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Comparison between paravertebral injections of ozone and epidural injections of corticosteroids used in the treatment of lumbosacral pain: scoping review

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From the Contents

Abstract

Paravertebral ozone injections have been used in the treatment of lumbosacral pain with or without radicular irradiation and have been reported to be effective in reducing pain when compared with placebo, physiotherapy programs or drug treatments; nevertheless, their effectiveness in comparison with minimally invasive procedures using corticosteroids is unknown. The main objective of this review was to explore the role of paravertebral ozone injections in the treatment of lumbosacral pain with radicular irradiation in comparison with minimally invasive procedures using corticosteroids. A systematic search was performed in electronic databases including PubMed, EMBASE, Central Cochrane and Web of Science, from January 2000 to December 2024; for clinical studies that compared paravertebral ozone injections with minimally invasive procedures using corticosteroids in the treatment of lumbosacral pain with radicular irradiation and were performed using the methodology of a scoping review. Four clinical trials met the inclusion criteria and were included in this review, gathering a total of 501 individuals. In the within-group comparison of every study, statistically significant reduction in pain was observed in both interventions. No side effects or serious adverse reactions were reported in the treated patients. Paravertebral ozone injections appear to have a favorable therapeutic effect in reducing pain in the short and medium terms, in individuals with lumbosacral pain with radicular irradiation, and this effect appears to be similar to that of epidural corticosteroid injections. No definitive recommendations are possible, for more clinical trials are needed to conduct meta-analytic reviews that clarify the results of this comparison.

Key Words: corticosteroids; disc herniation; disc protrusion; epidural injections; low back pain; lumbosacral pain; ozone; paravertebral injections; radicular pain; sciatica

Introduction

Low back pain is one of the main causes of medical attention and functional limitation worldwide,[1,2] presenting a prevalence of 84% during life[3,4] and an incidence of 36% per year.[4] The etiology of low back pain is multifactorial and it is classified based on the mechanism of injury, etiology, time of evolution and the presence of radicular pain,[5,6] there the need to establish multimodal treatment programs in patients with low back pain. The multimodal treatment includes conservative treatment strategies such as education, modification of activities, pharmacological treatment, physiotherapy programs based on therapeutic physical exercise and some therapeutic physical modalities.[5-8] The multimodal treatment of low back pain may also include the use of minimally invasive interventional procedures when the conventional treatment is not effective.[5,9,10] Minimally invasive interventional procedures include facet injections; sacroiliac joint injections; epidural corticosteroid injections (ECIs) with caudal, interlaminar or transforaminal anatomical approach; or periforaminal corticosteroid injections.[5,9,10]

ECIs are one of the most commonly used minimally invasive procedures in the treatment of low back pain with radicular pain,[11] and their short-term effectiveness in reducing lumbosacral radicular pain has already been reported.[12] Although the transforaminal anatomical approach appears to be slightly more effective in reducing lumbosacral radicular pain,[13] periforaminal injections with corticosteroids have also been used for treating unilateral lower lumbar radicular pain, with good efficacy in reducing pain in the short term.[14,15]

Other substances have also been used to perform minimally invasive procedures in the lumbar spine, such as the oxygen-ozone mixture.[16] For instance, ozone injections have been used for treating lumbar pain secondary to herniated disc,[17,18] degenerative disease of the lumbar spine,[19] lumbar spinal stenosis,[20] spondylolisthesis[20] and failed surgery syndrome.[21] The use of ozone in the treatment of these spinal pathologies has been performed via several routes including intradiscal,[17,18] intraforaminal epidural,[22,23] periforaminal,[24,25] caudal epidural[21] and injections into lumbar paravertebral muscles.[26,27]

One review reported that ozone injections were more effective in reducing low back pain and sciatica than the pharmacological treatment or minimally invasive procedures with corticosteroids (MIPC) in the short and medium terms[28]; however, that review only included studies where the ozone application was intradiscal. Other review studies have reported similar results, indicating a greater efficacy of ozone in reducing pain when compared with placebo or other interventions such as

