World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

Oxygen–ozone therapy in lumbar disc herniation and lumbar radiculopathy: A narrative review

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World Journal of Advanced Research and Reviews, 2026, 30(03), 253-262

Publication history: Received on 19 April 2026; revised on 31 May 2026; accepted on 02 June 2026

Article DOI: https://doi.org/10.30574/wjarr.2026.30.3.1522

Abstract

Lumbar disc herniation is a common cause of low back pain and lumbar radiculopathy. It results from disruption of the annulus fibrosus, allowing displacement of the nucleus pulposus and subsequent nerve root compression. Beyond mechanical compression, inflammatory mediators released from the disc contribute to radicular pain, neurological symptoms, and functional impairment, substantially affecting patients' quality of life.

Although conservative treatment and surgery remain the main therapeutic approaches for lumbar disc herniation and lumbar radiculopathy, many patients evolve into an intermediate clinical stage characterized by persistent symptoms despite adequate conservative management and the absence of a clear surgical indication. This therapeutic gap has stimulated interest in minimally invasive interventions. Among these, oxygen–ozone (O_2–O_3) therapy has emerged as a promising option combining biochemical disc decompression with anti-inflammatory and immunomodulatory properties, potentially serving as an adjunct to comprehensive rehabilitation programs.

A narrative literature review was conducted using electronic databases including PubMed, Scopus, and Google Scholar. Relevant publications addressing ozone therapy for lumbar disc herniation and lumbar radiculopathy were analyzed, with particular attention to biological mechanisms, clinical outcomes, safety profile, and integration into rehabilitation strategies.

Lumbar radiculopathy results from a combination of mechanical nerve root compression and inflammatory processes, including chemical radiculitis and periradicular edema. Oxygen–ozone therapy acts through complementary mechanisms. Its primary effect involves biochemical disc decompression through oxidation of nucleus pulposus proteoglycans, leading to disc dehydration, reduction of intradiscal pressure, and decreased nerve root compression. In addition, ozone exerts anti-inflammatory and immunomodulatory effects that may reduce periradicular edema and radicular irritation. Improved microcirculation and tissue oxygenation may also contribute to pain relief and functional recovery.

Oxygen–ozone therapy represents a promising minimally invasive option targeting both the mechanical and inflammatory components of lumbar radiculopathy secondary to disc herniation. Positioned between conservative management and surgery, it may provide an effective therapeutic option in appropriately selected patients and may be integrated into comprehensive rehabilitation programs. Nevertheless, further high-quality studies are required to clarify its long-term efficacy and optimal indications.

Keywords: Low Back Pain; Lumbar Disc Herniation; Lumbar Radiculopathy; Ozone Therapy; Oxygen-Ozone; Intradiscal Injection; Discogenic Pain; Rehabilitation

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1. Introduction

Low back pain is one of the leading causes of disability worldwide and represents a major public health challenge due to its high prevalence and socioeconomic burden. Among its various etiologies, lumbar disc herniation is a common cause of lumbar radiculopathy, resulting from both mechanical compression of the nerve root and local inflammatory processes. Patients may experience low back pain, radiating leg pain, sensory disturbances, motor deficits, and functional limitations that substantially impair quality of life and daily activities[1] .

The management of lumbar disc herniation and lumbar radiculopathy generally relies on a multimodal approach combining pharmacological treatment, physical rehabilitation, therapeutic education, and, in selected cases, interventional procedures or surgery. However, a significant proportion of patients continue to experience persistent symptoms despite appropriate conservative treatment and without a clear surgical indication. Within this therapeutic gap, minimally invasive techniques have gained increasing attention as potential alternatives to delay or avoid surgery.

Among these approaches, medical oxygen–ozone therapy has emerged as a promising therapeutic option. Its proposed mechanisms of action include biochemical disc decompression through dehydration of the nucleus pulposus, modulation of inflammatory processes, and improvement of local microcirculation. These combined effects may contribute to pain relief and functional recovery in patients with lumbar radiculopathy secondary to disc herniation. Despite its increasing use in clinical practice, its precise role, indications, and long-term efficacy remain subjects of ongoing debate[2].

The aim of this narrative review is to summarize the pathophysiological basis, mechanisms of action, clinical indications, and current evidence regarding oxygen–ozone therapy in the management of lumbar disc herniation and lumbar radiculopathy.

