Turk J Phys Med Rehab 2025;71(4):520-530
DOI: 10.5606/tftrd.2025.16087
Available online at www.turkishjournalpmr.com

Original Article

Efficacy of fluoroscopy-guided transforaminal epidural steroid injection with or without ozone in patients with lumbar radiculopathy: A single-center study

Derya Bayram, İbrahim Aşık

Department of Pain Medicine, Ankara University Faculty of Medicine İbni Sina Hospital, Ankara, Türkiye

ABSTRACT

Objectives: This study aims to assess the clinical effectiveness and safety of transforaminal epidural injections of steroid and ozone mixture versus steroid alone in patients with low back and radicular pain.

Patients and methods: This retrospective study reviewed the files of 120 patients (60 males, 60 females; mean age: 48.5±12.0 years; range, 18 to 75 years) who underwent fluoroscopy-guided transforaminal epidural steroid or steroid plus ozone injection between June and December 2020. The patients' clinical and demographic information were noted. Visual Analog Scale (VAS) and Oswestry Disability Index (ODI) scores were recorded at baseline and one, three, six, and 12 months after the procedure. MacNab scores were evaluated at baseline and 12 months. Postprocedure outcomes were compared with baseline and between the two groups.

Results: Patient characteristics were similar, and both treatment groups showed significant differences in mean VAS and ODI scores compared to baseline ($p<0.001$). However, the results showed a greater decrease in the combination therapy group ($p<0.001$). The mean ODI scores were comparable at one, three, and six months but differed at 12 months, with more favorable outcomes in patients who received additional ozone. After a prolonged observation, 61.6% of patients received steroid injections and 78.3% of those who underwent combined treatment were satisfied. The long-term follow-up revealed the absence of significant complications in both treatment groups.

Conclusion: Transforaminal injection of steroid alone and its combination with ozone were both effective in short- and long-term pain and disability. Additionally, ozone had a moderate effect on the results. Therefore, combining steroids and ozone could be a complementary treatment for better outcomes.

Keywords: Epidural, injections, low back pain, ozone, steroids.

Low back and radicular lower extremity pain are the common presenting symptoms in the field of pain medicine. The prevalence of low back pain ranges from 15 to 45%.[1] It is one of the prominent causes of disability worldwide, has a negative impact on daily lives, contributes to a significant economic impact due to work absenteeism, and results in high healthcare costs.[2-4]

For patients with chronic low back and radicular lower extremity pain, pain relief can be achieved through minimally invasive interventional procedures under fluoroscopic guidance. Since some patients may experience persistent pain and the potential development risk of failed back surgery syndrome, minimally invasive procedures are preferred as a presurgical intervention.[5-7]

Epidural steroid injections are the most commonly used nonsurgical interventions for disc herniation.[8] Corticosteroids can be used alone or in combination with other drugs such as hyaluronidase and local anesthetics.[9,10] Ozone therapy has also started to be used as frequently

Corresponding author: Derya Bayram, MD. Mardin Eğitim ve Araştırma Hastanesi, Ağrı Kliniği, 47100 Artuklu, Mardin, Türkiye.
E-mail: deryak.bayram@gmail.com

Received: November 17, 2024 **Accepted:** March 22, 2025 **Published online:** November 09, 2025

Cite this article as: Bayram D, Aşık İ. Efficacy of fluoroscopy-guided transforaminal epidural steroid injection with or without ozone in patients with lumbar radiculopathy: A single-center study. Turk J Phys Med Rehab 2025;71(4):520-530. doi: 10.5606/tftrd.2025.16087.

as steroids. Previous studies have shown that ozone can be given intradiscally, into the epidural space, and into paravertebral muscles.[11] Additionally, studies comparing the efficacy of intraforaminal ozone injection versus steroids reported that ozone injection was more effective than steroids.[12] Ozone is thought to modulate levels of cytokines and prostaglandins, minimize reactive oxidant species levels, and improve local periganglionic circulation.[5]

The objective of this study was to assess the short- and long-term clinical efficacy of transforaminal epidural steroid and steroid plus ozone injection in patients presenting with low back and radicular lower extremity pain and to determine the treatment method most beneficial in reducing pain.

PATIENTS AND METHODS

Files of 138 patients who applied to the outpatient clinic of the Ankara University Faculty of Medicine, Department of Pain Medicine, between June 2020 and December 2020 with lower back and radicular lower extremity pain were analyzed retrospectively. Eighteen patients were excluded from the study due to missing information in their records. Hence, the study included 120 patients (60 males, 60 females; mean age: 48.5±12.0 years; range, 18 to 75 years) with degenerative disc disease who underwent transforaminal epidural steroid or a combination of steroid and ozone injection. A flowchart of the study is illustrated in Figure 1. The inclusion criteria were as follows: age between 18 and 75 years, body mass index (BMI) <35, Visual Analog Scale (VAS) score ≥4, radicular lower extremity pain not responding to conservative therapy related to lumbar disk herniation, duration of pain >3 months, patients who received transforaminal injection with steroid or steroid in combination with ozone. Pregnancy, major progressive neurologic deficits, infective or inflammatory diseases, uncontrolled diabetes or other severe internal comorbidities, malignancy, international normalized ratio >1.2, and glucose-6-phosphate dehydrogenase deficiency were considered exclusion criteria. Written informed consent was obtained from the participants. The study protocol was approved by the Ankara University Faculty of Medicine Human Research Ethics Committee (Date 13.01.2022, No: I01-04-22). The study was conducted in accordance with the principles of the Declaration of Helsinki. The clinical trial registration number of this article was NCT06503835 (Clinicaltrials.gov).