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pharmacological treatment or MIPC[29,30]; in the included studies, however, ozone injections were applied using different routes such as intradiscal, intraforaminal, periforaminal or paravertebral intramuscular, and these routes of administration were not evaluated separately. Only one review study has evaluated the efficacy of ozone injections applied to lumbar paravertebral muscles, reporting that these injections were more effective in reducing low back pain and sciatica than placebo, physical therapy or pharmacological treatment in the short and medium terms.[31] No review study has specifically explored the effects of ozone injections into lumbar paravertebral muscles as a therapeutic strategy for reducing low back pain with radicular irradiation, compared with MIPC.

Therefore, the aims of this scoping review were to explore the role of paravertebral ozone injections (POIs) in the treatment of lumbosacral pain with radicular irradiation (LPRI), in comparison with MIPC (including facet injections; epidural injections with caudal, interlaminar or transforaminal anatomical approach; and periforaminal or periradicular injections) in order to describe and analyze the characteristics of the treatment and to determine the possible beneficial and side effects of POIs in the treatment of LPRI. Based on the above, we hypothesized that POIs are a therapeutic intervention that may be just as effective as MIPC in the treatment of LPRI.

Methodology

The preparation of this scoping review was based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines.[32]

The methodology was focused on five actions: (1) identification of research questions, (2) identification of relevant studies: sources of information and search strategy, (3) selection and classification of studies, (4) data extraction and definition of the study variables, and (5) analysis and report of results.

Identification of research questions

The established research questions were: How many clinical studies have compared POIs with MPIC in the treatment of individuals with LPRI? What are the characteristics of the POI technique used for treating individuals with LPRI, in comparison with the characteristics of MIPC? What results have already been reported regarding the beneficial effects and adverse reactions when comparing POIs with MIPC in the treatment of LPRI?

Identification of relevant studies: sources of information and search strategy

To identify potential articles, a systematic search was performed using the National Library of Medicine (PubMed), Cochrane Central Register of Controlled Trials (CENTRAL), Excerpta Medica Data Base (EMBASE) and Web of Science databases, up until December 2024. Additionally, other sources such as Google Scholar and Semantic Scholar were searched to identify manuscripts that are published in peer-reviewed journals but are not indexed in databases.

The search terminology used was a combination of Medical Subject Headings (MESH) terms, ENTRY terms and related terms. The complete search strategies are detailed for each database in **Additional Table 1**. Additionally, the bibliographic references of the studies found were reviewed to identify other studies that were not in the databases searched. The search comprised all the manuscripts reported in literature without language restrictions.

Selection and classification of studies

The PCC framework was used to identify the characteristics of the possible studies to include: (P) Population: individuals with LPRI, (C) Concept: Clinical studies in which individuals with LPRI were treated with POIs and were compared with individuals with LPRI who were treated with MIPC, and (C) Context: Studies published internationally from January 2000 to December 2024.

The studies included in this review met the following inclusion criteria: Randomized clinical trials or comparative observational studies (non-randomized) in which POIs were compared with MIPC in the treatment of individuals with LPRI. The participants were individuals over 18 years of age, of both sexes, with LPRI, who presented pain and functional alterations. Studies in which LPRI was secondary to diagnosed lumbar disc herniation, lumbar osteoarthritis or stenosis lumbar were included. The diagnoses had to be established by clinical and imaging evaluation.

The exclusion criteria were: Studies in which ozone was applied by a route other than intramuscular paravertebral (periradicular, periforaminal, transforaminal, caudal epidural or intradiscal) or when ozone was applied in combination with systemic applications (such as rectal insufflation or autohemotherapy) were excluded. Studies where electromyographic tests revealed neurogenic injury and/or denervation, diagnosis of cauda equina syndrome, peripheral neuropathy; and history of vertebral fracture, spinal surgery or spinal neoplasia, were excluded. Studies where co-interventions were not performed uniformly in every studied group, were also excluded.