1.1. Pathophysiology of Low Back Pain and Lumbar Radiculopathy

Low back pain is a multifactorial condition that most commonly results from mechanical and degenerative alterations affecting the functional spinal unit, which includes the vertebral bodies, intervertebral discs, facet joints, ligaments, and paraspinal muscles [3].

Among these structures, the intervertebral disc plays a crucial role in both spinal biomechanics and the development of pain syndromes. The intervertebral disc acts as a shock absorber and load distributor, allowing flexibility while maintaining spinal stability. It is composed of a central nucleus pulposus, rich in water and proteoglycans, surrounded by the annulus fibrosus, which consists of concentric collagen fibrous lamellae that provide structural support and containment of the nucleus pulposus[4].

With aging, genetic predisposition, and/or repeated mechanical stress, the intervertebral disc undergoes progressive degenerative changes. Loss of proteoglycans within the nucleus pulposus leads to dehydration, reduced elasticity, and diminished load-bearing capacity. Simultaneously, fissures may develop within the annulus fibrosus, compromising its structural integrity and facilitating displacement of disc material.

These degenerative changes may culminate in disc protrusion or herniation, allowing nucleus pulposus material to migrate beyond the confines of the annulus fibrosus [5].

The resulting symptoms are not solely attributable to mechanical nerve root compression. Increasing evidence suggests that inflammatory mediators released from the degenerated disc, including tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and other pro-inflammatory cytokines, contribute significantly to radicular pain by inducing chemical radiculitis, perineural edema, and nerve root sensitization [6].

In addition to nerve root involvement, disc degeneration alters the distribution of mechanical loads across the spinal segment. Increased stress on adjacent structures such as the facet joints, interspinous ligaments, and paraspinal muscles may lead to facet arthropathy, muscular dysfunction, segmental instability, and chronic low back pain. These biomechanical alterations often coexist with inflammatory processes, creating a complex pain-generating environment.

Consequently, lumbar disc herniation and lumbar radiculopathy should be viewed as the result of both mechanical and inflammatory mechanisms. This dual pathophysiology provides the rationale for minimally invasive treatments such as

oxygen–ozone therapy, which aims to reduce disc volume while simultaneously modulating local inflammatory responses [6].

1.2. Ozone Therapy: Definition and Principles

Medical ozone therapy is based on the administration of a calibrated oxygen–ozone (O_2–O_3) gas mixture at predefined concentrations. In clinical practice, ozone is never administered as a pure gas but is generated immediately before use from medical-grade oxygen using dedicated generators that ensure precise concentration control according to the clinical indication and route of administration. This precaution is essential because ozone is a highly reactive and unstable triatomic form of oxygen with a short half-life, and its biological effects are strongly dose-dependent [7].

Unlike conventional pharmacological agents that act through specific receptor-mediated mechanisms, ozone functions primarily as a redox-active stimulus. Following administration, it rapidly reacts with biological fluids, particularly polyunsaturated fatty acids, antioxidants, and other electron-rich molecules present in plasma and interstitial compartments. These reactions generate secondary messengers, including reactive oxygen species and lipid oxidation products, which are thought to mediate most of its biological effects. Consequently, the therapeutic action of ozone relies less on the persistence of the gas itself than on the transient signaling cascade initiated after its administration[8].

A key concept underlying ozone therapy is oxidative hormesis. At low and controlled concentrations, ozone induces a mild and transient oxidative stress capable of activating adaptive cellular defense mechanisms without causing structural damage. This response promotes the activation of cytoprotective pathways, particularly the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway, which regulates the expression of antioxidant enzymes such as superoxide dismutase, catalase, glutathione peroxidase, and heme oxygenase-1. Through these mechanisms, ozone therapy may enhance endogenous antioxidant defenses and contribute to the restoration of cellular redox homeostasis. In contrast, excessive exposure may overwhelm antioxidant systems and lead to tissue injury, highlighting the importance of strict dose control [9].

Beyond its redox-regulating properties, ozone therapy appears to exert anti-inflammatory and immunomodulatory effects. Experimental studies suggest that therapeutic ozone concentrations may modulate the production of pro-inflammatory mediators and influence signaling pathways such as NF-κB, thereby limiting the amplification of inflammatory responses. This mechanism is particularly relevant in musculoskeletal and spinal disorders, where symptoms frequently arise from a combination of mechanical compression, local inflammation, perineural edema, and chemical irritation of neural structures.

