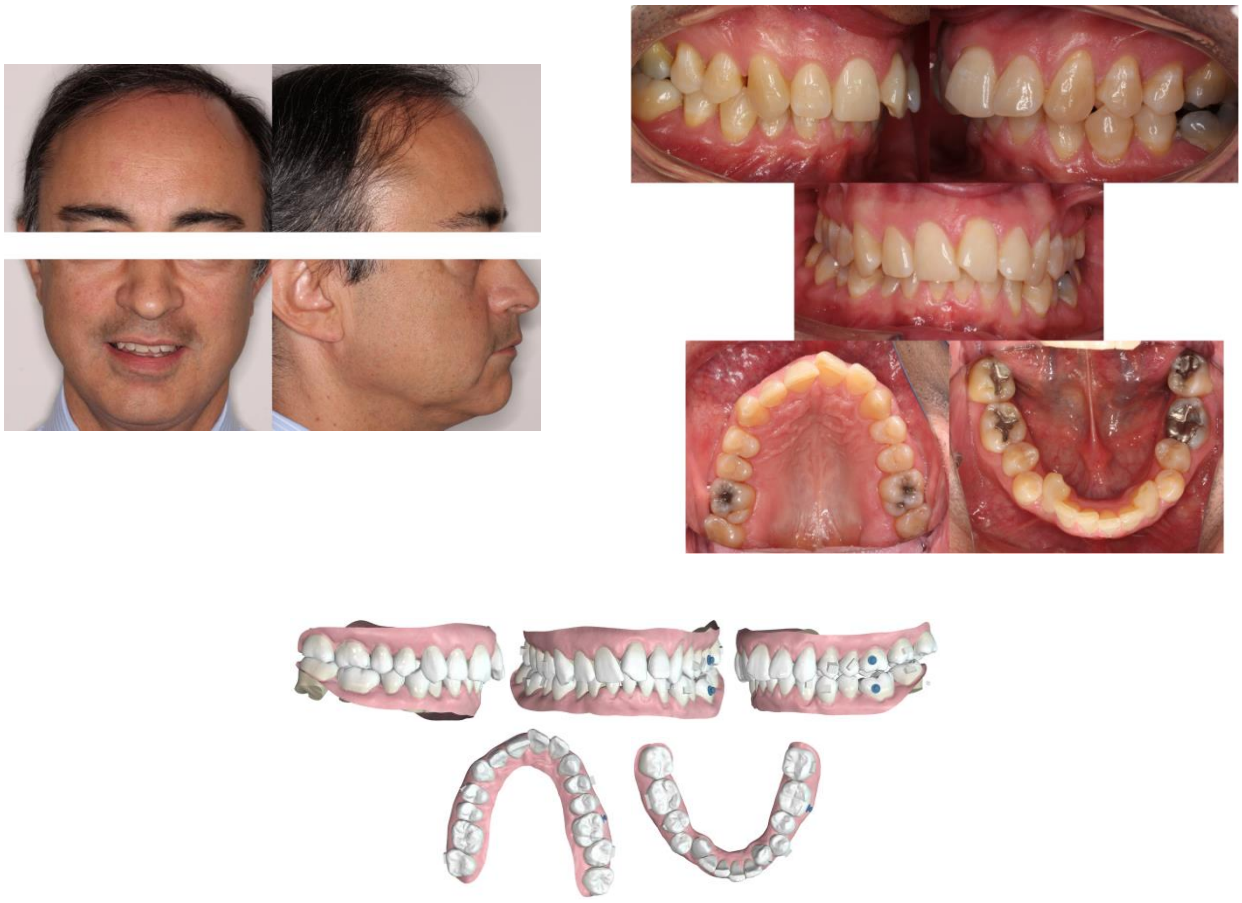

Fig. 1. *Pre-treatment photographs and models.*

The cephalometric analysis (Fig. 2) showed skeletal class I relationship (ANB = 4°, Wit's appraisal = 0.04 mm), prognathic maxilla and the correct position of the mandible (SNA = 86°, SNB = 82°), proper inclination of upper maxillary incisors and slightly retroclined the mandibular incisors (IMPA = 82°, U1-SN =101 °), and normal facial height (Sn-GoMe =31°) as shown in Table I.

