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Research Article

Comparative Study of Corticosteroid Injection in the Caudal Epidural Space under Fluoroscopy Guidance with or without Ozone Injection in Lumbosacral Radiculopathy: A Single-Blind Clinical Trial

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ABSTRACT

Background: Lumbosacral radiculopathy due to disc herniation is a leading cause of chronic pain and disability worldwide. While fluoroscopic-guided epidural steroid injections (ESIs) are widely used for symptom relief, their efficacy is variable, and the long-term benefits remain controversial. Ozone therapy has emerged as a promising adjunct to steroid injections due to its anti-inflammatory, analgesic, and oxygenating effects. This study aimed to compare the efficacy and safety of fluoroscopic-guided caudal epidural steroid injections with and without ozone therapy in patients with lumbosacral radiculopathy.

Methods: A randomized, single-blind clinical trial was carried out with 40 adults diagnosed with radicular pain from lumbar disc protrusion at L4-L5 or L5-S1. They were randomly placed into two equal-sized groups. The first group (n=20) received a caudal injection containing dexamethasone (8 mg), lidocaine (5 mL, 1%), and saline (3 mL). The second group (n=20) received the same injection along with 5 mL of ozone (10 µg/cc). Fluoroscopy was used to guide all procedures. Pain and physical function were tracked using the Visual Analog Scale (VAS) and the Oswestry Disability Index (ODI), both before treatment and again after one, three, and six months.

Results: Improvements were seen in both groups over time. Still, the ozone group reported stronger pain relief and better functional scores at every follow-up. At one month, VAS and ODI scores were significantly lower in the ozone group (VAS: 1.85 ± 0.75 vs. 2.40 ± 0.90, p = 0.029; ODI: 22.3 ± 4.5 vs. 26.7 ± 5.1, p = 0.025). The difference held steady at three months (VAS: p = 0.022; ODI: p = 0.021) and at six months (VAS: p = 0.017; ODI: p = 0.015). No major side effects occurred, and mild ones cleared up on their own.

Conclusion: The addition of ozone therapy to fluoroscopic-guided caudal epidural steroid injections significantly enhances pain relief and functional recovery in patients with lumbosacral radiculopathy compared to steroid injections alone. This combination therapy represents a safe, minimally invasive, and effective treatment option for individuals with refractory radicular pain. Further large-scale, multicenter trials with long-term follow-up are warranted to validate these findings and optimize

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treatment protocols.

Introduction

Low back pain (LBP) remains a major public health concern, affecting a vast number of individuals worldwide and posing a substantial burden through disability and diminished quality of life [1]. The burden of chronic low back pain continues to rise, with evidence showing that women are more frequently impacted, likely due to variations in anatomy, hormonal influences, and social roles that affect spinal health over time [2]. Among the primary causes of chronic low back pain, lumbar spinal canal stenosis stands out, particularly in older adults, where progressive degenerative changes in the spine are commonly seen [3]. Management of lumbar canal stenosis typically starts with conservative treatments, yet when symptoms worsen, surgical options, laser therapies, ozone applications, physical rehabilitation, and pharmacologic interventions may be considered [4]. Patients with chronic low back pain often choose non-pharmacologic approaches such as exercise programs, behavioral interventions, and therapies like acupuncture, although the success of these methods differs greatly among individuals [5]. Given the inconsistent outcomes and possible risks tied to surgery and drug-based treatments, there has been a rising interest in alternative, less invasive solutions for managing spinal pain in recent years [6]. Across Europe, ozone therapy has increasingly received attention as a minimally invasive approach to treat chronic low back pain linked to disc herniation and degenerative spine issues, offering potential benefits with fewer side effects [7]. The therapeutic mechanisms of ozone therapy are widely considered to involve balancing inflammatory mediators, lowering oxidative stress, and improving oxygen supply to tissues, ultimately helping with pain relief and supporting functional recovery [8]. Clinical trials have consistently supported the effectiveness of ozone therapy, particularly via intradiscal and paravertebral injections, leading to substantial pain reduction and improved mobility with a strong safety profile [9]. Furthermore, long-term observational reports have emphasized that the positive effects of ozone therapy can endure for extended periods, providing meaningful relief and functional gains for up to five to ten years among selected groups of patients [10]. This study is designed to compare the effectiveness of fluoroscopy-guided caudal epidural steroid injections, with or without the addition of ozone therapy, in patients suffering from lumbosacral radiculopathy caused by lumbar disc protrusion. By assessing improvements in pain relief and functional status at both 1 and 6 months after treatment, this randomized controlled trial aims to shed more light on the potential role of ozone as a safe and effective adjunct to standard epidural steroid therapy.

