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Effects of Ozone Disc Nucleolysis in Management of Herniated Lumbar Intervertebral Disc: A Retrospective Single-Center Study of 149 Patients

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Background: Lower back pain is a common problem in the general population. Medical treatment is the first choice for patients without severe pain and major motor weakness. If patients do not benefit from conservative treatment, minimally invasive treatment is recommended. Ozone nucleolysis has recently been used to reduce pain and inflammation in herniated discs and other spinal conditions. This retrospective study from a single center aimed to evaluate the effects of ozone disc nucleolysis in the management of 149 patients with herniated lumbar intervertebral discs from 2022 to 2024.

Material/Methods: Between 2022 and 2024, intradiscal ozone nucleolysis was performed under operating room C-arm scopy in 149 patients who received medical treatment and physical therapy without surgical indication but did not benefit, and the results were evaluated retrospectively. Visual Analog Scale (VAS) scores and Oswestry Disability Index (ODI) scores were recorded before the procedure, and at 1 month, 3 months, 6 months, and 1 year.

Results: The study enrolled 149 patients, comprising 61 males and 88 females, with an overall mean age of 43.9±4.7 years. The procedure was performed as 1 level in 138 patients and 2 levels in 11 patients. Among patients who underwent procedures based on lumbar MRI findings, 15 involved the L3-L4 intervertebral disc, 3 involved both the L3-L4 and L4-L5 discs, 90 involved the L4-L5 disc, and 31 involved the L5-S1 disc. Post-procedure VAS scores were significantly different at 1 month and 6 months ($P<0.05$). Post-procedure ODI scores were also significantly different at 1 month and 6 months.

Conclusions: Due to its low complication rate and effectiveness in treating lumbar disc herniation, ozone chemonucleolysis should be considered for use in patients who do not have a surgical indication or do not accept surgical intervention and did not benefit from medical treatment and physical therapy.

Keywords: Low Back Pain • Ozone • Lumbar Vertebrae • Intervertebral Disc Chemolysis • Intervertebral Disc Disease

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Introduction

The incidence of low back pain is high in people aged 30-50 years, which is considered the most productive age [1]. Approximately 80% of people have low back pain at some point in their lives [1]. Its prevalence is 60-80%, the incidence is 5%, and 1-3% of low back pain cases involve lumbar pathology that requires surgical intervention. In most cases, the prognosis is good and recovery occurs without medical treatment or intervention of any kind. The male-to-female ratio is equal [2].

In many cases, lower back pain is related to muscles and ligaments. However, in some cases, lower back pain and accompanying sciatica is due to lumbar discopathy. In most patients with lumbar discopathy, no specific cause can be found [1].

Lumbar disc herniation is a clinical condition that can often be resolved with medical treatment. Drop foot and cauda equina syndrome emergency constitute important indications for surgery. Surgery may be required for patients with persistent radicular pain that does not improve despite 4-6 weeks of conservative treatment and progressive neurological deficits during follow-up. Neurological deficit, especially if it includes motor losses, is considered a surgical indication [3].

Numerous therapeutic strategies have been developed for the treatment of pain associated with lumbar disc herniation. These range from conservative options such as medical treatments (eg, paracetamol, steroids, nonsteroidal anti-inflammatory drugs, and muscle relaxants), rehabilitation programs, and exercises, to algological interventions such as facet blockages, minimally invasive interventional treatments (eg, mechanical, laser, heat), and nucleolysis [2]. Medical treatment is the first choice for patients with pain but no major motor weakness. If patients do not benefit from conservative treatment, minimally invasive treatment is recommended [2].

Invasive pain interventions such as radiofrequency thermocoagulation and laser nucleoplasty are also used in conjunction with ozone for intradiscal application. In recent years, medical ozone applications have gained acceptance overall and have found application as an option for the effective treatment of many diseases. Intradiscal ozone application has become one of the most commonly used methods among invasive intradiscal procedures today [4].

Medical ozone has been introduced to take advantage of its pain-relieving activity, anti-inflammatory properties, and antiseptic activity [4]. Medical ozone is an allotrope of oxygen, consisting of 3 oxygen atoms, making it the most active form of oxygen. It exhibits strong activity and exerts a potent oxidizing effect on proteoglycans, lipids, bacteria, viruses, and other microorganisms [4]. When water retention is reduced by ozone's ability to break down proteoglycans and neutralize the negative charge of sulfate side chains, it leads to a decrease in hernia volume. Intra-disc applications have been utilized to harness this mechanism [5,6]. Ozone reduces inflammation around the nerve and helps shrink disc volume.