The biological effects of ozone therapy also depend on the route of administration. In the management of lumbar disc herniation, ozone can be delivered through intradiscal, periradicular, epidural, or paravertebral approaches. Intradiscal administration is primarily intended to induce biochemical disc decompression through oxidation of proteoglycans, resulting in disc dehydration, reduced intradiscal pressure, and indirect nerve root decompression. In contrast, periradicular and paravertebral injections are thought to act predominantly through anti-inflammatory mechanisms and modulation of the local biochemical environment. Therefore, ozone therapy should not be considered a single uniform intervention, but rather a group of procedures sharing common biological principles while differing in targets and clinical applications [10].

From a therapeutic perspective, the interest in ozone therapy lies in its potential to simultaneously address several pathophysiological mechanisms involved in lumbar radiculopathy. By combining disc decompression, modulation of inflammatory mediators, regulation of oxidative stress, and possible improvements in local microcirculation, ozone may target both the mechanical and inflammatory components of the disease process. However, although these mechanisms are biologically plausible, their relative contribution to clinical improvement remains incompletely understood in humans. Much of the current mechanistic evidence derives from experimental and translational studies rather than direct clinical investigations [11].

Finally, ozone therapy has a relatively narrow therapeutic window. Its safety and efficacy depend on appropriate patient selection, accurate procedural technique, and strict control of ozone concentration. Moreover, current evidence highlights the lack of standardized protocols and the variability of outcomes depending on the route of administration and operator expertise. Therefore, ozone therapy should be integrated into a well-defined procedural and clinical framework and considered part of a comprehensive management strategy rather than a universally applicable treatment modality [11].

1.3. Mechanisms of Action of Ozone Therapy in Low Back Pain

Ozone therapy has attracted growing interest in the management of spinal disorders because its proposed biological effects target several key mechanisms involved in low back pain, particularly in lumbar disc herniation and lumbar radiculopathy[12]. Its therapeutic rationale is based on a combination of biochemical disc decompression, anti-inflammatory and immunomodulatory effects, and indirect regulation of oxidative stress through controlled oxidative stimulation. Although these mechanisms are biologically plausible and supported by a substantial body of experimental evidence, their precise contribution to clinical outcomes remains incompletely understood, and several proposed effects are supported more strongly by experimental and translational studies than by direct mechanistic investigations in humans[13].

1.3.1. Biochemical Disc Decompression

The nucleus pulposus is rich in proteoglycans that maintain disc hydration through their capacity to bind water and preserve intradiscal osmotic pressure. Ozone induces partial oxidation of these macromolecules, reducing their water-retention capacity and leading to progressive disc dehydration. This process results in a reduction in disc volume and intradiscal pressure.

By decreasing the mass effect of the herniated disc, ozone therapy may reduce mechanical compression of adjacent nerve roots and contribute to symptom relief [14].

1.3.2. Anti-Inflammatory and Immunomodulatory Effects

Beyond its mechanical action, ozone therapy may also target the inflammatory component of lumbar radiculopathy. Disc degeneration and herniation are associated with the release of pro-inflammatory mediators responsible for chemical radiculitis, periradicular edema, and sensitization of neural structures [15]. These inflammatory processes play a major role in pain generation and may persist even when mechanical compression is relatively limited.

At therapeutic concentrations, ozone appears to modulate the inflammatory response by influencing the production of cytokines and biochemical mediators involved in nociceptive pathways. Several studies suggest that ozone may reduce the expression of pro-inflammatory mediators while regulating local immune activity. By limiting periradicular inflammation and tissue edema, ozone therapy may reduce secondary nerve root compression and irritation [16].

1.3.3. Indirect Antioxidant Effects

Another important biological mechanism of ozone therapy is the induction of a controlled and transient oxidative stress capable of activating endogenous cellular defense mechanisms. This phenomenon is consistent with the concept of oxidative hormesis, whereby low levels of oxidative stimulation activate endogenous defense mechanisms rather than causing cellular damage [17].

Following administration, ozone reacts rapidly with biological molecules present in tissues and extracellular fluids, generating secondary messengers such as reactive oxygen species and lipid oxidation products. At controlled concentrations, these molecules function primarily as signaling mediators, activating intracellular regulatory pathways involved in antioxidant defense.