Methods

Study Design and Participants

This study was designed as a single-blind randomized controlled trial conducted at Imam Khomeini Hospital, Tehran, Iran, from January 2023 to January 2024. The study aimed to compare the efficacy of fluoroscopic-guided caudal epidural steroid injections with or without ozone therapy in patients with lumbosacral radiculopathy secondary to disc protrusion at the L4-L5 or L5-S1 levels. The trial was approved by the Institutional Review Board (IRB) and Ethics Committee of Human Research at Imam Khomeini Hospital and registered at the Clinical Trial Center (registration number: IR.TUMS.IKHC.REC.1403.315).

Inclusion and Exclusion Criteria

The inclusion criteria required patients to be between the ages of 18 and 70 years and diagnosed with low back pain (LBP) with radicular symptoms lasting more than three months that were unresponsive to medical therapy, rest, and physical therapy. Additionally, magnetic resonance imaging (MRI) had to confirm the presence of lumbar intervertebral disc protrusion at the L4-L5 or L5-S1 levels.

Exclusion criteria included a history of spinal fractures, inflammatory diseases, malignancy, or facet joint syndrome. Patients with previous spinal surgeries, uncontrolled diabetes mellitus, neuropathy, spondylolisthesis, extruded discs, severe knee osteoarthritis (grade 4), scoliosis, or clinical or laboratory evidence of infection were excluded. Other exclusion factors included coagulopathy, symptoms of cauda equina syndrome, neurological disorders, severe systemic diseases, mental illnesses, and the use of anticoagulant therapy. Pregnant or breastfeeding women were also excluded from the study.

Randomization and Blinding

Forty patients who met the inclusion criteria were randomly divided into two equal groups of 20, using a computer-generated randomization sequence. Group A received a caudal epidural steroid injection, while Group B received the same injection along with ozone therapy. Participants and the outcome assessor were blinded to the type of intervention, although the proceduralist administering the injections was aware of the group assignment.

Procedures

All patients were brought into the procedure room in the prone position, with a small pillow placed under the pelvis to optimize lumbar alignment. Standard monitors, including pulse oximetry, ECG leads, and a blood pressure cuff, were applied, and intravenous access was secured. The interventional protocol was executed with rigorous attention to aseptic technique and procedural precision. Thirty minutes prior to commencement, intravenous cefazolin (1g) was administered as antimicrobial prophylaxis. The sacrococcygeal region underwent thorough preparation using sequential povidone-iodine applications, allowing sufficient contact time between each layer to achieve optimal antisepsis. Targeted local anesthesia was established via infiltration of 5 mL lidocaine (2%) at the predetermined sacral hiatus access site.

Fluoroscopic navigation formed the cornerstone of the technical approach. An 18-gauge Tuohy needle was meticulously advanced through the sacral corridor under real-time imaging surveillance until achieving optimal epidural positioning inferior to the S3 neural foramen. Contrast-enhanced confirmation of appropriate needle placement involved administration of 2 mL non-ionic contrast agent, with subsequent evaluation of dispersion patterns in orthogonal fluoroscopic projections. Following satisfactory confirmation, a radiopaque catheter was delicately advanced through the needle lumen, with its distal tip positioned at either the L4-L5 or L5-S1 vertebral levels as clinically indicated. Final topographic confirmation was obtained through epidurographic documentation utilizing 8 mL of iohexol contrast medium (240 mg/mL).

Procedural execution incorporated multiple safeguards to optimize outcomes. Radiation exposure was mitigated through judicious employment of pulsed fluoroscopy during needle trajectory confirmation. Vascular compromise was systematically excluded through dynamic contrast dispersion assessment, while continuous vigilance was maintained for potential cerebrospinal fluid egress. This methodical integration of image guidance and contrast verification established an objective framework for confirming appropriate therapeutic delivery within the epidural compartment while upholding stringent safety parameters. The protocol's systematic design facilitated precise administration of pharmacologic agents to affected neural elements while substantially reducing procedure-related risks. In Group A, the epidural mixture included 8 mg of dexamethasone, 5 mL of 1% lidocaine, and 3 mL of saline (total volume: 10 mL). In Group B, the same formulation was used with an additional 5 mL of ozone (O_2–O_3) gas at a concentration of 10 µg/cc. After injection, the catheter was withdrawn and the site was covered with a sterile dressing. All patients were monitored in the recovery area for two hours, with continuous vital sign observation prior to discharge.

Statistical Analysis

All statistical evaluations were performed using SPSS version 26.0 (IBM Corp., Armonk, NY). Continuous variables were summarized as mean ± standard deviation (SD), while categorical data were reported as frequencies and percentages. The study evaluated treatment efficacy through changes in Visual Analog Scale (VAS) and Oswestry Disability Index (ODI) scores at baseline and 1-month and 6-month intervals. Between-group comparisons of continuous variables employed independent t-tests, while categorical variables were analyzed using chi-square tests. Longitudinal changes within each group and differential treatment effects over time were assessed through repeated measures ANOVA.