Demographic information, pain intensity, localization, pattern (neuropathic, nonneuropathic, or mixed), and patients' quality of life, and the

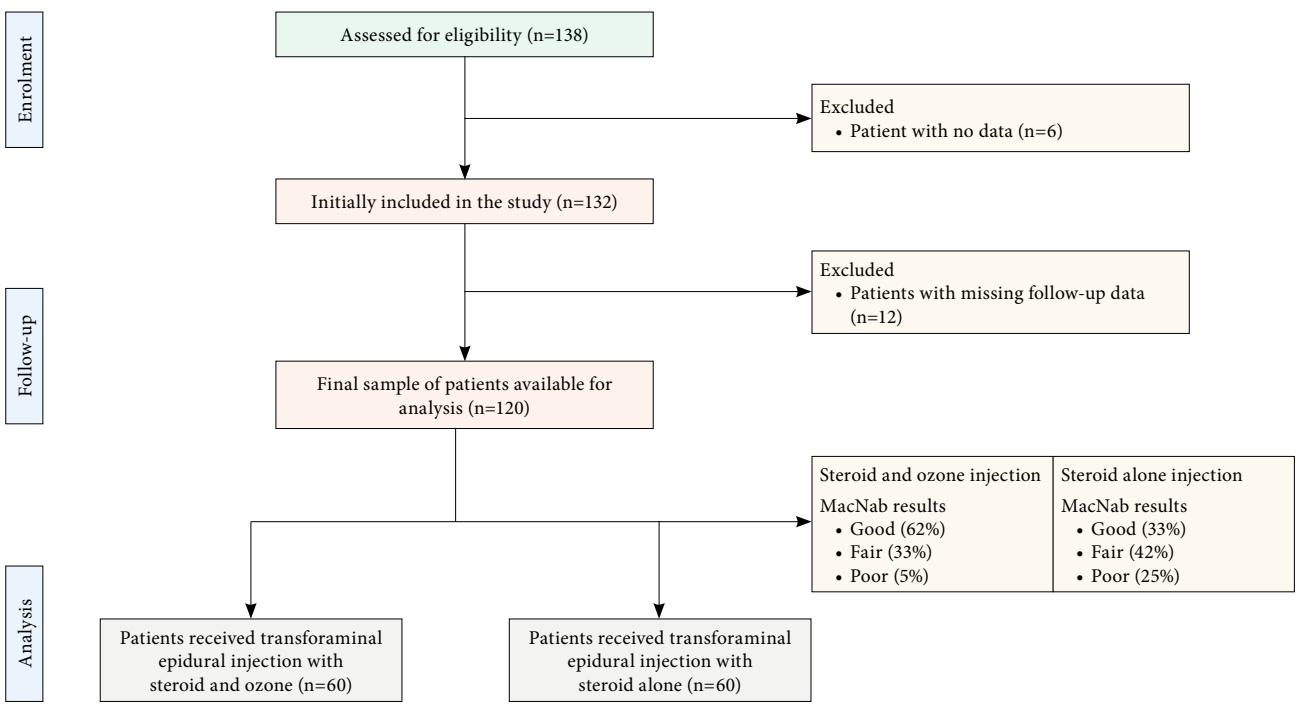

Figure 1. Flowchart of the selection process of the study participants.

treated level (the innervation territories of L2, L3, L4, L5, or S1) were analyzed. The pain was classified as neuropathic, nonneuropathic, or mixed type based on the Douleur Neuropathique 4 (DN4) questionnaire.[13] Pain intensity was assessed using the VAS, and patient disability was evaluated with the Oswestry Disability Questionnaire (ODI).

Patients were divided into two treatment groups: *(i)* those who received 2 mL of dexamethasone (8 mg) and 3 mL of saline for each transforaminal epidural injection level, and *(ii)* those who received 5 mL of ozone at a concentration of 28 µg/mL in addition to steroids. In our clinic, a combination of steroids and ozone was utilized as a standard treatment method for patients presenting with long-term pain and magnetic resonance imaging findings of multiple-level disc herniation. The recommendation and administration of epidural ozone injections were at a concentration of 10 to 30 µg/mL in studies. On the other hand, studies of interlaminar, transforaminal application of ozone to the epidural space have generally used 5 to 8 mL doses of 20 to 30 µg/mL.[5,14,15] Therefore, a 5 mL ozone injection at a concentration of 28 µg/mL, which is in a safe range for patients, was preferred in our clinic.

A single experienced practitioner (more than 20 years of experience) performed all procedures under light sedation in a sterile operating room. Ozone was created by an ozone generator (Dr. J. Hänsler Ozonosan, Iffezheim, Germany). The C-arm was adjusted so that the X-rays were parallel to the cover plates of the injection level and rotated until the processes spinosus protruded over the contralateral facet column. A 10-cm long (or 15-cm long for obese patients), 22-gauge Quincke needle (Egemen International, İzmir, Türkiye) was inserted as the tunneled vision in the medial part of the intervertebral foramen. Subsequently, the depth of the needle tip was evaluated in a lateral view. Appropriate diffusion of the nonionic contrast agent into the periradicular and epidural area was verified through anteroposterior and lateral fluoroscopic images, as shown in Figure 2. The injections were then safely performed. Following the administration of steroid injections at each level, ozone injections were subsequently applied using a separate injector. Patients were injected at multiple levels where disc herniation was identified. After discharging patients, the follow-up period for each patient was 12 months.