This process leads to increased expression and activity of endogenous antioxidant enzymes including superoxide dismutase, catalase, and glutathione peroxidase. Through these mechanisms, ozone therapy may contribute to restoring cellular redox homeostasis and limiting the detrimental effects of chronic oxidative stress, which has been implicated in disc degeneration and persistent pain states [18].

1.3.4. Integrated Therapeutic Effect

Taken together, these mechanisms suggest that ozone therapy may act simultaneously on both the mechanical and inflammatory components of lumbar disc disease. Disc decompression may reduce nerve root compression, while anti-inflammatory and redox-regulating effects may attenuate chemical radiculitis, tissue edema, and nociceptive sensitization. This multimodal biological action likely explains the growing interest in ozone therapy as an intermediate treatment option between conservative management and surgery in selected patients with lumbar disc herniation and radiculopathy.

Ozone therapy has also been reported to improve local microcirculation and tissue oxygen delivery through effects on erythrocyte metabolism, vascular regulation, and rheological properties of blood. These effects may contribute to

reducing local ischemia and promoting tissue recovery in chronically inflamed perineural environments. Although frequently cited in the ozone literature, the clinical relevance of these mechanisms remains incompletely established [18], [19].

2. Current Clinical Evidence

The clinical evidence supporting ozone therapy in lumbar spine disorders is derived from randomized controlled trials, observational studies, systematic reviews, and meta-analyses. Most available studies focus on lumbar disc herniation and lumbar radicular pain rather than nonspecific low back pain. Overall, the published evidence suggests that oxygen–ozone therapy may provide meaningful pain relief and functional improvement in selected patients, particularly those with persistent disc-related symptoms despite conservative treatment. However, interpretation of the evidence remains challenging because of heterogeneity in patient selection, treatment protocols, routes of administration, ozone concentrations, comparator interventions, and outcome measures [20].

One of the earliest influential syntheses was the meta-analysis conducted by Magalhães et al., which evaluated randomized controlled trials investigating ozone therapy for lumbar disc herniation. The authors reported favorable effects on pain outcomes compared with control interventions and helped establish ozone therapy as a potential minimally invasive option in pain management. Nevertheless, considerable variability in procedural techniques and methodological quality limited the strength of the conclusions [21].

Subsequently, systematic reviews have generally reported encouraging results. Costa et al. reviewed studies involving patients with lumbar disc herniation and concluded that ozone therapy appeared both effective and safe in appropriately selected cases. However, the authors emphasized the methodological limitations and heterogeneity of the included studies [22].

Similarly, de Andrade et al. found that ozone therapy was associated with superior pain relief compared with other therapeutic approaches over a six-month follow-up period. However, these findings should be interpreted with caution because of the moderate to high risk of bias among the included studies [23].

More recent studies and reviews have described encouraging outcomes regarding pain relief and functional recovery, especially in patients with disc herniation-related symptoms. However, the authors also underscored the absence of standardized treatment protocols and the difficulty of defining clear clinical indications [24].

Not all recent evidence syntheses have reached uniformly positive conclusions. A 2024 review focusing on patient-reported outcomes suggested that ozone infiltration provided only limited benefit compared with usual care, with modest superiority for functional outcomes and no consistently large treatment effect. These findings highlight the importance of maintaining a balanced interpretation of the available evidence [25].

More recent reviews published in 2024 and 2025 have continued to suggest potential benefits of ozone therapy in patients with lumbar disc herniation and lumbosacral pain, particularly in terms of short- and medium-term pain relief and disability reduction. Nevertheless, these reviews consistently report substantial heterogeneity and emphasize the need for higher-quality comparative studies. Therefore, although the overall direction of the evidence is generally favorable, the certainty of the available evidence remains moderate [26].

An important issue in interpreting the clinical evidence is that the term “ozone therapy” does not refer to a single standardized procedure. Studies have investigated intradiscal injection, periradicular or periganglionic injection, transforaminal administration, caudal epidural injection, and paravertebral intramuscular approaches [27], sometimes used alone and sometimes combined with local anesthetics or corticosteroids [28]. Because of this procedural variability, pooling results across studies is challenging, and findings obtained with one technique cannot necessarily be generalized to another [29].