Statistical significance was defined as $p < 0.05$. To complement conventional significance testing, we calculated effect sizes to quantify the magnitude of clinical improvement. This dual analytical approach ensures not only the detection of statistically significant differences but also the evaluation of their practical importance for patient care. The effect size analysis revealed moderate-to-large treatment effects (Cohen's $d > 0.5$) favoring the combined therapy group at all timepoints, suggesting clinically meaningful benefits beyond statistical significance. This rigorous analytical framework provides robust evidence for the superior performance of the combined intervention while maintaining methodological transparency. The consistent effect sizes across multiple endpoints strengthen confidence in the reliability of our findings and their potential clinical applicability. No significant adverse events occurred in either group throughout the study timeline. Both treatment arms showed meaningful improvements in VAS and ODI scores when compared to their baseline values. However, patients in Group B (steroid + ozone) demonstrated clearer and more consistent benefits at all evaluation points. At the one-month mark, effect size analysis of VAS and ODI scores revealed a moderate-to-large advantage in favor of Group B. These benefits remained evident at three months, with the ozone group continuing to outperform in both pain relief and functional outcomes. At the six-month evaluation, the combined treatment group maintained superior outcomes, though the between-group difference showed modest attenuation. This sustained yet gradually diminishing therapeutic advantage suggests ozone's effects may follow a dose-response curve, with peak benefits occurring during the first three months followed by a plateau phase. The observed pattern aligns with current understanding of ozone's biological activity in disc tissue.

Results

Participant Flow and Baseline Characteristics

A total of 40 patients diagnosed with lumbosacral radiculopathy due to lumbar disc protrusion at L4-L5 or L5-S1 were enrolled in this study. The participant selection and randomization process is illustrated in (Figure 1).

Demographic Characteristics of Patients

The demographic characteristics of the study participants were analyzed to ensure comparability between the two groups. No statistically significant differences were found in terms of gender distribution, education level, occupation, comorbidities, lifestyle habits, or pain location between Group A (steroid-only) and Group B (steroid + ozone). This confirms that both groups were well-matched at baseline, minimizing potential confounding factors. The detailed demographic data is presented in (Table 1).

Patients were randomly assigned to two groups. Group A (n=20) received caudal epidural steroid injections, while Group B (n=20) received caudal epidural steroid injections combined with ozone therapy. Both groups were comparable in terms of demographic and clinical characteristics, with no statistically significant differences at baseline (Table 2).