We evaluated the patients' records of VAS and ODI scores on the day of the procedure, at 24 h (for VAS only), and at one, three, six, and 12 months after the procedure. Patients' satisfaction was assessed using MacNab scale scores at one and 12 months. The posttreatment outcomes of the patients were compared between the two groups and with baseline.

The VAS score for pain assessment ranges between 0 and 10 (min. and max. pain degree). The ODI is a questionnaire in which the level of disability increases as the total score increases.[16]

A score of at least 4/10 on the DN4 questionnaire indicated neuropathic pain. The DN4 contains seven items relating to symptoms (e.g., sensations of burning, electric shock, painful cold, and tingling) and three items relating to physical examination.[13] The MacNab scale scores were used for success in pain decrease (excellent, good, fair, and poor). The "excellent" and "good" results were accepted as

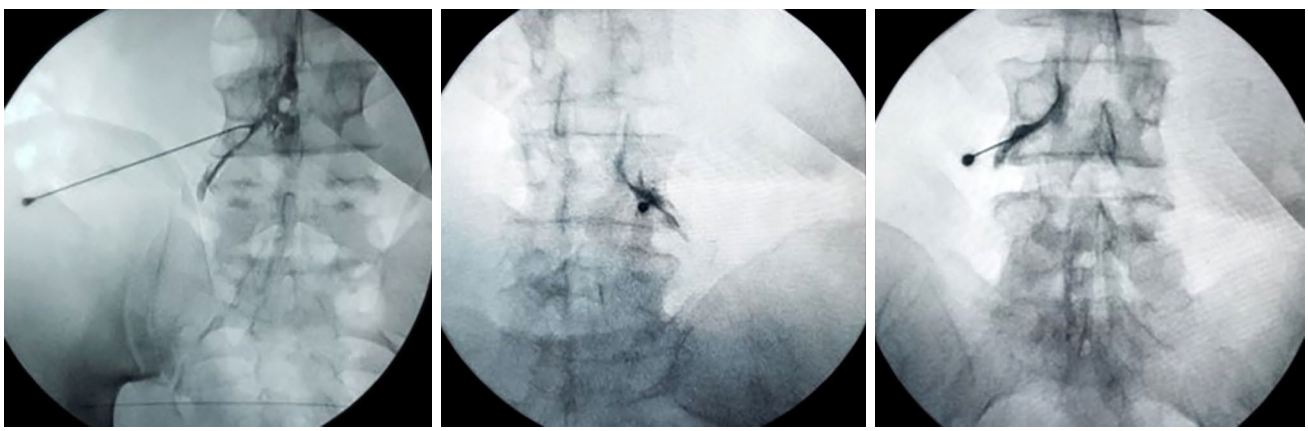

Figure 2. Fluoroscopic images of transforaminal epidural injections.

favorable outcomes, and the "fair" and "poor" results were considered unsatisfactory.[17]

Statistical analysis

Statistical analysis was performed with the IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as mean ± standard deviation (SD) or median (min-max) for quantitative variables and frequency (percentage) for qualitative variables. The one-sample Kolmogrov-Smirnow test was performed to assess the distribution pattern of the data sets. The chi-square test and Fisher exact test were used for the comparison of categorical variables. Student's t-test was used to compare normally distributed quantitative data, and the Mann-Whitney U test was used for nonparametric data. Repeated measures were analyzed using the Friedman test, and differences of pairwise groups were shown using post hoc tests. The Mann-Whithey U test was used to compare mean VAS and ODI scores between groups. The correlations between VAS scores, ODI scores, and demographic data were assessed by the correlation coefficient (Spearman's rank correlation coefficient). A *p*-value <0.05 was considered statistically significant.

A power analysis was conducted before the study using the G*Power version 3.1 software (Heinrich-Heine Universität Düsseldorf, Düsseldorf, Germany) to determine the required sample size. The type of statistical test was selected as means: difference between two independent means (two groups). A sample size of 53 individuals per group was determined, with an effect size of 0.554, alpha of 0.05, and power of 0.80, by selecting two in the tail section. The ODI scores at four weeks (mean and standard deviation values) were taken as the basis for the analysis.[9]

RESULTS

The mean age of the group receiving combination therapy was 48±12.4 years, whereas the mean age of the patients who received steroid injections was 49.0±11.9 years. There were no significant differences in age, sex, BMI, pain duration, or the distribution of treated nerve root levels and number of operations between groups. The demographic and clinical characteristics of the patients are detailed in Table 1.

The number of patients with persistent spinal pain syndrome was 19 in the combination group and 13 in the steroids alone group. "Persistent spinal pain syndrome" is a newly suggested term that is considered to be a more appropriate and clinically meaningful alternative to failed back surgery syndrome.[18]

In the combination therapy group, 53 patients were using gabapentinoid, whereas 48 patients were using gabapentinoid in the steroid-alone group. While 25 patients in the combination therapy group and 20 patients in the steroid-alone group experienced a decrease in the gabapentinoid dose, eight and 17 patients increased the gabapentinoid dose, and 27 and 23 patients used the same dose, respectively (p=0.030 for the combination group, p=0.793 for the steroid-alone group).

Significant decreases were observed in mean VAS scores during at 12 months in both injection groups (p<0.001); however, the combination treatment group had better results at one-, three-, six-, and 12-month follow-up visits, as shown in Table 2.