Therefore, this retrospective study from a single center aimed to evaluate the effects of ozone disc nucleolysis in the management of 149 patients with herniated lumbar intervertebral discs from 2022 to 2024.

Material and Methods

Ethics Statement

The Declaration of Helsinki 2013, ICJM recommendations, COPE"s International Standards for Editors and Authors, and other relevant bioethical guidelines were considered during the conduct of the study. The Health Sciences University Ethics Committee approved the study (no. 09/2023-137).

Inclusion Criteria

- Patients with back pain and/or radicular pain associated with protrusion or extruded intervertebral disc herniation on magnetic resonance imaging (MRI).
- Cases that received medical treatment for 4-8 weeks and did not benefit from conservative treatment were evaluated by a physical therapist.
- Numbness throughout the dermatomal distribution corresponding to the herniated disc as seen on MRI.
- The patient accepts the procedure to be performed.
- Cases that are stated by anesthesiologists and relevant consultant physicians as being at high risk due to age, comorbidities, and chronic diseases, and who do not accept surgery.

Exclusion Criteria

- Clinical evidence of motor deficit corresponding to a herniated disc.
- Positive red flags for axial skeleton-like infection, trauma, or malignancy.
- The patient rejects the procedure to be performed.
- Patients with sequestered disc herniation.
- Uncontrolled hypertension.
- Hyperthyroidism.
- Uncontrolled diabetes mellitus.
- Glucose-6-phosphate dehydrogenase enzyme deficiency.
- Neurologic deficits.
- Liver and kidney failure.
- Coronary artery disease.

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Study Design

In this study, 149 patients who presented to the outpatient clinic between 2022 and 2024 with lumbar disc-related pain, and who either did not require surgical intervention or declined it, were included. Patients with low back pain and/or sciatica, who attended outpatient clinic consultations, and underwent neuroimaging revealing lumbar protrusion or extruded disc herniation, were also included. Patients with a clear surgical indication before the procedure were excluded. For the remaining cases, initial medical treatment was administered for an average of 4-8 weeks, followed by referral to a physical therapy rehabilitation physician, with subsequent follow-up appointments. If symptoms did not improve during follow-up, algological interventions, including ozone chemonucleolysis, were considered. Detailed information about the procedure, along with potential complications, was provided to patients who then provided informed consent.

Ozone chemonucleolysis injections were performed under local anesthesia and sterile conditions in an operating room equipped with C-arm fluoroscopy. Each patient underwent a 1.5 Tesla lumbar MRI interpreted by a spinal neuroradiologist before the procedure. After the procedure, a follow-up MRI was conducted at the same facility using the same device, and it was interpreted by the same neuroradiologist at the 2-month follow-up.

VAS scores were recorded before the procedure and at 1 month, 3 months, 6 months, and 1 year. ODI scores were recorded before the procedure and at 1 month, 3 months, 6 months, and 1 year.

Radiological images of all patients were evaluated by accessing the hospital database system. Informed consent was obtained from all patients before the procedure.

Procedure

The entire surgical procedure was performed by an experienced surgeon who has been working as a specialist physician for 14 years and has been performing algological interventions for approximately 16 years. The patient was placed on the surgical table in the prone position. The abdomen was supported with pillows. The patient was monitored and vascular access was established. The patient was stained with povidone-iodine 3 times and covered with sterile drapes. Imaging was conducted using C-arm fluroscopy (Philips Corp., The Netherlands).

The level was first determined with C-arm fluroscopy. Subsequently, a 20-cm, 22-G spinal needle was inserted with oblique fluoroscopy views to ensure accurate placement. Local anesthetic (procaine) was applied to the point where the level was determined approximately 10 cm lateral from the midline on the side where the patient had pain, and the first needle attempt was made at a 45-degree angle towards the medial side. The procedure was started under approximately 35-40 degrees oblique fluroscopy. The procedure proceeded by targeting the disc space behind the facet joint, and its placement was confirmed again using anterior-posterior (A-P) and sagittal images (**Figures 1-4**). After making sure that the disc space was entered, the needle was advanced by an average of 3 cm. A 25-mL mixture of oxygen-ozone (O2-O3), with a concentration of 30 micrograms/mL of ozone, was administered intradiscally. Subsequently, the patient underwent a neurological examination. Following a 2-h observation period in the ward, the patient was discharged.