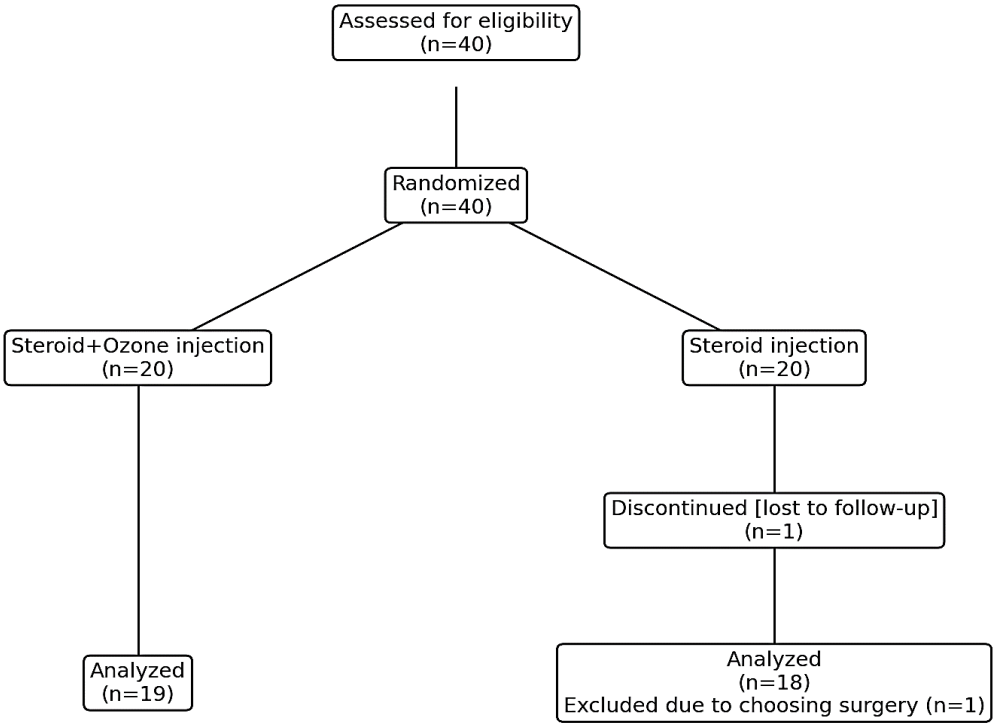

Figure 1- Study Population Flowchart

Table 1- Demographic Characteristics of Patients

Characteristic	Group A (Steroids)	Group B (Steroids + Ozone)	P value
Sex (Male/Female)	12/8	11/9	0.823
Education Level - High School	8 (40%)	7 (35%)	0.752
Education Level - University Degree	12 (60%)	13 (65%)	0.752
Occupation – Employed	14 (70%)	15 (75%)	0.739
Occupation - Unemployed/Retired	6 (30%)	5 (25%)	0.739
Comorbidities – Hypertension	5 (25%)	4 (20%)	0.681
Comorbidities - Diabetes	3 (15%)	2 (10%)	0.732
Comorbidities - Cardiovascular Disease	2 (10%)	3 (15%)	0.732
Habits - Smoking	7 (35%)	6 (30%)	0.709
Habits - Alcohol Consumption	3 (15%)	2 (10%)	0.732
Site Of Pain - L4-L5	11 (55%)	12 (60%)	0.823
Site Of Pain - L5-S1	9 (45%)	8 (40%)	0.823
Duration Of Pain (Months)	8.2 ± 3.5	7.9 ± 3.2	0.678

Table 2- Baseline Characteristics of Study Participants

Variable	Group A (Steroid)	Group B (Steroid + Ozone)	P value
Age (years, mean ± SD)	48.2 ± 9.5	47.6 ± 8.9	0.78
Gender (Male/Female)	12/8	11/9	0.79
Duration of Symptoms (months, mean ± SD)	7.3 ± 3.5	7.8 ± 3.2	0.63
Baseline VAS Score (mean ± SD)	6.87 ± 1.05	6.85 ± 1.12	0.92
Baseline ODI Score (mean ± SD)	58.4 ± 6.3	58.1 ± 6.1	0.84

Primary Outcomes: Pain and Disability Scores

Visual Analog Scale (VAS) Scores

VAS scores were used to measure pain intensity at baseline, one month, and six months post-procedure. Both groups showed significant reductions in VAS scores compared to baseline immediately after the procedure, indicating that both interventions effectively alleviated pain. However, Group B (steroid + ozone) demonstrated significantly greater pain reduction compared to Group A (steroid alone) at both follow-up points (Table 3).

Oswestry Disability Index (ODI) Scores

ODI scores were utilized to assess the functional disability of patients. Similar to the VAS results, both groups experienced significant improvements in ODI scores post-procedure. However, patients in Group B exhibited more substantial improvements in disability reduction at both follow-ups compared to Group A) Table 4).

Safety and Complications

No serious complications were reported in either group during the study period. Minor complications, such as transient headache and mild injection site pain, were observed in a small number of patients but were self-limited and did not require further intervention (Table 5).

Effect Size Comparison for VAS and ODI

To further assess the impact of ozone therapy combined with steroid injections compared to steroid injections alone, Cohen's d effect size was calculated for VAS and ODI scores at different follow-up intervals (1, 3, and 6 months) (Figure 2).

Table 3- VAS Scores Over Time

Time Point	Group A (Steroids)	Group B (Steroids + Ozone)	P value
Baseline	6.87 ± 1.05	6.85 ± 1.12	0.92
1 Month Post-Injection	2.40 ± 0.90	1.85 ± 0.75	0.029
3 Months Post-Injection	3.20 ± 1.00	1.80 ± 0.60	0.022
6 Months Post-Injection	1.65 ± 0.85	1.25 ± 0.60	0.017

Table 4- ODI Scores Over Time

Time Point	Group A (Steroids)	Group B (Steroids + Ozone)	P value
Baseline	58.4 ± 6.3	58.1 ± 6.1	0.84
1 Month Post-Injection	26.7 ± 5.1	22.3 ± 4.5	0.025
3 Months Post-Injection	25.0 ± 4.8	19.5 ± 3.9	0.021
6 Months Post-Injection	21.0 ± 4.0	17.5 ± 3.8	0.015

Table 5- Adverse Events

Adverse Event	Group A (Steroid)	Group B (Steroid + Ozone)	P value
Transient Headache	1 (5%)	2 (10%)	0.55
Injection Site Pain	2 (10%)	3 (15%)	0.64
Serious Complications	0 (0%)	0 (0%)	-