There were significant decreases in the mean ODI scores at 12 months (p<0.001) in both groups. No significant differences in the mean ODI scores were found among the groups except for the 12th month. The mean ODI scores in the 12th month were in favor of the patients who received steroid plus ozone treatment.

In the combination therapy group, pairwise comparisons for low back pain demonstrated significant differences between all time using post-hoc tests, except between the 24th h and third month (p=0.341), the 24th h and sixth month (p=0.788), the first and third months (p=0.232), and the third and sixth months (p=0.223). For lower extremity pain, significant differences were observed between all time intervals, except between the 24th h and first month (p=0.130), the 24th h and third month (p=0.449), the 24th h and sixth month (p=0.242), and the third and sixth months (p=0.678). Regarding the Oswestry Disability Index (ODI) scores, a statistically significant difference was found between all time intervals, except between the first and third months (p=0.470). The efficacy of the treatment initiated 24 h after the procedure for low back and radicular lower extremity pain increased during first month for low back pain and continued similarly between three and six months. Although the efficacy decreased at 12 months compared to six months, pain severity at 12 months remained lower than at baseline.

TABLE 1
Demographic and clinical characteristics of patients

	Ozone+steroid injection (n=60)					Steroid alone injection (=60)					
	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	*p*
Age (year)			48.0±12.4					49.0±11.9			0.663[a]
Sex											0.999[c]
Male	30					30					
Female	30					30					
BMI (kg/m^2)			24.9±3.3					24.8±2.9			0.771[a]
Nerves											0.267[b]
L2	2	3.3				7	11.7				
L3	39	65				23	38.3				
L4	56	93.3				44	73.3				
L5	39	65				43	71.6				
S1	13	21.7				13	21.7				
Duration (mo)				13	3-72				13	3-36	0.885[b]
Stabilization											0.399[d]
Yes	7	11.7				4	6.6				
No	53	88.3				56	93.3				
Number of operation											0.204[b]
0	41	68.3				47	78.3				
1	12	20				9	15				
2	7	11.7				4	6.7				
Spinal stenosis											0.573[d]
Yes	11	18.3				5	8.3				
No	49	81.6				55	91.6				
The character of pain											0.663[d]
Neuropathic	38	63.3				33	55				
Nonneuropathic	16	26.7				15	25				
Mix type	6	10				12	20				
Side											0.569[d]
Right	23	38.3				22	36.6				
Left	26	43.3				27	45				
Bilaterally	11	18.3				11	18.3				
VAS before intervention											
Low back				8	4-10				7	5-10	0.546[b]
Leg				8	4-10				7	5-10	0.413[b]
ODI before intervention				42	30-68				42	20-62	0.645[b]

SD: Standard deviation; BMI: Body mass index; VAS: Visual Analog Score; ODI: Oswestry Disability Index; [a] Independent Samples t test; [b] Mann-Whitney U test; [c] Chi-square test; d Fisher exact test, (p<0.001).

In the steroid-only group, post hoc pairwise comparisons for low back and lower extremity pain showed statistically significant differences, except for VAS at 24 h *vs.* one month (p=0.714, p=0.770) and VAS at three *vs.* six months (p=0.232, p=0.661). The efficacy for low back and radicular lower extremity started at 24 h and kept the same effect for up to one month, continued to increase until the third month, and showed similar efficacy between the third and sixth months. Although the pain level started to increase after six months, it was statistically significantly lower than the baseline at six and 12 months.

The disability score for both groups started to decrease significantly from the first month and remained the same in the third month for the combination therapy group. Although there was an increase in disability scores for both groups at six months, disability scores at six and 12 months were still low in comparison with baseline.

No statistically significant relations were found between age, BMI, pretreatment VAS or ODI scores, and the posttreatment outcomes. The results of the treatment were found to be unaffected by factors such as age, the number of previous operations,

TABLE 2
Visual Analog Scale and ODI scores for both groups at baseline and one, three, six, and 12 months

	Steroid and ozone injection		Steroid alone injection		
	Median	Min-Max	Median	Min-Max	p^b
Low back					
VAS basal	8	4-10	7	5-10	0.546
VAS 24th	4	1-9	4	2-8	0,532
VAS 1 (mo)	3	1-8	4	3-8	**0.003**
VAS 3 (mo)	4	2-7	5	3-8	**<0.001**
VAS 6 (mo)	4	3-7	5	3-6	**<0.001**
VAS 12 (mo)	5	4-7	6	4-7	**<0.001**
p^a	**<0.001**		**<0.001**		
Lower extremity					
VAS basal	8	4-10	7	5-10	0.413
VAS 24th	4	1-9	4	2-8	0.052
VAS 1 (mo)	3	1-8	4	3-8	**<0.001**
VAS 3 (mo)	4	2-7	5	3-8	**<0.001**
VAS 6 (mo)	4	3-7	5	4-6	**<0.001**
VAS 12 (mo)	6	3-9	7	4-8	**<0.001**
p^a	**<0.001**		**<0.001**		
ODI score					
Basal	42	30-68	42	20-62	0.645
1 (mo)	27	14-44	24	16-56	0.209
3 (mo)	28	18-42	28	20-56	0.352
6 (mo)	28	22-42	30	24-56	0.103
12 (mo)	30	24-44	40	26-56	**<0.001**
p^a	**<0.001**		**<0.001**		

ODI: Oswestry Disability Index; VAS: Visual Analog Score; [a] Friedman test was used; [b] Mann-Whitney U test was used, (p<0.001).

the duration of the pain, and the presence of spinal stenosis or stabilization.