Statistical Analysis

SPSS 15.0 for Windows was utilized for statistical analysis. Results within the groups were expressed in both numerical values and percentages, and descriptive statistics, including the mean, highest and lowest values, and standard deviations, were calculated and examined. For comparisons between 2 independent groups, the *t* test was employed if the data had normal distribution, and if the data deviated from normality, the Mann-Whitney U test was utilized instead. Additionally, within-group analyses were conducted using the Wilcoxon test for paired samples. To address the issue of multiple comparisons in nonparametric data, Bonferroni adjustment was applied. A significance level of $P<0.05$ was selected for interpreting the results, indicating statistical significance.

Results

Patients Characteristics

We included 149 patients in the study, comprising 61 males and 88 females, with an overall mean age of 43.9±4.7 years (range, 22-71 years) (**Table 1**). The procedure was applied at a single level for 138 patients and 2 levels for 11 patients. Among the cases, 15 involved the L3-L4 intervertebral disc, 3 involved both the L3-L4 and L4-L5 discs, 90 involved the L4-L5 disc, and 31 involved the L5-S1 disc (**Table 2**).

Analysis of Patients' VAS and ODI Scores

Statistically significant results were obtained when the pre-procedure VAS scores (7.5±1.2) were compared with the 1-month (3.2±0.9) and 6-month VAS scores (2.4±0.7) after the procedure ($P<0.05$) (**Table 3, Figure 5**). Statistically significant results were obtained when the pre-procedure ODI scores (21.7±8.2) were compared with the 1-month (12.6±7.3) and 6-month ODI scores (11.8±7.7) after the procedure ($P<0.05$) (**Table 3, Figure 6**).

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Figure 1. Obliq scopy image during the intradiscal ozone procedure.

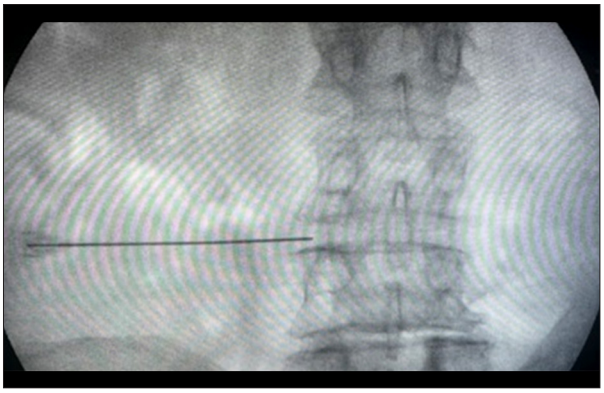

Figure 2. A-P scopy image during the intradiscal ozone procedure.

Table 1. Demographic properties.

Age	43.9±4.7 years
Gender (%)	61 (40.9%) males and 88 (59.1%) females
Male	61
Female	88
BMI	24.7±2.4
Duration of pain (Months)	3.2

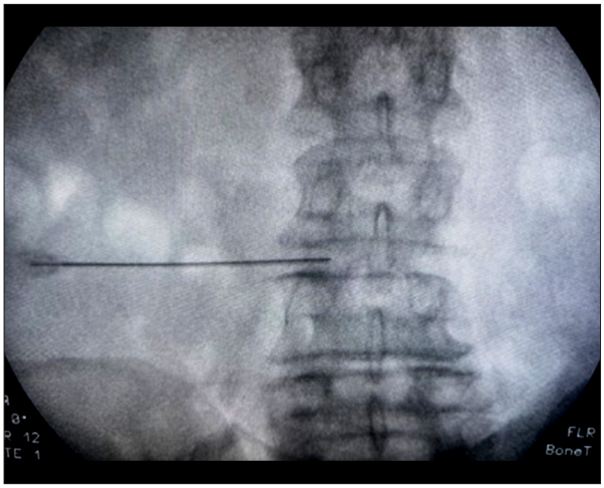

Figure 3. A-P scopy image during the intradiscal ozone procedure.