Data extraction and definition of the study variables

The characteristics of the interventions used in the included studies were: All the participants were treated with one or multiple sessions of POIs applied exclusively by intramuscular paravertebral route. Individuals in the control group were treated with MIPC via facet, periradicular, periforaminal, transforaminal, caudal epidural or intradiscal injections. Co-interventions were allowed as long as they were uniform in all groups. Every study selected described in detail the intervention performed, methods of assessment and the results. Two reviewers independently examined the titles, abstracts and full texts and determined the eligibility of each study (PIAV and RGCA). Disagreements were resolved by the opinion of a third reviewer (RQG).

Analyzing and reporting the results

The variables to be collected for each included study were: Bibliometric variables: authors, year of publication, and country of origin. Study variables: design type, level of evidence, characteristics of the disease, demographic characteristics, characteristics of the intervention used, results and adverse reactions or side effects.

The level of evidence for each study was determined using the American Society of Surgeons Scale for studies evaluating therapeutic interventions, which determines the level of evidence according to the study design.[33]

Results

Search results

A total of 1556 citations were identified, excluding 1187 in duplicate. The titles and abstracts of the remaining 369 studies were studied, excluding 196 basic or animal model studies, editorials, comments, protocols and other unrelated studies. 173 studies were studied in full text, of which 169 were excluded for the following reasons: review studies (n = 42); studies in which ozone application was performed intradiscally (n = 93); studies where ozone application was performed via transforaminal, caudal, periforaminal or periradicular routes (n = 18); studies where patients were treated with POIs but there was no comparison group or were compared against interventions other than MIPC (n = 16). Finally, four studies were eligible for inclusion in the scoping review,[34-37] in which POIs were compared with MIPC. The flow chart of the systematized search is shown in **Figure 1**.

Characteristics of the studies

The four studies included in this review were randomized clinical trials.[34-37] Two studies were performed in Italy,[33,34] one in Egypt[36] and one in Iran.[37]

This scoping review included 501 individuals who presented LPRI secondary to disc pathology[34-36] and lumbar stenosis.[37] A total of 245 individuals were included in the POIs groups, who were treated with intramuscular injections of ozone into the lumbar paravertebral muscles, while 236 individuals were included in the MPIC groups. In the four included studies the MPIC performed were ECIs including epidural injection via interlaminar[34,35] or epidural injection via caudal[36,37] with corticosteroid alone[34,35] or combined with local anesthetic[35,37] or hyaluronidase.[37] Additionally, one of the studies included 20 individuals, who belonged to an additional control group and were treated with intramuscular paravertebral injections of bupivacaine.[34]

Treatment characteristics of paravertebral ozone injections

Regarding the characteristics of the treatment in the POIs groups, we found that all the included studies applied 1 to 8 sessions, with a mode of 3 sessions. The frequency of applications was 1–3 times per week with a mode of once per week. The volume of gas used per application was 5–20 mL, with a mode of 5 mL. The ozone concentrations used were 10–20 µg/mL, with a mode of 20 µg/mL. On the other hand, the application technique in all studies was through intramuscular injections in the lumbar paravertebral muscles at approximately 4 cm of depth, on the sides of the spine of the affected level, including or not the immediate upper and lower levels, performing 2–6