At the 12-month follow-up, 62% of patients in the combined therapy group were satisfied, while 33% were fair, and 5% were unsatisfied with the procedure. In the steroid-alone group, 33% of the patients were satisfied, while 42% were fair, and 25% were unsatisfied with the procedure, as shown in Figures 3 and 4.

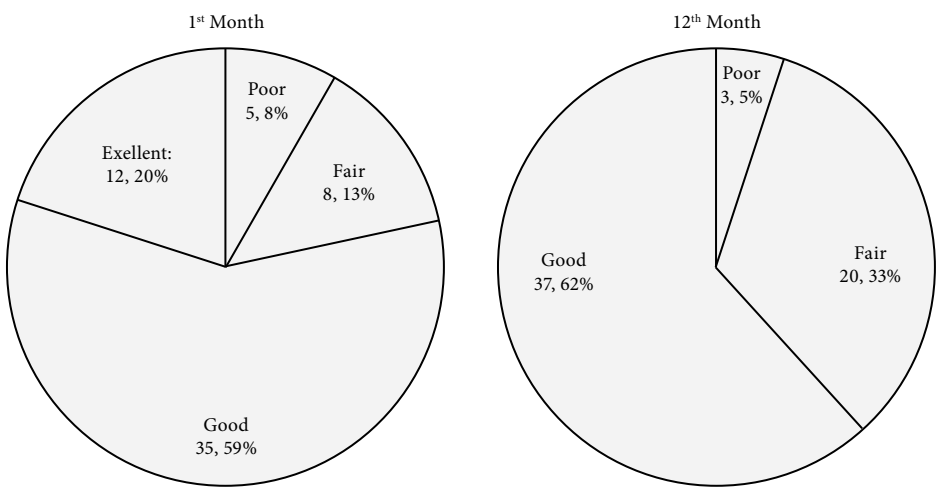

Figure 3. MacNab results of patients at the end of the first and 12th months for the ozone plus steroid injection group.

Figure 4. MacNab results of patients at the end of the first and 12th months for the steroid-only group.

None of the patients reported complications such as neuralgia, paresthesia, bleeding, dural puncture, or infection related to the procedure.

DISCUSSION

This study demonstrated that transforaminal epidural steroid injection and the combination of steroids and ozone were both effective and safe methods for the treatment of low back and radicular lower extremity pain in the short and long term. A notable reduction in pain intensity and disability was observed in patients compared to the initial assessment, and treatment outcomes were better in the combined therapy group, particularly at 12 months.

Several studies on the use of ozone therapy for spinal-origin pain have been published in the literature, with the majority focusing on intradiscal interventions.[19,20] Ozone has been demonstrated to oxidize proteoglycans, which has been shown to enhance nerve root sensitivity to pain in the nucleus pulposus. Ozone also inhibits the synthesis and release of prostaglandins and bradykinin. A reduction in disc volume and the alleviation of chemical radiculitis result in pain alleviation.[21] In addition, Perri et al.[22] reported that ozone discolysis obtained the best results in the case of extrusions and protrusions and even in the presence of discal degeneration ranging from mild to moderate grade. The diminished amount of disc water present in severe disc degeneration may restrict the expected therapeutic response to ozone discolysis. As the herniation size becomes larger, the possibility of nerve root compression and a greater inflammatory response might increase. The disc shrinkage and periganglionic anti-inflammatory effects of ozone may have strengthened its efficacy in these pathologies. Due to the nature of the present study, it was not feasible to evaluate the efficacy of injections on bulging, protrusion, or extrusion in patients with varying degrees of disc herniation at multiple levels.

It has been demonstrated that intraforaminal ozone injection is significantly more effective than steroid injection in several studies.[12,15,23,24] Zambello et al.[23] reported that 47.3% (n=351) of patients treated with epidural steroids and 77.1% treated with ozone had excellent or good long-term outcomes with low back pain. Bonetti et al.[12] conducted a study with 306 patients with acute or chronic low back pain and sciatic nerve pain and compared periradicular ozone at 25 µg/mL concentration with periradicular steroid injection. After six months, they found that the periradicular ozone was significantly more effective than periradicular steroid injection, particularly in patients with disc disease, suggesting its use as the primary treatment for epidural injections. This outcome could be as a result of the long-term effects of ozone, such as its reactions with amino acids and carbohydrates, good tissue diffusion as a result of its beneficial effect on microcirculation, and anti-edema mechanism.[25]

The occurrence of epidural steroid-induced rebound pain, arising three to six months after injection, has been documented in some studies