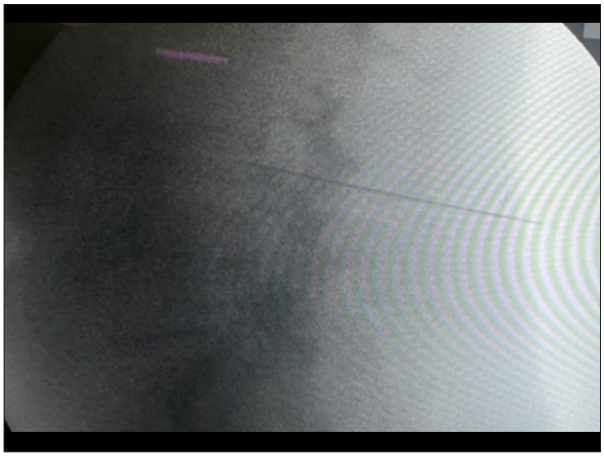

Figure 4. Lateral scopy image during the intradiscal ozone procedure.

Table 2. Applied lumbar disc level with intradiscal ozone.

	Mean±SD (Min-Max)	
	n	%
Level of LDDD		
L3-L4	20	13.4
L4-L5	90	60.4
L5-S1	34	22.8
L3-L4+L4-L5	5	3.3

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Table 3. Pain and disability changes in groups.

	VAS Mean±SD	ODI Mean±SD
1st day	7.5±1.2	21.7±8.2
1st month	3.2±0.9	12.6±7.3
6 months	2.4±0.7	11.8±7.7
P	<0.001	<0.001

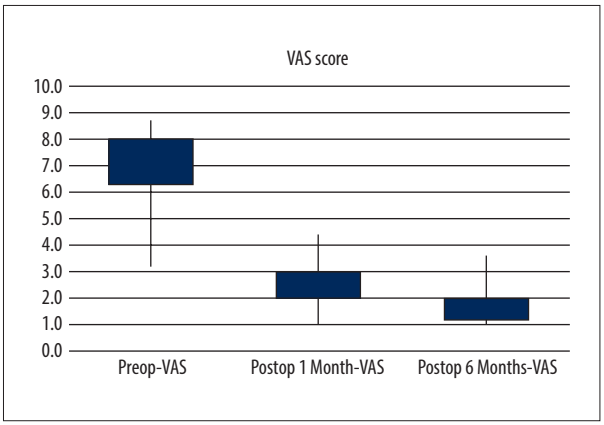

Figure 5. Preoperative/postoperative Visual Analog Scale (VAS) score.

Post-Procedure Patient Outcomes

Pre- and post-procedure MRIs of the patients were evaluated by the radiologist in the same sagittal and axial planes. They were classified as completely regressed (90-100%), moderately regressed (40-80%), and mildly regressed (10-30%). In this measurement, the disc size was measured and evaluated. In the 2nd postoperative month, it was observed that the disc was completely regressed in 89 patients, moderately regressed in 25 patients, mildly regressed in 10 patients, and the hernia was not regressed in the remaining 25 patients (**Figures 7, 8**).

Regressions were detected in the 2nd month of the control lumbar MRI. In the 1st month after the procedure, 3 patients were operated on. These patients were evaluated with a lumbar MRI in the 1st month after the procedure, as the pain did not subside and the sciatalgia became more pronounced. It was observed that the patient's discs enlarged and the root and canal compression increased. The patients were offered surgery. Patients who agreed to surgery underwent a microsurgery discectomy.

Discussion

In our study, 149 patients were followed up for an average of 1 year. Four of the ozone-treated patients required surgical

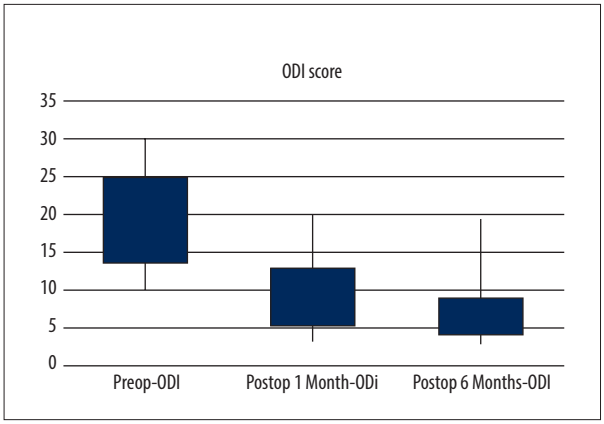

Figure 6. Preoperative/postoperative Oswestry Disability Index (ODI) score.

intervention, while 6 patients did not require surgical intervention but experienced persistent symptoms. There were no serious complications in the patients. Statistically significant decreases were achieved in the 1-month and 6-month VAS scores and ODI scores.