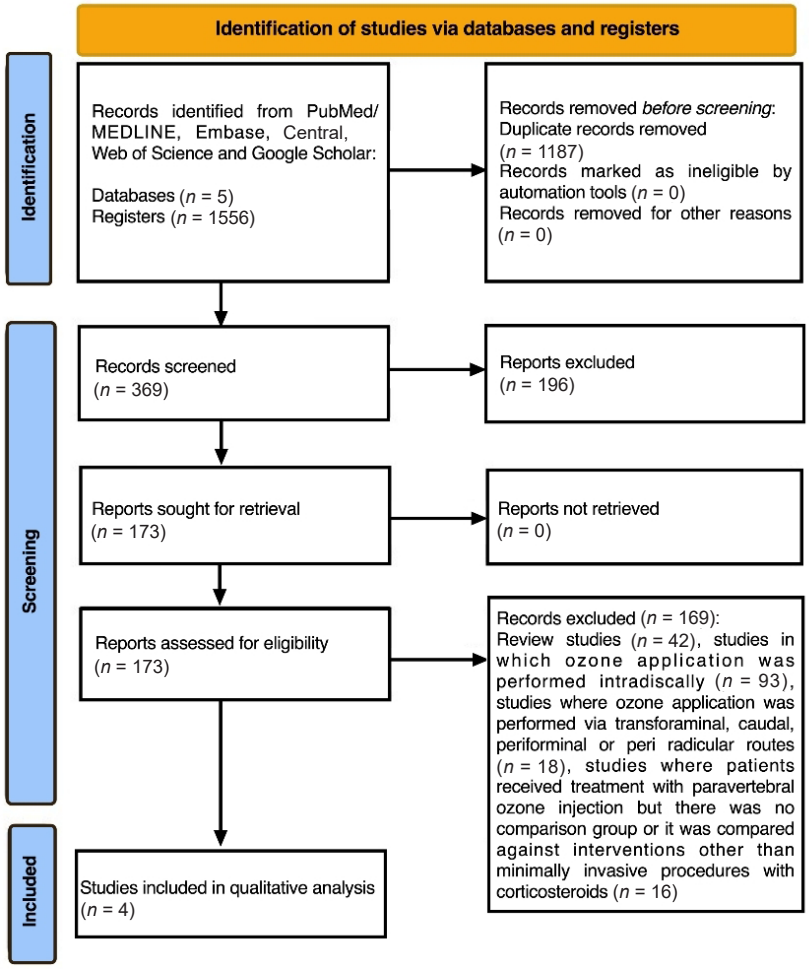

Figure 1 | **Systematic review flow diagram.**
A total of 1556 citations were identified in all databases, 1187 were duplicates and were excluded. 369 studies were reviewed, of which 365 were excluded. Finally, 4 studies were eligible for inclusion in the scoping review.

punctures per session.

Beneficial effects of paravertebral ozone injections

The four included studies[34-37] reported that in the groups treated with POIs a statistically significant reduction in pain was observed, when comparing the baseline evaluation with post-treatment evaluations.

When comparing POIs and ECIs groups, all studies reported a statistically significant reduction in pain for both interventions in the within-group comparison.[34-37]

In the short term between-group comparison, two studies reported a statistically significant pain reduction in favor of the POIs groups[34,35]; while two studies reported pain reduction in favor of the ECIs groups.[36,37] In the medium term, two studies reported statistically significant pain reduction in favor of the POIs groups,[35,37] and only one study reported pain reduction in favor of the ECIs group.[36]

Gjonovich et al.[34] compared eight sessions of POIs versus two sessions of ECIs in the treatment of LPRI secondary to disc herniation; at 2 weeks follow-up they observed more than 50% pain reduction in 75% of the patients treated with POIs, and in 55% of patients treated with ECIs.

Zambello et al.[35] compared 1–3 sessions of POIs *versus* 1–3 sessions of ECIs in the treatment of LPRI secondary to disc herniation; at 3 weeks follow-up they observed that pain had disappeared in 72% of patients in the POIs group, as well as in 45% of patients in the ECIs group. When evaluated at 6-month follow-up, 70% of individuals treated with POIs remained pain-free, while in individuals treated with ECIs group only 41% remained pain-free.

Abulkassem et al.[36] compared four sessions of POIs *versus* two sessions of ECIs when treating LPRI secondary to herniated disc; they observed a statistically significant pain reduction in both treatment groups at 4 and 12 weeks follow-ups, but in favor of the group treated with ECIs.

Parvin et al.[37] compared three sessions of POIs versus one session of ECIs when treating LPRI secondary to lumbar spinal stenosis, reporting a statistically significant pain reduction in both treatment groups at 2, 4 and 8 weeks follow-ups, with results in favor of ECIs at 2 and 4 weeks, but in favor of POIs at 8 weeks.