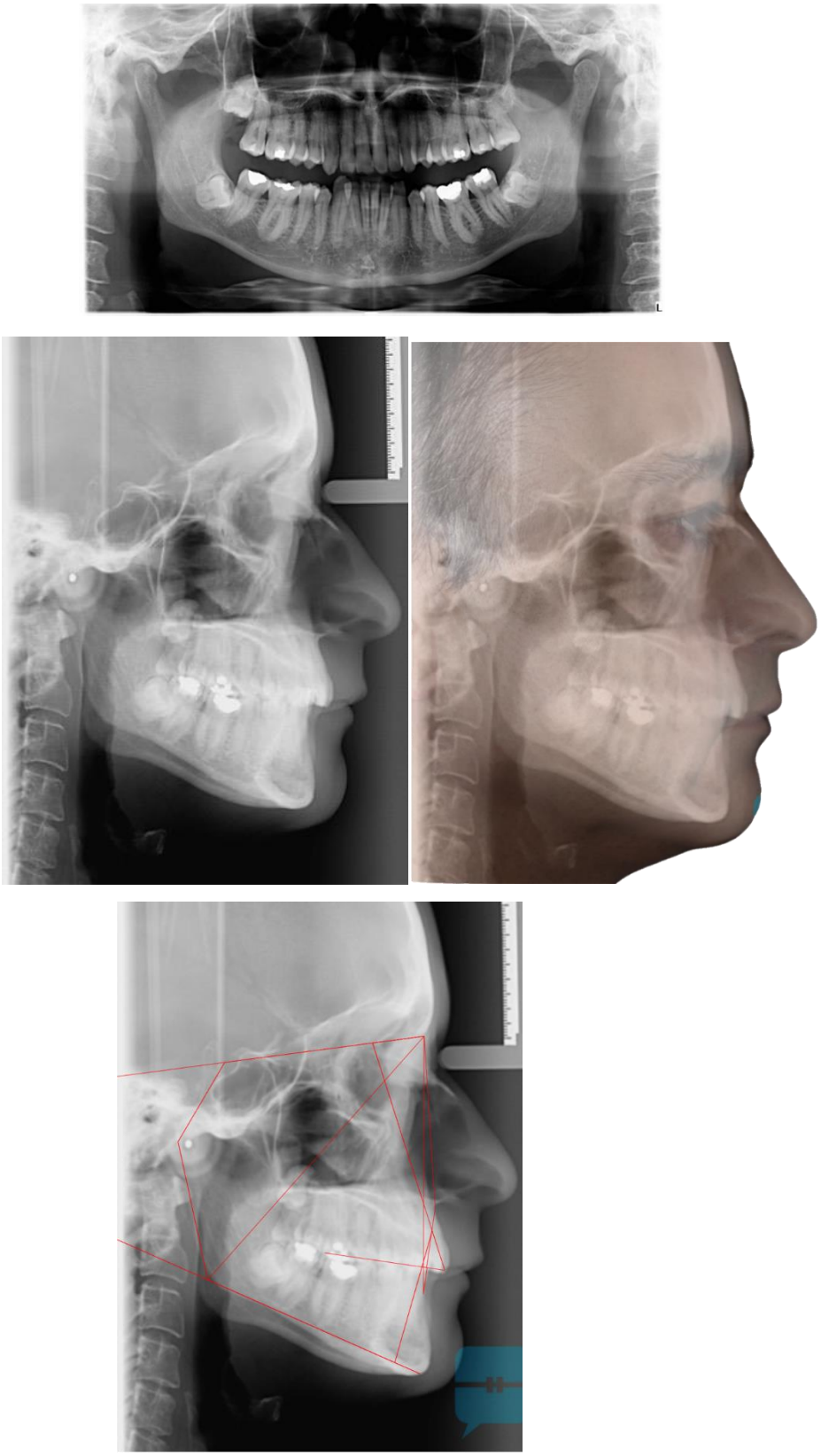

Fig. 2. *Pre-treatment radiograph and cephalometric analysis.*

Table I. *Cephalometric analysis pre- and post-treatment.*

Measurement	Pre-treatment	Post-treatment	Norm
Skeletal component			
SNA	86°	83°	**81°**
SNB	82°	80°	**79°**
ANB	4°	3°	**2°**
Wits appraisal	0,04 mm	2 mm	**-1 to 1 mm**
Gonial Angle	126°	128°	**130° ± 7°**
Upper gonial angle	54°	53°	**52°- 55°**
Lower gonial angle	72°	75°	**70° - 75°**
N-S-Ar-Go-Gn	391°	393°	**396°**
S-N/Go-Me	31°	34°	**32°**
Dentoalveolar compenent			
UI-SN	101°	103°	**102° ± 2°**
IMPA	82°	89°	**90° ± 3°**
Interincisal angle	147°	139°	**135°**

Treatment planning

The treatment plan based on the Malagón Method centered on utilizing Spark Aligners (manufactured by Ormco Corporation) for upper distalization, taking advantage of the aligner system's flexibility and precision. The objectives included correcting the Class II malocclusion, restoring incisor alignment, and enhancing the lower facial profile.

Treatment objectives and treatment plan

Over 8 months, the patient underwent a phased treatment involving 31 Spark Aligners (manufactured by Ormco, advanced clear aligner technology with TruGenTM materials). The treatment timeline consisted of three appointments, each marking the progression to a new set of aligners. We used 3D controls in the virtual simulator (Spark Approver) to achieve a predictable clinical outcome for class II correction. The primary treatment goals were to achieve class I canines and molars bilaterally using upper molar distalization orthodontic approaches. This treatment aimed to move the upper molars backward (distally) to correct the relationship between the upper and lower arch, resulting in a more harmonious occlusion. Additional objectives were to relieve the crowding in both arches, restore a pleasant smile with optimal lip line and smile arch, and enhance the patient's profile. Distalization of the upper arch was chosen as a treatment option to improve the position of the upper lips relative to the chin and lower lip. Non-invasive direct restoration (BOPT technique) using composite resins on anterior teeth 11, 12, 13, 21, 22, and 23 were performed after achieving a stable and coordinated occlusion. All procedures were carried out in accordance with the ethical standards outlined in an appropriate version of the Helsinki Declaration.

Therapeutic intervention or treatment protocol