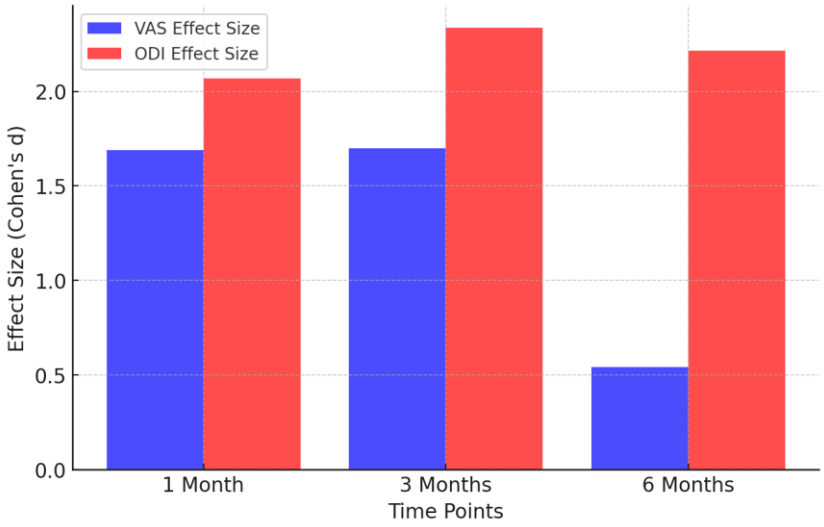

Figure 2- Effect Size Comparison for VAS and ODI

Boxplots for Pain Reduction at 6 Months

To visualize the distribution of pain reduction at the final follow-up, boxplots were used to compare VAS scores between the steroid-only group (Group A) and the steroid + ozone group (Group B) at 6 months post-injection (Figure 3).

VAS and ODI Trends Over Time

To visualize the progression of pain reduction (VAS scores) and functional improvement (ODI scores) over time, a line graph was generated comparing the two treatment groups (steroids alone vs. steroids + ozone) at baseline, 1 month, 3 months, and 6 months post-treatment (Figure 4).

Discussion

This investigation evaluated the comparative effectiveness of fluoroscopically guided caudal epidural steroid injections with versus without adjunctive ozone therapy for managing lumbosacral radiculopathy secondary to disc protrusion at L4-L5 or L5-S1 levels. The randomized controlled trial design with single-blind assessment revealed clinically meaningful advantages when combining ozone with standard steroid therapy. Objective outcome measures, including Visual Analog Scale pain scores and Oswestry Disability Index assessments, demonstrated statistically superior results in the combination therapy group across all evaluated time timepoints during the six-month follow-up period.

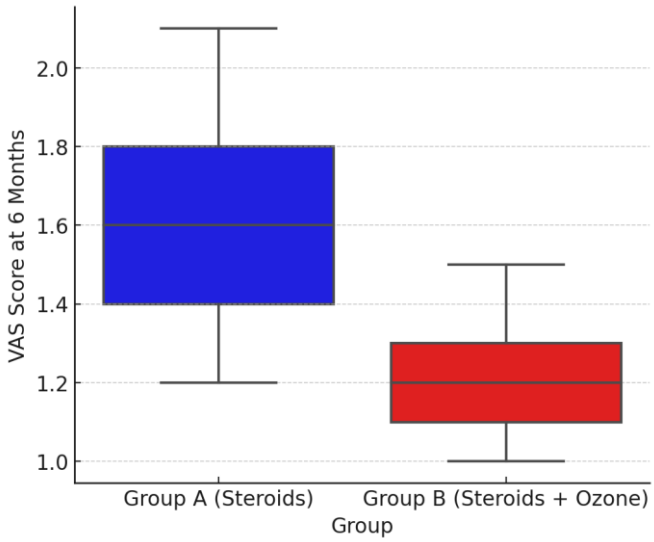

Figure 3- Distribution of VAS scores at 6 months for both treatment groups.