Ozone was initially employed as an antiseptic in operating rooms and for disinfecting surgical instruments. Subsequently, it found was used in medical practice for treating tuberculosis. Historical records indicate its use in treating soldiers' wounds during the First World War [7]. Today, ozone is utilized in various capacities and dosages for treating numerous diseases. In cases of lumbar disc disease, an ozone-oxygen mixture can be intradiscally injected into the facet joint or paravertebral muscles [6].

In lumbar disc herniation (LDH), ozone therapy (OT) was first introduced in Italy during the 1980s. Following intradiscal injection, ozone begins to dissolve in the intradiscal fluid within the nucleus pulposus. The dissolved ozone then reacts with proteoglycans and glycosaminoglycans present in the nucleus pulposus structure. These reactions lead to oxidation and disruption of the three-dimensional configuration of macromolecules such as galactose, glucuronic acid, glycine, and 4-hydroxyproline. Consequently, reabsorption begins, resulting in decreased pressure within the disc. This reduction in disc pressure alleviates pressure on the nerve root, consequently providing pain relief. The dosage of ozone gas can be adjusted to 25-40 µg/mL [8].

In addition to intradiscal ozone therapy, transforaminal steroid injections or lumbar caudal steroid injections can also be performed in the same session. Comparative studies in the literature have combined these applications. For instance, in 2013 Zhang et al conducted a study involving 172 patients with lumbar disc herniation aged 23-59 years. These patients were randomly divided into 2 groups: one group received only ozone into

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Figure 7. Preoperative/postoperative 2-month T2 sagittal MRI.

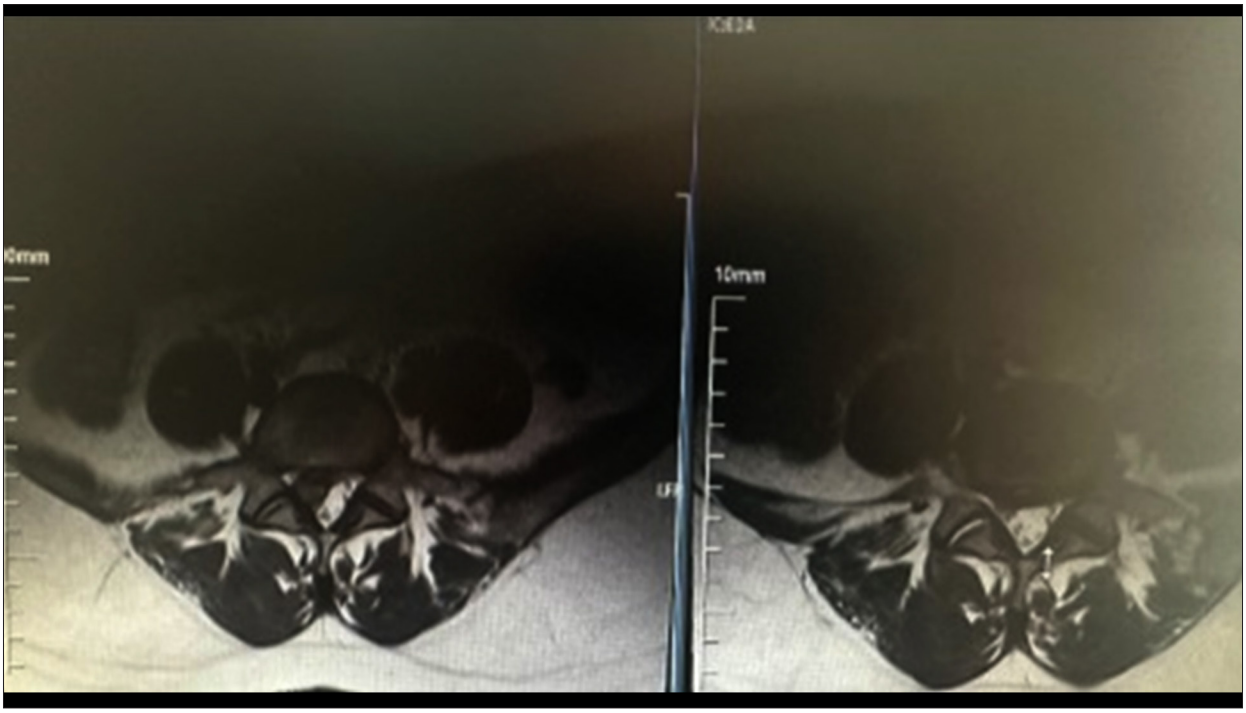

Figure 8. Preoperative/Postoperative 2- month T2 sagittal MRI.