following regular use of repeated epidural steroid injections in the treatment of disc herniation.[24,26,27] Regardless of rebound pain, the increased risk of infection and the development of scar tissue, which are the local effects that may occur with repeat epidural steroid injections, may also be important limiting factors. Despite this, ozone therapy is a reproducible and long-lasting treatment. In recent years, the lack of adverse effects and the ability to administer the treatment repeatedly have contributed to an increase in the frequency of ozone therapy use. Some researchers have suggested the combination of intradiscal and epidural ozone applications. Muto et al.[28] performed three studies with 2,200 patients and reported 80% and 75% success rates at six and 18 months using computed tomography-guided 3 to 4 mL intradiscal ozone injection and 10 mL intraforaminal ozone at 30 µg/mL concentration. Zhang et al.[29] divided 172 patients into two groups and administered intradiscal and intraforaminal ozone to one group and ozone plus steroids to the other group. At three weeks, the group that received additional steroids showed better recovery rates. For longer follow-up (six or 12 months), this study found no significant differences between the two treatments. The authors indicated no significant difference between ozone and a combination of ozone and steroid. They suggested ozone therapy without requiring steroid addition. This underscores the idea that ozone treatment, independently, is a highly effective solution, eliminating the necessity for steroid supplementation in managing disc-related conditions. In addition, ozone injections may be an alternative treatment modality, particularly in patient groups where steroid use may be challenging, such as those with a history of steroid-related complications, immunosuppression, diabetes, or osteoporosis. In contrast to these two studies, our study did not include intradiscal treatment. However, although disability scores at 12 months showed a statistically significant decrease in both groups compared with baseline, the results were statistically better in the ozone-added group than in the steroid-only group.

On the other hand, several studies and case reports have reported that combined treatment is more effective than the use of pure steroids and demonstrated the cumulative effects of epidural ozone and steroids.[10] Additionally, the combination of steroids, local anesthetic agents, and ozone has been demonstrated to be more effective than ozone injection alone. A study by Gallucci et al.[21] included two treatment groups. They administered a combination of steroids and local anesthetics (1 mL intradiscal and 1 mL intraforaminal) to the first group and a combination of steroids, local anesthetics, and ozone (5 to 7 mL intraforaminal and 5 to 7 mL intradiscal at 28 µg/mL) to the second group under computed tomography guidance. According to the results of the study, there was no significant difference between the success rates of the two groups in the short term (2 weeks and 3 months), while the success rate was significantly higher in the ozone-added group in the long term (6 months). They attributed this result to the long-acting effect of ozone. Therefore, they suggested that combined ozone, steroid, and local anesthetic injection at intradiscal and intraforaminal levels should be considered more effective than steroid and local anesthetic injection. Similarly, in a study of 600 patients, Andruela et al.[30] reported that the success rate was higher in patients (n=300) who received a steroid, ozone, and local anesthetic combination than the patients (n=300) who were injected with ozone (intradiscal and periganglionic). On the other hand, in their study of 178 patients, Ryska et al.[8] found that the VAS score immediately after treatment with transforaminal steroid and local anesthetic was lower than that achieved with transforaminal ozone. However, in the third and sixth months after treatment, the mean VAS scores did not demonstrate a statistically significant difference. Furthermore, no significant differences were observed in ODI values between the groups at any of the follow-up visits. Patient eligibility and assessment methods may account for the differences between the studies. A retrospective study by Chemeisani et al.,[15] conducted with 100 patients, noted that transforaminal epidural steroid injection in fifty patients was more effective in the short term (1 to 3 months), but fifty patients who received transforaminal ozone injection had long-term (6 months) pain relief in chronic low back pain. By studying patients with different radiculopathies, they suggested that ozone was better than steroids in both short- and long-term treatments. A recent study including two groups of 40 patients, reported that 24-h, one-month, and three-month VAS and ODI scores were not statistically different in the two treatment groups consisting of transforaminal epidural steroid injection with ozone and transforaminal injection of epidural steroid alone.[31] They attributed the results to their sample size. As in previous studies, a longer follow-up period may have been

beneficial to more clearly observe the long-term effects of ozone. In the present study, we found that VAS scores improved significantly in both groups when compared to baseline measurements. The pain scores were similar between the two groups. Furthermore, disability scores also showed a significant reduction compared to baseline, with a notable difference in favor of patients who received additional ozone therapy, particularly at 12 months. The methodology of the trials, the different types of steroids used, the volume of the injectate, the number of ozone injections, the use of ozone with steroids or alone, the timing of the evaluation, and the follow-up of the patients varied between the trials, leading to inconsistent results.[31] Spinal stenosis, postoperative adhesions, recurrent herniated discs, and the presence of extruded or sequestered discs with significant nerve compression may also lead to treatment failure.

The administration of ozone may result in some side effects, including insomnia, itching, gastritis, dizziness, tachycardia, and hot flashes.[32] Furthermore, there was one case of thunderclap headache following an inadvertent intrathecal puncture and one case of paresthesia and hypoesthesia following percutaneous intradiscal infiltration of ozone for an L4-L5 disc herniation.[33,34] However, it is important to note that these side effects were not caused directly by ozone, and the method of application was important.[35] In their study, Vanni et al.[32] observed the presence of hard adhesions between the root and dural sac or fragmented disc in patients who previously underwent ozone therapy. They suggested that the incidence of significant complications associated with the use of ozone may be underreported. Furthermore, they emphasized the necessity for the development of more comprehensive guidelines and protocols for the utilization of ozone.

The main limitation of our study was its retrospective nature. The absence of a sham-treated or ozone-only group was another limitation. Further research including randomized controlled studies with larger samples is required to standardize the dose, duration, and volume to make more precise assessments of the efficacy of epidural ozone injection. To our knowledge, a comparative analysis of fluoroscopy-guided transforaminal epidural steroid and steroid plus ozone treatments is a relatively undeveloped area of research, particularly in the long term. As such, this study represents a valuable contribution to the field.