The digital setup (Approver) involved using computer software to create a virtual representation of the patient's teeth and jaws, allowing the orthodontist to plan the precise movements required to achieve the desired result. On the upper arch, reciprocal movements represented by upper incisor proclinations during molar and premolar distalization were critical in preventing anterior anchorage loss. The treatment was completed without the extraction of the upper third molars.

Orthodontic setup of the upper arch, distalization protocol.

Sagittal plane: The second molars were distalized simultaneously to upper incisors proclination (reciprocal movement), which should last until 5s are in class I. After 4 aligners, distalization of the upper first molars began, which involved a 1mm opening space useful for increasing the surface to be covered by aligners for tipping maintenance. Distalization of the second premolars started when the second molars reached their final and correct position, and so on with the first premolars. Distalization was performed every 4 aligners and not more than 2 posterior teeth at the same time. Anterior teeth retrusion and intrusion from 13 to 23 were completed at 115°, and the second premolars reached their final position. Additional palatal root torque compensation was prescribed to incisors to avoid retroclination and achieve the incisors' bodily movement during retrusion.

Transversal plane: Constriction by palatal-crown torque of the upper second molars as well as distopalatal rotation and relative extrusion. Similarly, the first molars were expanded by mesiobuccal rotation, followed by the compensation of molars and premolars by 10° of buccal root torque (to maintain the initial torque and avoid the tendency of over inclination and potential posterior open bite) until an oval arch shape was obtained. Premolar and canine were also expanded.

Prescription of attachments

Only the first and second molars in the upper arch had HRGB (horizontal gingival beveled attachments). No additional attachments were required to allow aligners to cover the entire buccal surface. The HRGB attachments work as active attachments on the upper second molars since I need extrusion (relative extrusion thanks to the required palatal crown torque). On the upper first molars, the same attachments, HRGB, these attachments work as passive attachments because the expansion requires pushing from palatine out the molar, pressing close to the center of resistance (the higher on the palatal surface, the better), and the attachments on buccal surface act creating a system of forces to avoid the potential undesired over inclination.