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the disc and foramina, while the other group received ozone and 1 mg of betamethasone. VAS and JOA (Japon Orthopedic Association) scores were monitored at 3 weeks, 6 months, and 12 months of follow-up to evaluate clinical outcomes, showing decrease in VAS score from 7.68 to 2.17 in Group A and from 7.49 to 2.23 in Group B, with notable improvements in mean JOA score and improvement rate in both groups at each follow-up. Moreover, at the 3-week follow-up, the JOA recovery rate of Group B was significantly higher than that of Group A. However, no significant differences were found between the 2 groups at 6 and 12 months. Therefore, oxygen-ozone nucleolysis appears to provide excellent pain relief in most hernia patients who do not respond to conservative treatment. Additionally, we found that there was no significant statistical differences between the treatment groups receiving oxygen-ozone and steroid combination and those receiving oxygen-ozone alone at 6-month and 12-month follow-ups, and therefore, O2-O3 appears to be effective as an analgesic and should be the first-choice treatment before resorting to surgery or when surgery is not possible [9]. In our study, there were significant improvements in VAS score and ODI score at 1-month and 6-month follow-ups, and there were significant regressions of the herniated disc in the second month of the control lumbar MRI.

In a comprehensive multicenter study involving 8000 patients, ozone therapy was evaluated using the VAS and ODI in terms of pain, functional improvement, and complication rate. The results revealed that ozone therapy yielded similar successful outcomes to surgical discectomy for lumbar disc herniation in patients aged 13-94 years, with a complication rate below 0.1% [10].

A 2021 study by Clavo et al revealed that intradiscal ozone injection reduced the frequency of patients needing surgery [11,12], and the rate of subsequent surgery was 20% in the group in which intradiscal ozone injection was performed [11]. The general rate of complications related to ozone therapy is 0.1% [13]. Giudice et al reported a case of bilateral vitreoretinal hemorrhage due to high-volume application [14]. Additionally, cases of headache, paresthesia, and hypoesthesia due to intrathecal administration have been described [15]. Corea et al reported a case ofvertebrobasilar stroke [16]. In our series of 149 patients, spondylodiscitis was observed in 1 case.

A 2023 study by Kelekis et al assessed 49 patients to determine whether intradiscal ozone therapy could reduce the rate of surgery in patients who present with back and leg pain who do not benefit from conservative methods and who are candidates for lumbar microsurgery, showing the need for surgery was reduced by 71%. In our study, intradiscal ozone was applied to cases that did not benefit from conservative methods, and by reducing pain scores and ODI index, the rate of surgery was reduced [12].

Ghatge et al, in their study on 2089 patients in 2023, evaluated patients with lumbar disc herniation and applied intradiscal ozone therapy with their VAS and ODI scores. At the end of the study, ozone disc nucleolysis was found to be optimally effective and most effective for herniated lumbar intervertebral disc with a significant decrease in the disability rate. They stated that it is a less invasive treatment option [17].

Steppan et al performed a meta-analyses of 12 studies on oxygen/ozone therapy outcomes for approximately 8000 patients from multiple centers. The mean improvement was 3.9 for VAS and 25.7 for ODI. The probability of complication was 0.064%. They found that oxygen/ozone therapy for the treatment of herniated discs is an effective and extremely safe procedure [18].

A major limitation of the present study is the lack of a control or comparator group. The short follow-up period and small number of patients are other limiting factors.

Conclusions

Ozone chemonucleolysis has a low complication rate and can be effective patients with lumbar disc herniation who do not have a surgical indication or do not accept surgical intervention and did not benefit from medical treatment and physical therapy. In some cases, patients refuse spinal surgery. Although some patients are willing to undergo surgery, anesthesiologists and relevant consultant physicians may deterine they are poor surgical candidates due to high risk from age, comorbidities, and chronic diseases. Conservative treatments may be inadequate in such patients. Intradiscal ozone should be kept in mind as the primary option in such patients.

Department and Institution Where Work Was Done

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Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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