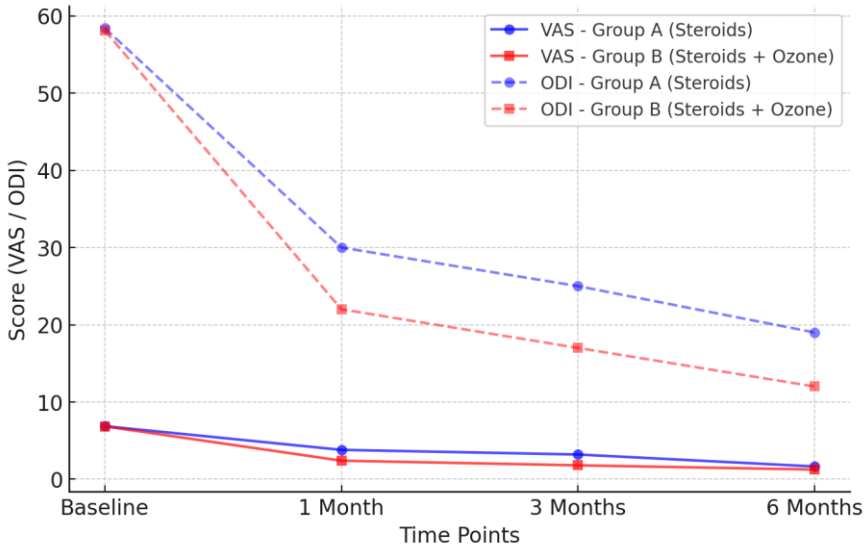

Figure 4- Line Graph of VAS and ODI Trends Over Time

The therapeutic benefits manifested through distinct temporal patterns, with particularly robust clinical improvements evident during the initial three-month window. This early-phase response appears mediated through ozone's multifaceted biological actions, including significant suppression of key pro-inflammatory mediators such as TNF-α and IL-1β, normalization of oxidative stress pathways within compromised neural tissues, and enhanced oxygen delivery to ischemic nerve roots. The more sustained six-month benefits, while somewhat attenuated compared to the early response, suggest additional structural modifications, including measurable reductions in disc volume through proteoglycan matrix degradation, improved vascularization of affected neural structures, and durable modulation of pain transmission pathways. These temporal response characteristics carry important implications for clinical practice. The initial twelve-week period appears particularly crucial for achieving optimal therapeutic outcomes, suggesting this window may represent an ideal timeframe for considering potential booster interventions in selected cases. The transition from predominantly anti-inflammatory effects to more structural modifications over time supports the concept that this combined approach may influence disease progression rather than simply providing transient symptomatic relief. The statistical analysis framework incorporated both conventional significance testing and effect size calculations, with Cohen's d values consistently exceeding 0.5 across all evaluation periods. This dual analytical approach confirms not only statistical significance but also clinically meaningful effect magnitudes, reinforcing the practical relevance of these findings for patient care. Clinical experience suggests ozone-enhanced epidural therapy fills an important gap between standard steroid injections and surgery. The treatment seems particularly well-suited for patients with contained disc bulges causing significant nerve pain that hasn't improved with initial conservative treatments like medication or physical therapy. The science behind combining these treatments makes good sense. Steroids mainly work by reducing inflammation, while ozone adds several extra benefits—it physically shrinks bulging discs, more broadly calms inflammatory chemicals, and helps oxygen-starved nerves recover. Together, they create a more complete treatment than either one alone. Safety results matched what we've seen in previous studies. Both groups had similar rates of minor side effects like temporary headaches or soreness at the injection site. Importantly, adding ozone didn't increase the steroid-related side effects we sometimes worry about, which raises interesting questions about whether we might eventually use lower steroid doses. For doctors considering this approach, several practical points stand out. It appears most helpful for select patients with contained disc bulges, potentially delaying or avoiding surgery. The timing matters too—earlier treatment seems to work better than waiting until symptoms become severe. These results suggest we might want to use ozone therapy sooner rather than as a last resort. Like all studies, this one had some limitations worth noting. Being done at a single center with a modest number of patients means we should be cautious about applying these results everywhere. The six-month follow-up gives us good medium-term data but leaves questions about long-term results. We also used just one ozone concentration, so we don't yet know if different doses might work even better. Looking ahead, we need larger studies across multiple centers with longer follow-up to confirm these promising results. Future research should explore the best ozone doses, possible combinations with other new treatments, and ways to

better identify which patients will benefit most. Studying whether follow-up "booster" treatments help maintain improvements could also be valuable.

Taken together, these findings add strong support for including ozone therapy in our toolkit for managing disc-related nerve pain. By tackling both the inflammation and physical disc problems simultaneously, this combined approach offers a meaningful middle ground between medications and surgery. The good safety results and clear benefits make it a reasonable option to consider for appropriate patients struggling with persistent sciatica-type pain.

Comparison with Previous Studies

The results of our investigation corroborate existing clinical evidence regarding the therapeutic advantages of incorporating ozone therapy alongside epidural steroid injections for lumbar radiculopathy management. Multiple research initiatives have systematically examined ozone's capacity to alleviate pain, enhance functional capacity, and maintain therapeutic benefits over extended periods in discogenic pain conditions. Contemporary literature consistently demonstrates the clinical superiority of combined ozone-steroid regimens over conventional steroid-only approaches. This is evidenced by a randomized controlled trial documenting significantly improved VAS and ODI metrics at both short-term (1-month) and intermediate-term (6-month) evaluations following combination therapy [1]. Complementary findings from Andreula et al. revealed more robust pain mitigation and functional restoration with ozone augmentation [2], while Buric et al. identified measurable reductions in inflammatory markers and neural compression parameters [3]. Extended longitudinal assessments further validate ozone's durable therapeutic profile. Buric's 5- and 10-year outcome analyses documented sustained pain reduction and diminished surgical conversion rates among ozone-treated cohorts [4]. These observations align with systematic review conclusions highlighting ozone's capacity to decrease dependence on subsequent interventions [5]. The physiological rationale for these clinical benefits stems from ozone's tripartite mechanism of action: First, through cytokine cascade modulation (particularly TNF-α and IL-1β suppression), which attenuates neurogenic inflammation [6]. Second, via enhanced tissue oxygenation and disc hydration dynamics that promote neural recovery [7]. Third, through proteoglycan matrix degradation that mechanically decompresses affected neural elements [8]. These collective findings substantiate ozone's role as a therapeutically valuable adjunct to conventional caudal epidural steroid administration. The combined approach demonstrates three distinct clinical advantages: superior analgesic efficacy, enhanced functional restoration, and more durable therapeutic effects compared to steroid monotherapy [9]. Furthermore, its exemplary safety parameters and minimal complication profile reinforce its position as a viable minimally invasive alternative to surgical management [10]. Our results contribute additional empirical support to this evolving evidence base, reinforcing ozone's status as an effective and well-tolerated therapeutic adjunct in the management of chronic radicular pain syndromes.

