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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%)

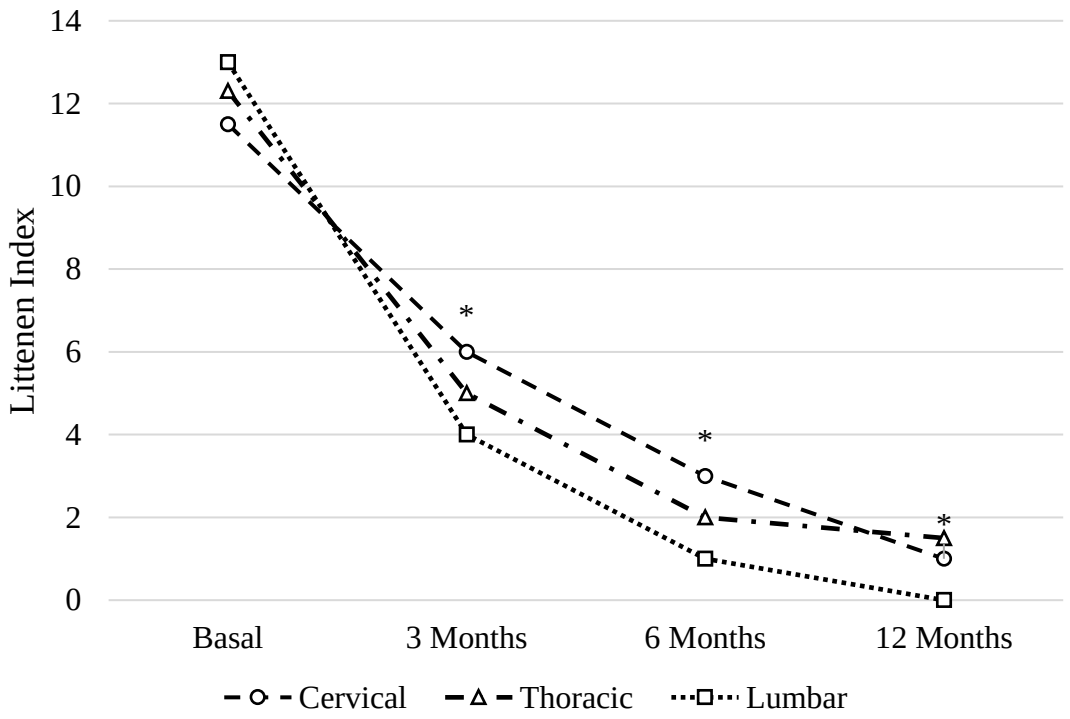

Fig. 1. *Evolution of patients according to the Lattinen scale and according to the location of the hernia;* ***represents significant differences ($p<0.05$) compared to baseline time. No significant differences ($p>0.05$) were found between the 3 locations evaluated in each time period.*

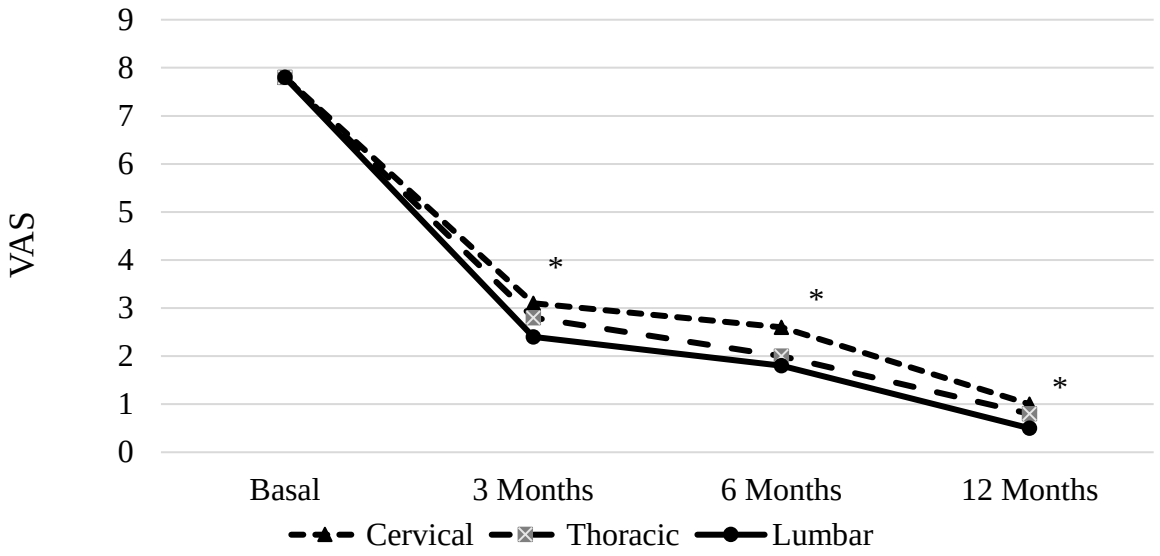

Fig. 2. *Evolution of patients according to the VAS scale; *****represents significant differences (p<0.05) compared to baseline time. No significant differences (p>0.05) were found between the 3 locations evaluated in each time period.*