Adverse effects of paravertebral ozone injections

The four included studies[34-37] reported no side effects or adverse reactions in the patients treated. The results regarding the origin and study design, intervention characteristics, as well as favorable and adverse effects of the included studies are shown in **Table 1**.

Discussion

The objectives of this scoping review were to identify and analyze clinical studies where POIs were compared with MIPC when treating patients with LPRI, in order to describe and analyze the characteristics of the treatments and the benefits and side effects.

Previous reviews have evaluated the efficacy of ozone injections in reducing lumbosacral pain secondary to disc herniation[28]; these reviews, however, have included studies where ozone was applied intradiscally. Similarly, other review studies have performed a combined analysis of studies where ozone was applied by various routes such as intradiscal, intraforaminal, periradicular or intramuscular paravertebral,[28,30] which does not allow a specific analysis of the benefits and adverse reactions of POIs. Only one systematic review[31] has specifically analyzed the efficacy of POIs in the treatment of lumbosacral pain with or without radicular irradiation; nonetheless, this review included case series studies (without a control group), observational studies and clinical trials that compared POIs with interventions such as placebo, physical therapy or pharmacological treatment, not showing the benefits of POIs in comparison with MIPC.

Our review identified and analyzed studies in which POIs were compared with MIPC (specifically ECIs), in the treatment of LPRI. Four controlled clinical trials with low numbers of patients were included in this scoping review, which correspond to level II evidence for intervention studies.[33] In our review, we found that in all the included studies,[34-37] a reduction in LPRI was observed when comparing the baseline evaluation with subsequent evaluations in individuals treated with POIs, suggesting a therapeutic effect. When comparing POIs with ECIs, in the within-group comparisons, a statistically significant reduction in pain was reported in every study for both interventions. In the between-group comparisons, some studies reported a greater therapeutic effect of POIs and other studies reported favorable effects in favor of ECIs, with results varying according to the follow-up time. Two studies reported greater efficacy of POIs in reducing LPRI in the short term,[34,35] while two studies reported that ECIs were more effective in reducing LPRI in the short term.[36,37] These results appear contradictory and do not allow us to define which intervention is more effective in the short term; nevertheless, both had a favorable effect in reducing pain.

In the medium term, two studies reported greater efficacy of POIs in reducing LPRI,[35,37] and only one study reported greater efficacy of ECIs. These results suggest a slightly better effect of POIs in the medium term.

ECIs are a minimally invasive procedure, well established and commonly used for treating radicular lumbosacral pain.[11] Its efficacy has been demonstrated with a statistically significant reduction in pain in short-term follow-ups observed in individuals with LPRI.[12] ECI mechanism is based on the deposit of corticosteroids in the

Table 1 | Characteristics of the interventions and results of the included studies