By covering the whole tooth surface (buccal, lingual, occlusal, mesial, and distal) during upper molar distalization, we avoided the distal crown tipping that usually happens using traditional multibracket biomechanics with round wires and low friction mechanics.

Orthodontic setup of the lower arch

Transversal plane: Constriction of lower molars and lingual root torque (to avoid increasing the curve of Wilson) and distolingual rotation of second molars were planned simultaneously with the expansion of first molars, premolars, and canine to achieve an oval arch.

Sagittal and vertical plane: Round tripping and IPR from 33 to 43 to correct anterior crowding.

Prescription of attachments

Passive HRGB (Horizontal Occlusal Beveled Attachment) was placed on the buccal surfaces of lower first and second premolars to avoid potential misfitting of the aligners during the severe intrusion of lower incisors.

RESULTS

The case report focuses on managing the lower third of the face through upper distalization in a 54-year-old patient with the primary motivation of restoring incisors. The initial presentation revealed a Class II malocclusion attributed to maxillary causes. The Malagón treatment protocol involved the use of Spark Aligners, with a total of 31 aligners utilized over 8 months.

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After the 8-month treatment period, the patient exhibited remarkable improvements in both functional and aesthetic aspects, and the predetermined objectives were met, yielding satisfactory results. Aesthetic Arnett analysis revealed an improvement in the aesthetic profile: a reduced upper lip projection and a more opened nasolabial angle. The success of the upper distalization process was evident in the comprehensive assessments conducted at each of the three appointments throughout the treatment period. The effective correction of the Class II malocclusion and the harmonious alignment of the upper dentition contributed to the overall enhancement of the lower third of the patient's face.

The concise treatment duration and minimal number of appointments underscore the efficiency of the protocol employed, demonstrating the potential for targeted orthodontic interventions in addressing specific concerns with optimal outcomes (Fig. 3, 4). The patient expressed satisfaction with the achieved results and discussions regarding retention strategies, including the incorporation of a retainer (Spark aligners, Trugen XR material) with a prescription to wear it for 22 hours a day during the first month after finishing the active treatment, 16 hours a day during the next 2 months and 12 hours a day the next 3 months, to ensure the longevity of the orthodontic improvements.