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

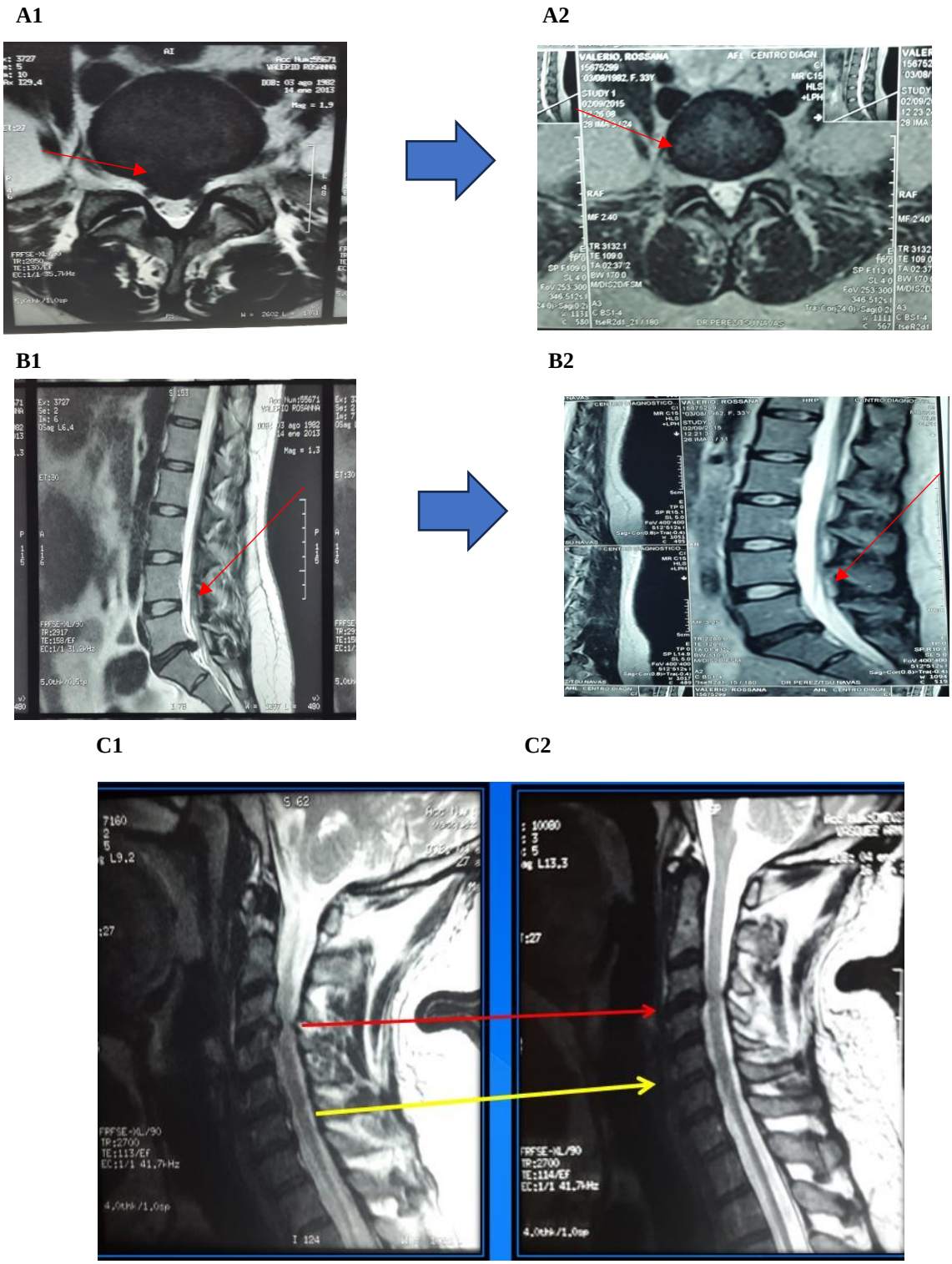

Fig. 3. *Representative photographs of the evolution of patients with herniated discs.* ***A1****): patient with L5-S1 disc herniation axial cut T2 pretreatment;* ***A2****): patient A1 post-treatment (6 months post-dicolysis);* ***B1****): patient with herniated disc L5-S1 sagittal cut T2 pre-treatment;* ***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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