Study	Year	Country	Level of evidence*	Design	Study groups	Results	Adverse reactions and/or side effects
Gjonovich et al.[34]	2001	Italy	II	Clinical trial that included 60 patients (22–55 yr old) with lumbosacral pain with radicular irradiation, secondary to disk pathology diagnosed by computed tomography or magnetic resonance imaging, of more than 45 d of evolution and with failure in conventional treatment.	POIs group: 20 patients treated with 8 sessions of POIs. In each session, two injections were applied (both sides of the affected level). At each point, 15–20 mL of ozone was applied at a concentration of 15 µg/mL, with an application frequency three times per week.	The results were expressed as a percentage of patients who presented pain reduction greater than 50% in relation to initial value, at 2 wk of follow-up.	Absence of complications or serious adverse effects was reported in patients of both groups.
					ECIs group: 20 patients treated with three epidural injections with 8 mg of phosphate de dexamethasone diluted in 15 mL of physiological saline solution in the intervertebral space corresponding to the affected disc, with a weekly application frequency.	The percentage of patients with a favorable response to treatment was statistically significant for both treatment groups, but in favor of the POIs group.	
					PBI group: 20 patients treated with one intramuscular paravertebral injection of 10 mL of 0.25% bupivacaine on both sides of the affected level.		
Zambello et al.[35]	2006	Italy	II	Clinical trial that included 351 patients (average age of 49.5 yr) with chronic lumbosacral pain with radicular irradiation, secondary to disk pathology diagnosed by magnetic resonance imaging and with failure in conventional pharmacological treatment.	POIs group: 180 patients treated with 1–3 sessions of POIs. In each session, six injections were applied (both sides of the affected level and one level below and above the affected level). At each point, 5 mL of ozone was applied at a concentration of 10–20 µg/mL, with a weekly application frequency.	The results were expressed as a percentage of patients who presented pain reduction at three wk and 6 mon of follow-up.	Absence of complications or serious adverse effects was reported in patients of both groups.
					ECIs group: 171 patients treated with 1 to three epidural injections with 80 mg of triamcinolone acetonide diluted in 20 mL of physiological saline solution in the intervertebral space corresponding to the affected disc, with a weekly application frequency.	The percentage of patients with a favorable response to treatment was statistically significant for both treatment groups in the short and medium terms, but in favor of the POIs group.	
Abulkassem et al.[36]	2013	Egypt	II	Clinical trial that included 60 patients (22–55 yr old) with lumbosacral pain with radicular irradiation, secondary to disk pathology diagnosed by computed tomography or magnetic resonance imaging, with more than 3 mon of evolution and with failure in conventional treatment.	POIs group: 30 patients treated with 4 sessions of POIs. In each session, four injections were applied (both sides of the affected level and one level below). At each point, 15 mL of ozone was applied at a concentration of 10 µg/mL, with weekly frequency.	Pain reduction expressed in the VAS.	Absence of complications or serious adverse effects was reported in patients of both groups.
					ECIs group: 30 patients treated with 2 caudal epidural injections with 14 mg of betamethasone, 5 mL of 2% Lidocaine and 5 mL of 0.5% Bupivacaine diluted in 30 mL of physiological saline solution, with a weekly application frequency.	No statistically significant difference between groups at 2 wk follow-up. Statistically significant pain reduction in both treatment groups at 4 wk and 3 mon of follow-up, but in favor of the ECIs group in the intergroup analysis.	
Parvin et al.[37]	2024	Iran	II	Clinical trial that included 30 patients (55–75 yr old) with lumbosacral pain with radicular irradiation, secondary to degenerative spinal canal stenosis diagnosed by magnetic resonance imaging, with more than 3 mon of evolution and with failure in conventional treatment.	POIs group: 15 patients treated with 3 sessions of POIs. In each session, two injections were applied (both sides of the affected level). At each point, 5 mL of ozone was applied at a concentration of 20 µg/mL, with weekly frequency.	Pain reduction expressed in the VAS.	Absence of complications or serious adverse effects was reported in patients of both groups.
					ECIs group: 15 patients treated with caudal epidural injections of methylprednisolone 80 mg, 4 mL of 0.5% bupivacaine and hyaluronidase 1500 IU.	In both groups, a statistically significant reduction in pain was reported compared to baseline. At 2 and 4 wk of follow-up, the reduction in pain was in favor of the ECIs group; at 8 wk of follow-up, it was in favor of the POIs group.	

*Level evidence determined using the American Society of Surgeons Scale for studies evaluating therapeutic interventions. ECIs: Epidural corticosteroid injections; PBI: paravertebral bupivacaine injections; POIs: paravertebral ozone injections; VAS: Visual Analogue Scale.

epidural space, generating an anti-inflammatory stimulus that decreases cyclo-oxygenase and lipoxygenase production, as well as the levels of prostaglandins, thromboxanes and leukotrienes; this reduces intraneural and perineural edema and inhibits nerve transmission in nociceptive C fibers. Finally, ECIs contribute to the decrease of the inflammatory state that occurs in the epidural space and spinal nerve roots as a consequence of the intervertebral disc degeneration.[11]

On the other hand, the use of ozone injections for treating lumbar pain is a minimally invasive procedure that is still under development.[38] Up until now, POIs have been an effective intervention in reducing low back pain with or without radicular irradiation, in the short and medium terms, in comparison with placebo interventions,

physical therapy programs and pharmacological treatments.[31] Our review suggests that POIs may also have a beneficial effect in reducing LPRI compared with other minimally invasive treatments such as ECIs.