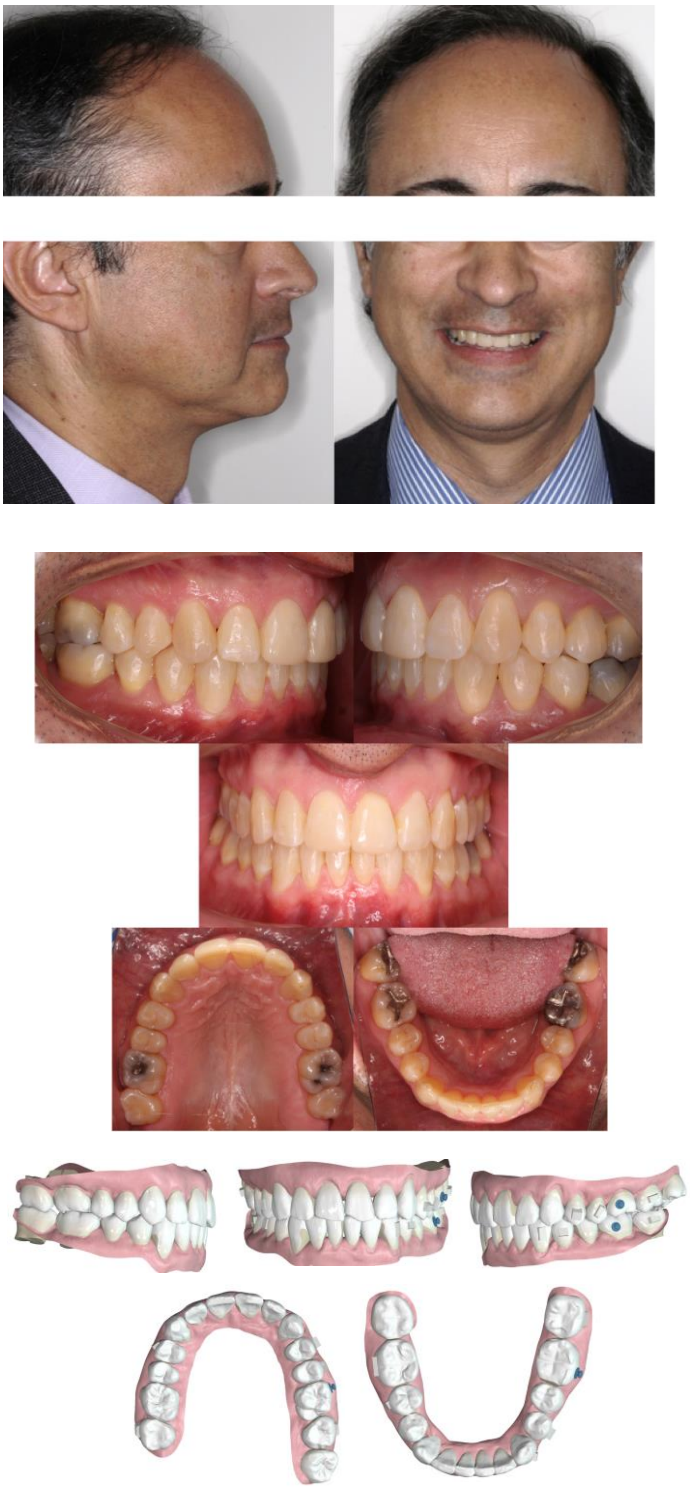

Fig. 3. *Post-treatment photographs and models.*

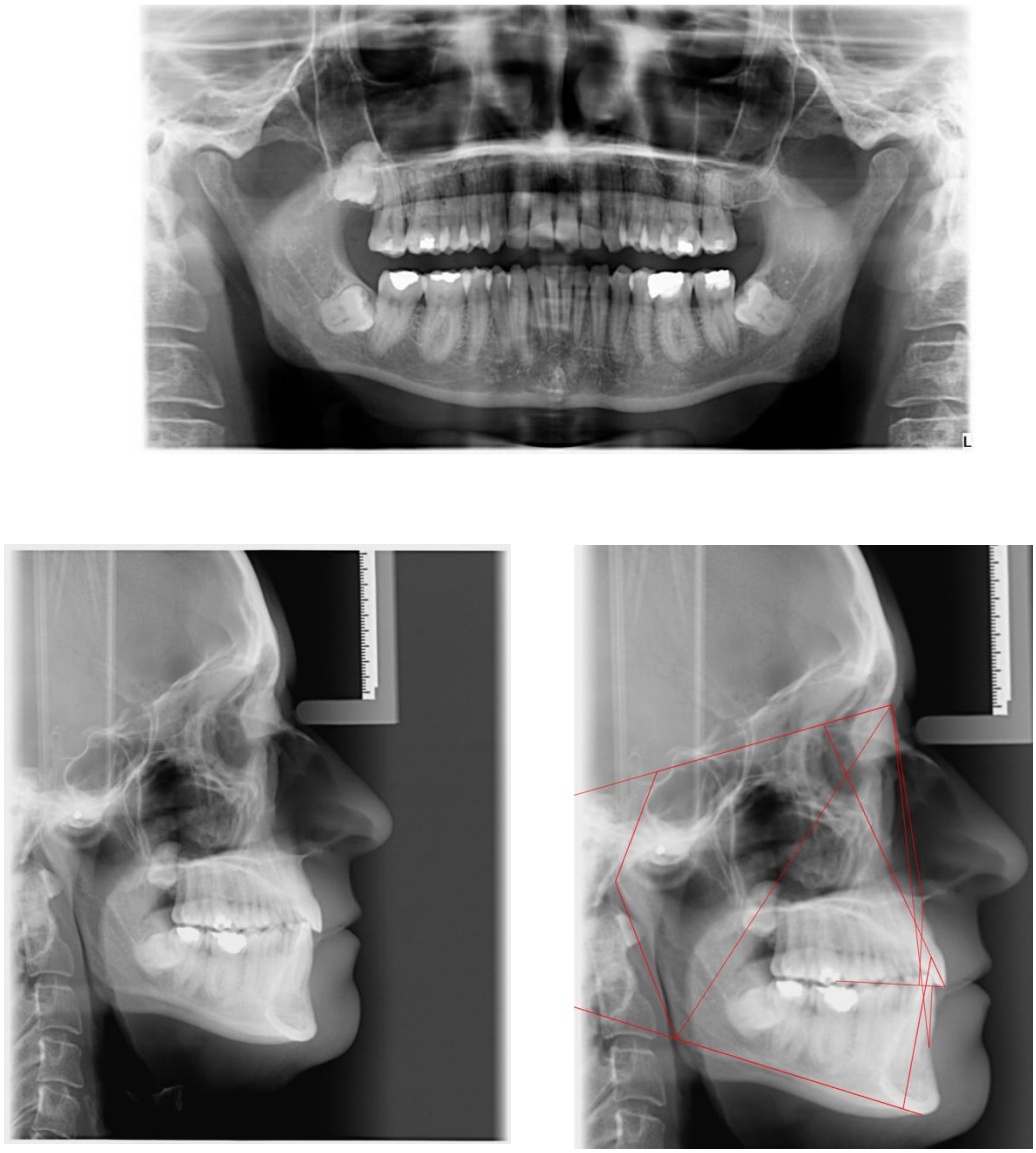

Fig. 4. *Post-treatment radiograph and cephalometric analysis.*

After 6 months of removable retention, the patient came to a new appointment to check the occlusion, the thickness of the periodontal ligaments, and the stability of the case so that, having reached the objectives, he started wearing the removable retainers only nights for 8 hours a day. Overall, the case highlights that the Malagón method is a successful and efficient approach to managing the lower third of the face through upper distalization in an adult patient population.

Post-treatment panoramic radiography revealed good root parallelism, no crestal bone height reduction, and no evidence of apical root resorption. Table 1 shows cephalometric results that show a reduced ANB angle (SNA from 86° to 83° and an SNB angle from 82° to 80°), good vertical control (S-N/Go-Me from 31° to 34°), correct incisor inclination (UI-SN from 101° to 103° and IMPA from 82° to 89°), and optimal overjet (from 4 mm to 2 mm) and overbite (from 5mm to 2mm).

DISCUSSION

The successful management of the lower face through upper distalization in our 54-year-old patient with Class II malocclusion highlights the effectiveness of targeted orthodontic interventions in addressing dental and aesthetic concerns in adult patients. Class II malocclusion, often associated with maxillary protrusion, can result in dental misalignment and impact the lower third of the face, influencing lip position, chin projection, and overall facial balance (6-8).

In this case, the utilization of Spark Aligners proved to be a valuable tool, facilitating the controlled and gradual distalization of the upper arch (5, 9-10). The 8-month treatment duration and the minimal number of appointments (three in total) underscore the efficiency of this contemporary orthodontic approach. The use of aligners