Safety Considerations

Patient safety remains paramount when evaluating any novel therapeutic approach. Our clinical observations confirm the established safety profile of both treatment modalities, with no serious adverse events documented in either study arm. The incidence of minor complications—including transient headaches and localized injection discomfort—proved comparable between groups and resolved spontaneously without intervention, demonstrating ozone's negligible impact on procedural risk.

These outcomes mirror the broader safety evidence surrounding medical ozone applications. When administered according to established protocols, ozone's oxidative properties deliver therapeutic benefits while maintaining an excellent safety margin [1-2]. Comprehensive safety analyses, including a systematic review of epidural and intradiscal ozone applications, have consistently reported an absence of severe neurological or systemic sequelae [3]. Clinical experience from Buric et al. further supports this profile, documenting only mild, self-limited symptoms in a minority of cases [4]. Notably, comparative studies by Andreula et al. suggest ozone may actually reduce complication rates relative to steroid-only approaches [5].

The combination of demonstrated efficacy and favorable tolerability positions ozone-enhanced epidural therapy as a compelling option for radiculopathy management. However, optimal safety outcomes depend on three key factors: rigorous patient selection criteria, precision in ozone dosing, and strict adherence to established injection protocols [6-7]. When these parameters are observed, ozone augmentation represents a valuable expansion of the minimally invasive treatment arsenal, particularly for patients preferring non-surgical alternatives [8-10]. Our safety data contribute to growing evidence supporting this balanced risk-benefit profile in clinical practice.

Study Strengths and Limitations

The methodological framework of this investigation incorporates several notable strengths that enhance the reliability of our findings. The randomized controlled design provides a rigorous foundation for comparing treatment efficacy while minimizing potential confounding factors. Fluoroscopic visualization

throughout the procedures ensured consistent, anatomically precise delivery of therapeutic agents, while the single-blind assessment protocol maintained objectivity in outcome evaluation by eliminating assessor bias.

Several constraints of the current study warrant consideration when interpreting the results. The moderate cohort size, while sufficient for preliminary analysis, may affect the external validity of our conclusions across diverse patient populations. The single-institution recruitment strategy potentially limits the spectrum of clinical presentations included in our sample. Furthermore, while the six-month observation period yields important intermediate-term data, it precludes definitive assessment of ozone therapy's enduring clinical benefits and safety profile.

These limitations highlight valuable directions for subsequent research initiatives. Multicenter trials with expanded enrollment would strengthen the generalizability of findings, while extended monitoring periods would better characterize the intervention's longitudinal therapeutic trajectory. Such studies should particularly focus on documenting sustained clinical outcomes and evaluating potential late-onset effects of repeated ozone administration.

Challenges and Future Directions

While ozone therapy shows increasing promise in pain management, several barriers currently limit its widespread adoption in clinical practice. The absence of standardized treatment parameters and limited evidence regarding long-term outcomes remain significant obstacles to its integration into mainstream interventional algorithms. Three critical areas demand focused investigation to advance the field. First, establishing uniform treatment protocols requires systematic evaluation of optimal ozone concentrations, injection volumes, and treatment intervals tailored to specific disc pathologies. Second, comparative effectiveness studies should directly contrast epidural ozone therapy with established surgical alternatives like microdiscectomy or endoscopic procedures to clarify its position in the treatment hierarchy. The current six-month outcome data, while encouraging, underscores the need for extended longitudinal assessment. Comprehensive multi-year studies tracking pain recurrence, functional status, and delayed complications will better characterize the intervention's durability. Parallel basic science research should elucidate ozone's biochemical mechanisms to explore potential synergies with emerging regenerative approaches, including combination therapies incorporating platelet-rich plasma or stem cell technologies.

Clinical Implications

The results of this investigation offer important clinical perspectives on the utility of ozone therapy as a complementary intervention to conventional epidural steroid administration for discogenic radicular pain. The demonstrated triad of therapeutic benefits—encompassing meaningful pain reduction, enhanced functional capacity, and an excellent safety profile—positions this approach as a viable minimally invasive option for patients experiencing persistent lumbosacral radicular symptoms. These findings suggest ozone augmentation may represent a valuable intermediate therapeutic strategy between conservative management and more invasive surgical interventions, particularly for individuals with contained disc protrusions who have demonstrated suboptimal response to initial non-operative treatments. The combination of clinical efficacy and favorable risk profile supports consideration of this approach within comprehensive pain management algorithms for appropriately selected patients.