In relation to the mechanisms, the POI technique is performed by applying ozone to the lumbar paravertebral muscles, on the sides of the spinous process at the affected vertebral level, at approximately 4 cm of depth; and it can be applied above and below the affected level.[34-37,39] Some authors have proposed that the application could be deeper and that the ozone may even be deposited very close to the lamina, in the vertebra at the affected level.[39] Clearly, the mechanisms of POIs and ECIs are different. In POIs, ozone is not deposited in the epidural space, these injections are administered in the paravertebral muscles and it is likely that ozone diffuses between the fascial planes, similar to what occurs with the erector spinae block, reaching nerve filaments coming from the dorsal branch of the affected root, then exerting its therapeutic effect.[40,41]

The therapeutic effects of ozone in spinal pathology are based on its anti-inflammatory effect and influence on oxidative stress regulation. A preclinical study reported that intrathecal injections with low concentrations of ozone reduce the overexpression of tumor necrosis factor-alpha, interleukin-6 and interleukin-1 in rats with chronic radiculitis model.[42] Other studies performed in animal models reported that the perineural application of ozone does not cause damage to the structure or function of the peripheral nerve,[43] and favors the activation of antinociceptive and anti-edema mechanisms[44]; ozone also favors the myelination process and restores the local redox balance,[45] without causing an increase in fibrotic tissue.[46]

In humans, it has been reported that the application of intradiscal ozone at medium concentrations in individuals with disc pathology decreases the expression of interleukins (such as interleukin-6) and immunoglobulins (such as IgG and IgM).[47] Similarly, León-Fernández et al.[48] demonstrated that POIs decrease local oxidative stress and restore local redox balance in individuals with disc pathology. Apparently, the anti-inflammatory and oxidative stress-modulating effects of ozone are related to an increase in phosphorylation of the nuclear factor erythroid 2 which stimulates the activity of the endogenous antioxidant enzymatic system while inhibiting nuclear factor kappa B, thereby decreasing the synthesis of proinflammatory cytokines.[49]

Both interventions POIs and ECIs, act through different application routes, but they share the anti-inflammatory effect as the main mechanism; ozone, however, has an additional effect on oxidative stress. Comparisons between both interventions raise the possibility of establishing advantages and disadvantages between them.

In terms of efficacy, ECIs represent a consolidated intervention that is commonly used in the treatment of LPRI.[11-13] POIs on the other hand, is an emerging intervention that has been reported to be more effective than placebo,[31,50] noninvasive treatments such as physiotherapy programs[31,51] and pharmacological treatment[31,52]; furthermore, it has been reported that POIs may be synergistic with these treatments.[53,54] The results of this review, indicate that POIs are a potential intervention for the treatment of LPRI, perhaps as an alternative to ECIs.[34,35,37]

Although ECIs are more commonly used than POIs for treating LPRI, the number of corticosteroid applications is usually limited given the complexity and risk of the procedure, as well as the possible deleterious effects of corticosteroids.[55] In the case of POIs, they can be applied several times without side effects, achieving pain control in recalcitrant cases. In the included studies, we were able to observe that more POI sessions than ECIs were applied per patient[34,36,37] almost in a 2:1 or 3:1 ratio. However, Gjonovich et al.[34] reported that POIs decreased lumbosacral pain after the first applications; but in radiated sciatic pain more applications were needed to decrease pain.