allowed for discreet correction and contributed to the patient's reported minimal discomfort and successful adaptation to the treatment. The restoration of incisors and the improvements in facial aesthetics demonstrate the multifaceted benefits of addressing Class II malocclusion in mature patients. Beyond the conventional goals of dental alignment, this case emphasizes the potential for orthodontic interventions to positively impact the overall facial profile and patient satisfaction, aligning with the growing emphasis on comprehensive aesthetic outcomes in orthodontic care (11).

Retention strategies (SPARK aligners TRUGEN XR materials) were crucial in maintaining the achieved results. As age-related changes in dentition and soft tissues continue, a well-planned retention phase becomes paramount for the long-term stability of the orthodontic correction (12-13).

While our case presents a successful outcome, it is essential to acknowledge the individualized nature of orthodontic treatment and the need for tailored approaches based on each patient's specific needs and characteristics.

Our case contributes to the evolving landscape of orthodontic management strategies, showcasing the potential for effective, efficient, and aesthetically pleasing outcomes in treating complex malocclusions in older age groups.

CONCLUSIONS

This case report underscores the effectiveness of the Malagón method in the upper arch distalization managing the lower third of the face in a 54-year-old male patient with Class II malocclusion. The restoration of incisors and the rejuvenation of the lower facial profile were successfully achieved using Spark Aligners within a concise treatment timeframe. This approach provides valuable insights into the potential of upper distalization as a comprehensive solution for addressing functional and esthetic concerns associated with aging-related changes in the dentofacial region.

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