In conclusion, this study aimed to compare the effects of minimally invasive fluoroscopy-guided transforaminal epidural steroid injections with the combination of steroid and ozone injections on pain and disability in patients with chronic radicular syndrome. The findings of the current study indicated that both treatments administered under fluoroscopic guidance resulted in short- and long-term pain relief, regardless of the treatment. However, the combination therapy group reported better treatment outcomes. Furthermore, although there was no difference in short-term efficacy, the ozone group demonstrated a significantly greater reduction in long-term disability. Ozone injections are safe, effective, and reproducible, with rare side effects. Based on our findings, the use of ozone and steroids in transforaminal epidural injection should be considered a complementary approach for treating chronic low back and radicular lower extremity pain associated with herniated discs, offering a viable alternative for better results.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Concept, design, supervision, analysis/interpretation, writing the article, critical review, references and fundings, materials: D.B., İ.A.; Data collection, literatur review: D.B.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Manchikanti L, Singh V, Falco FJ, Benyamin RM, Hirsch JA. Epidemiology of low back pain in adults. Neuromodulation 2014;17 Suppl 2:3-10. doi: 10.1111/ner.12018.
2. Silva GQ, NBR Alves F, R Afonso JP, MP Soares J, A Souza SK, M Rodrigues-Silva B, et al. Non-invasive therapeutic approaches for mechanical low back pain: an integrative systematic review: non-invasive therapeutic approaches for mechanical low back pain. Man Ther Posturology Rehabil J 2024,22. doi: 10.17784/mtprehabjournal.2024.22.1382.
3. Carregaro RL, Tottoli CR, Ben ÂJ, da Silva EN, Bosmans JE, van Tulder M. Cost-utility of Pilates versus home-based exercises in individuals with chronic non-specific low back pain: economic evaluation alongside a randomized controlled trial. JAFF 2024;9:139-40. doi: 10.22563/2525-7323.2024.v9.s1.p.124.
4. Adıgüzel E, Tecer D, Güzelküçük Ü, Taşkaynatan MA, Tan AK. The effectiveness of transforaminal epidural steroid injection in patients with radicular low back pain:

Combination of pain provocation with effectiveness results. Turk J Phys Med Rehabil 2017;63:117-23. doi: 10.5606/tftrd.2017.05882.
5. Bonetti M, Lauritano D, Ottaviani GM, Fontana A, Frigerio M, Zambello A, et al. New approach to chronic back pain treatment: A case control study. Biomedicines 2022;11:73. doi: 10.3390/biomedicines11010073.
6. Costa T, Linhares D, Ribeiro da Silva M, Neves N. Ozone therapy for low back pain. A systematic review. Acta Reumatol Port 2018;43:172-81.
7. Hashemi M, Poorfarokh M, Mohajerani SA, Jalili P, Akhyani V, Barikani A, et al. Injection of intradiscal o2-o3 to reduce pain and disability of patients with low back pain due to prolapsed lumbar disk. Anesth Pain Med 2014;4:e19206. doi: 10.5812/aapm.19206.
8. Ryska P, Jandura J, Hoffmann P, Dvorak P, Klimova B, Valis M, et al. Comparison of pulsed radiofrequency, oxygen-ozone therapy and epidural steroid injections for the treatment of chronic unilateral radicular syndrome. Medicina (Kaunas) 2021;57:136. doi: 10.3390/medicina57020136.
9. Fathy W, Hussein M, Ibrahim RE, Abdel-Aziz MM, Adel S, Soliman SH, et al. Comparative effect of transforaminal injection of Magnesium sulphate versus Ozone on oxidative stress biomarkers in lumbar disc related radicular pain. BMC Anesthesiol 2022;22:254. doi: 10.1186/s12871-022-01789-0.
10. Migliorini F, Maffulli N, Eschweiler J, Bestch M, Tingart M, Baroncini A. Ozone injection therapy for intervertebral disc herniation. Br Med Bull 2020;136:88-106. doi: 10.1093/bmb/ldaa032.
11. Bocci V, Borrelli E, Zanardi I, Travagli V. The usefulness of ozone treatment in spinal pain. Drug Des Devel Ther 2015;9:2677-85. doi: 10.2147/DDDT.S74518.
12. Bonetti M, Fontana A, Cotticelli B, Volta GD, Guindani M, Leonardi M. Intraforaminal O(2)-O(3) versus periradicular steroidal infiltrations in lower back pain: Randomized controlled study. AJNR Am J Neuroradiol 2005;26:996-1000.
13. Unal-Cevik I, Sarioglu-Ay S, Evcik D. A comparison of the DN4 and LANSS questionnaires in the assessment of neuropathic pain: validity and reliability of the Turkish version of DN4. J Pain 2010;11:1129-35. doi: 10.1016/j.jpain.2010.02.003.
14. Haseeb A, Abd El Hares A, Abd El Moez K, Mustafa A, Ahmed O. Comparative study between treatment of lumbar disc herniation with intra discal ozone and transforaminal steroid injection versus steroid injection only. The Egyptian Journal of Hospital Medicine 2019;74:705-20. doi: 10.21608/ejhm.2019.24068.
15. Chemeisani A, Tarhini H, Haj Ali T, Jibbawi AA, Yehya K, Msheik A. The benefit of epidural transforaminal injection of ozone in comparison with transforaminal steroids ınjection in the management of chronic low back pain in Lebanese population: One-year retrospective study. Cureus 202315:e34106. doi: 10.7759/cureus.34106.
16. Yakut E, Düger T, Oksüz C, Yörükan S, Ureten K, Turan D, et al. Validation of the Turkish version of the Oswestry Disability Index for patients with low back pain. Spine (Phila Pa 1976) 2004;29:581-5. doi: 10.1097/01.brs.0000113869.13209.03.
17. Macnab I. Negative disc exploration. An analysis of the causes of nerve-root involvement in sixty-eight patients. J Bone Joint Surg Am 1971;53:891-903.
18. Christelis N, Simpson B, Russo M, Stanton-Hicks M, Barolat G, Thomson S, et al. Persistent spinal pain syndrome: A proposal for failed back surgery syndrome and ICD-11. Pain Med 2021;22:807-18. doi: 10.1093/pm/pnab015.
19. Andreula C. Lumbar herniated disk and degenerative changes. Interventional spinal treatment with chemiodiscolysis with nucleoptesis with O3 and perigangliar infiltration in 150 cases. Rivista di Neuroradiologia 2002;14:81-8. doi: 10.1177/19714009010140S118.
20. Muto M, Avella F. Percutaneous treatment of herniated lumbar disc by intradiscal oxygen-ozone injection. Interv Neuroradiol 1998;4:279-86. doi: 10.1177/159101999800400403.
21. Gallucci M, Limbucci N, Zugaro L, Barile A, Stavroulis E, Ricci A, et al. Sciatica: Treatment with intradiscal and intraforaminal injections of steroid and oxygen-ozone versus steroid only. Radiology 2007;242:907-13. doi: 10.1148/radiol.2423051934.
22. Perri M, Marsecano C, Varrassi M, Giordano AV, Splendiani A, di Cesare E, et al. Indications and efficacy of O2-O3 intradiscal versus steroid intraforaminal injection in different types of disco vertebral pathologies: A prospective randomized double-blind trial with 517 patients. Radiol Med 2016;121:463-71. doi: 10.1007/s11547-015-0598-x.
23. Zambello A, Fara B, Tabaracci G, Bianchi M. Epidural steroid injection vs paravertebral O2-O3 infiltration for symptomatic herniated disc refractory to conventional treatment: A prospective randomized study. Rivista di Neuroradiologia 2006;5:123-127.
24. Joel JJ, Dutta D, Das G, Anand Kumar GS, Panchal J, Basak S. Efficacy of transforaminal epidural steroid injection versus intraforaminal or periforaminal ozone for low back pain with radiculopathy Indian J Pain. 2015;29:64-72. doi: 10.4103/0970-5333.155172.
25. Hidalgo-Tallón FJ, Torres-Morera LM, Baeza-Noci J, Carrillo-Izquierdo MD, Pinto-Bonilla R. Updated review on ozone therapy in pain medicine. Front Physiol 2022;13:840623. doi: 10.3389/fphys.2022.840623.
26. Spijker-Huiges A, Winters JC, van Wijhe M, Groenier K. Steroid injections added to the usual treatment of lumbar radicular syndrome: A pragmatic randomized controlled trial in general practice. BMC Musculoskelet Disord 2014;15:341. doi: 10.1186/1471-2474-15-341.
27. Karppinen J, Malmivaara A, Kurunlahti M, Kyllönen E, Pienimäki T, Nieminen P, et al. Periradicular infiltration for sciatica: A randomized controlled trial. Spine (Phila Pa 1976) 2001;26:1059-67. doi: 10.1097/00007632-200105010-00015.
28. Muto M, Andreula C, Leonardi M. Treatment of herniated lumbar disc by intradiscal and intraforaminal oxygen-ozone (O2-O3) injection. J Neuroradiol 2004;31:183-9. doi: 10.1016/s0150-9861(04)96989-1.
29. Zhang Y, Ma Y, Jiang J, Ding T, Wang J. Treatment of the lumbar disc herniation with intradiscal and intraforaminal injection of oxygen-ozone. J Back Musculoskelet Rehabil 2013;26:317-22. doi: 10.3233/BMR-130386.

30. Andreula CF, Simonetti L, De Santis F, Agati R, Ricci R, Leonardi M. Minimally invasive oxygen-ozone therapy for lumbar disk herniation. AJNR Am J Neuroradiol 2003;24:996-1000.
31. Nazemian NA, Khajehnasiri A, Sanatkar M, Samavatian M, Nikoo MR. Efficacy of lumbar transforaminal epidural steroid injection with or without ozone therapy on radicular pain. Arch Anesth & Crit Care 2024;10:377-84. doi: 10.18502/aacc.v10i4.16267.
32. Vanni D, Galzio R, Kazakova A, Pantalone A, Sparvieri A, Salini V, et al. Intraforaminal ozone therapy and particular side effects: Preliminary results and early warning. Acta Neurochir (Wien) 2016;158:491-6. doi: 10.1007/s00701-015-2545-y.
33. Devetag Chalaupka F, Caneve G, Mauri M, Zaiotti G. Thunderclap headache caused by minimally invasive medical procedures: Description of 2 cases. Headache 2007;47:293-5. doi: 10.1111/j.1526-4610.2006.00699.x.
34. Ginanneschi F, Cervelli C, Milani P, Rossi A. Ventral and dorsal root injury after oxygen-ozone therapy for lumbar disk herniation. Surg Neurol 2006;66:619-20. doi: 10.1016/j.surneu.2006.01.025.
35. Magalhaes FN, Dotta L, Sasse A, Teixera MJ, Fonoff ET. Ozone therapy as a treatment for low back pain secondary to herniated disc: A systematic review and meta-analysis of randomized controlled trials. Pain Physician 2012;15:E115-29.