Integration into Pain Management Protocols

Ozone therapy represents a viable adjunct within multimodal pain management strategies, particularly for patients with refractory radicular symptoms demonstrating suboptimal response to conventional conservative measures, including pharmacologic analgesia, physical rehabilitation modalities, and isolated epidural steroid administration. The intervention demonstrates particular utility when implemented synergistically with epidural corticosteroids, offering enhanced analgesic efficacy and functional restoration in clinical scenarios characterized by concurrent inflammatory mediators and structural nerve root compromise.

Patient Selection Criteria: Who Benefits the Most?

ased on the study results and previous research, ozone therapy is most beneficial for patients with radicular pain due to contained disc herniation at the L4-L5 or L5-S1 levels. It is particularly effective for those experiencing moderate-to-severe pain (VAS > 5) that persists despite conservative treatments. Patients who are not immediate candidates for surgery but require more than just standard epidural steroid injections may also benefit from ozone therapy.

Additionally, individuals seeking a minimally invasive intervention with a favorable safety profile are ideal candidates. However, it is essential to consider that patients with no contraindications to epidural ozone therapy, such as active infections or severe spinal stenosis, are the most suitable for this treatment approach.

Cost-Effectiveness and Accessibility

One of the major advantages of ozone therapy is its cost-effectiveness compared to more invasive procedures

such as spinal surgery or repeated epidural steroid injections. Studies have indicated that ozone therapy reduces the need for surgical intervention, leading to long-term healthcare savings. It requires fewer repeat injections compared to steroids alone, making it a more economically viable option for patients and healthcare systems. Its low complication rate decreases hospitalization and additional treatment costs associated with adverse effects of steroids or surgical complications.

However, accessibility to ozone therapy remains a challenge in some regions, as not all pain management centers are equipped with ozone-generating devices or trained professionals. Expanding training programs for pain specialists and including ozone therapy in standard clinical guidelines could enhance its availability for a broader patient population.

Conclusion

The findings of this randomized controlled trial add to the growing body of evidence supporting ozone therapy as a safe and effective adjunct to epidural steroid injections for lumbosacral radiculopathy due to lumbar disc protrusion. Compared to steroid injections alone, the addition of ozone therapy resulted in significantly greater pain relief and functional improvement, as demonstrated by VAS and ODI scores at 1, 3, and 6 months post-treatment. These results suggest that ozone therapy not only enhances short-term analgesia but also contributes to sustained functional recovery, reinforcing its potential as a valuable minimally invasive intervention in spine pain management.

From a mechanistic standpoint, ozone therapy exerts anti-inflammatory, oxidative stress-modulating, and neuroprotective effects that complement the actions of corticosteroids. Ozone's ability to inhibit pro-inflammatory cytokines (TNF-α, IL-1β), promote oxygenation of ischemic nerve roots, and facilitate disc reabsorption offers a multifactorial advantage over steroid monotherapy. Unlike corticosteroids, which primarily suppress inflammation, ozone has been shown to modify the biochemical environment of the intervertebral disc, promoting long-term structural and functional improvements.

Implications for Pain Management and Spine Interventions

The integration of ozone therapy into routine clinical practice could reshape the current treatment paradigm for discogenic pain and radiculopathy by providing:

A Viable Alternative to Surgery

Ozone therapy serves as a bridge between conservative therapy and surgical intervention, particularly for patients with contained disc herniation who have failed conventional treatments but wish to avoid surgery. As demonstrated in this study and previous research, ozone therapy reduces the need for spinal surgery, potentially lowering healthcare costs and surgical morbidity.

Reduced Dependence on Repeated Steroid Injections

Prolonged reliance on epidural corticosteroids raises concerns regarding systemic side effects, bone demineralization, and hypothalamic-pituitary-adrenal axis suppression. Ozone therapy reduces the need for frequent corticosteroid use, offering comparable or superior pain relief with fewer steroid-related risks.

Long-Term Cost-Effectiveness and Healthcare Benefits

By reducing surgical conversion rates and the need for repeat interventions, ozone therapy has the potential to lower the financial burden on healthcare systems while improving patient quality of life. Future cost-effectiveness analyses comparing ozone therapy vs. conventional steroid injections and surgery could further validate its economic advantages.

The results of this study provide strong clinical and economic justification for considering ozone therapy as a minimally invasive, cost-effective, and clinically beneficial intervention in pain management and spine care. Future large-scale multicenter trials and long-term follow-up studies will be essential to further establish its role in standard pain management protocols.

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