With regards to the application route and mechanisms, the injections into the epidural space represent a minimally invasive procedure that seeks to deposit corticosteroids as close as possible to the disco-radicular conflict in question.[11] POIs seek to generate an anti-inflammatory effect as well as an indirect modulating effect on oxidative stress, through the diffusion of ozone gas by the fascial planes.[40,41] ECIs are a more technically complex intervention, requiring the use of ultrasound or radiographic guidance for greater safety,[11,55] implying a higher level of training of the medical staff that performs it, and only a few medical specialists perform this technique. POIs on the other hand, need a less technically complex intervention,[39] which may or may not require ultrasound guidance, without affecting the efficacy of the procedure.[56] In this sense, Araimo Morcelli et al.[56] evaluated the efficacy and safety of POIs in individuals with low back pain, comparing paravertebral injections of 5 mL of ozone with ultrasound guidance, *versus* injections of 10 mL of ozone without ultrasound guidance, reporting no differences in efficacy between the two procedures; nonetheless, the ultrasound-guided group reported less discomfort during application, probably due to the lower volume of gas.

Regarding the safety of these procedures, it has been reported that ECIs are a generally safe intervention when performed correctly, with a minor complication rate of 2.4% per puncture, with the most frequent minor adverse reaction being post-puncture pain[55]; however, given the technical complexity and proximity to the anatomical structures, it is a procedure that can potentially be a source of severe neurological complications.[12,55] While POIs, being intramuscular-myofascial procedures, are perhaps the least complex of the minimally invasive procedures used to apply ozone in lumbar spine pathologies; then, the possibility of complications and their severity is lower. The main adverse reactions of POIs are discomfort or pain during application,[31] but it is suggested that this can be reduced with the application of low volumes of gas (up to 5 mL),[56] as well as with local anesthetics.[57] However, one case of paravertebral abscess secondary to the application of ozone in paravertebral muscles has been reported,[58] this could be related more to antiseptic conditions during the procedure and the patient's condition, than to the application complexity. It should be noted that intradiscal or intraforaminal ozone applications may have a higher risk of complications.[59,60] In our review, no side effects or severe adverse reactions were reported for any interventions studied, using ECIs or POIs. Perhaps POIs represent an intervention with a lower risk of complications or less severe complications than other interventions such as epidural injections or other forms of ozone application including intraforaminal or intradiscal, which could facilitate its use, requiring less infrastructure and being more accessible when added to multimodal treatments for treating LPRI.

It is important to note that our review has some limitations. Only four studies were included, gathering a total of 501 individuals, which represents a low number for a review. The variability in the reported diagnoses and the heterogeneity in the treatment regimens, made it impossible to perform a systematic review with meta-analysis to assess the efficacy or safety of POIs; for this reason, the scoping review design was used, in order to establish a first overview of this intervention that will help to determine whether POIs represent an alternative to ECIs in the treatment of LPRI. Preclinical studies are needed to confirm the mechanisms of ozone in pain control as well as more high-quality randomized controlled trials comparing POIs with ECIs, in order to clarify the benefits and side effects of both interventions. When more scientific evidence is available, other reviews with quantitative analysis could be performed to establish a good level of evidence when comparing POIs with ECIs. This scoping review included four clinical trials that compared POIs with ECIs in the treatment of LPRI. POIs appear to have a favorable therapeutic effect in reducing pain in the short and medium terms in individuals with LPRI, and in some studies, this effect was higher than ECIs. POIs are minimally invasive with low risk and low application complexity, which makes this treatment a potential tool for inclusion in multimodal programs for the treatment of LPRI. However, given the low number of studies analyzed in this Scoping Review, we conclude that more high-quality randomized clinical studies are necessary to perform meta-analytical studies to confirm the efficacy and safety of POIs in the treatment of LPRI.

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Conflicts of interest: *The authors declare that there are no conflicts of interest in producing this article and that they approve its publication.*

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no generative AI or AI-assisted technologies were used in the construction of this manuscript.

Data availability statement: *All data relevant to the study are included in the article or uploaded as Additional file.*

Additional file:

Additional Table 1: *Detailed information on search strategies.*

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