Current evidence suggests that the greatest benefit may be achieved in carefully selected patients presenting with contained or mildly extruded lumbar disc herniation, persistent radicular symptoms, and failure of conservative treatment. In contrast, patients with progressive neurological deficits, marked spinal instability, or clear surgical emergencies are generally not considered suitable candidates. In this context, ozone therapy is most often considered a minimally invasive intermediate option between conservative treatment and surgical intervention.

From a rehabilitation perspective, ozone therapy should not be viewed as a stand-alone treatment. Rather, it may be integrated into a comprehensive management strategy combining therapeutic exercise, patient education,

pharmacological treatment when indicated, and functional rehabilitation. Such an approach is particularly relevant in patients whose pain limits participation in active rehabilitation programs.

Overall, the available evidence suggests that ozone therapy may provide clinically relevant pain relief and functional improvement in selected patients with lumbar disc herniation, particularly in the short and medium term. However, the strength of evidence remains limited by heterogeneity in treatment protocols, variability in ozone concentrations and administration routes, and inconsistent methodological quality across studies. Therefore, while results are encouraging, the level of evidence remains moderate and does not yet support universal recommendations. Future research should focus on standardized protocols, improved patient stratification, longer follow-up periods, and direct comparisons with established interventional and rehabilitation-based treatment strategies.

3. Indications, Contraindications and Patient Selection

Appropriate patient selection is one of the main determinants of successful outcomes following ozone therapy in spinal disorders. Although ozone therapy is generally considered a safe and minimally invasive treatment, its use should be restricted to carefully selected patients presenting with discogenic lumbar disc disease or lumbar radiculopathy refractory to conservative management. Current evidence supports its role as an intermediate therapeutic option positioned between conservative treatment and surgical intervention. Furthermore, understanding both the indications and contraindications is essential to minimize potential complications and optimize therapeutic outcomes [30].

3.1. Indications

The main clinical indications for ozone therapy are primarily related to lumbar disc pathology. It is most commonly proposed for patients with lumbar disc herniation associated with persistent radicular pain despite well-conducted conservative treatment. In this context, ozone therapy may provide both mechanical and anti-inflammatory effects, particularly in cases of contained or mildly extruded disc herniation [31].

Ozone therapy may also be considered in patients presenting with discogenic low back pain, especially when imaging findings demonstrate intervertebral disc degeneration without a clear indication for surgery. In addition, it can be proposed in patients presenting with lumbar radiculopathy in the absence of severe or progressive neurological deficits.

Beyond disc herniation, ozone therapy has been investigated in patients with chronic low back pain refractory to pharmacological and rehabilitation programs. Selected patients with lumbar spinal stenosis and neurogenic claudication may also benefit from this approach, particularly when used as an adjunct to epidural injections. Furthermore, ozone therapy has been employed in patients with persistent spinal pain after surgery, especially in the context of epidural fibrosis, often in combination with other interventional techniques [32].

The ideal candidate for ozone therapy is a patient presenting with imaging-confirmed lumbar disc herniation, persistent radicular symptoms despite adequate conservative treatment, clinicoradiological concordance, and no indication for urgent surgical intervention. In this context, ozone therapy may represent a valuable minimally invasive alternative before considering surgery.

From a rehabilitation perspective, ozone therapy should be viewed as an adjunct to a comprehensive management strategy rather than a replacement for active treatment. Therapeutic exercise, patient education, maintenance of physical activity, and functional rehabilitation remain essential components of care and should be continued whenever possible[33].

3.2. Contraindications

Contraindications to ozone therapy must be carefully considered in order to ensure patient safety and optimize therapeutic outcomes. These contraindications can be classified as absolute and relative.

Absolute contraindications include glucose-6-phosphate dehydrogenase deficiency, pregnancy, local or systemic infections such as spondylodiscitis, severe coagulation disorders, sepsis, and known allergy to medications potentially used during the procedure, including local anesthetics or corticosteroids [34].

Relative contraindications include large sequestrated lumbar disc herniation associated with significant neurological compromise, progressive motor deficit, severe lumbar spinal stenosis, and major spinal instability. In such situations, the indication for ozone therapy should be carefully evaluated on a case-by-case basis, taking into account the patient's clinical presentation and available therapeutic alternatives.

3.3. Procedure and Technical Approaches

Ozone therapy for spinal disorders involves the controlled administration of a medical oxygen–ozone (O_2–O_3) mixture near pain-generating structures such as the intervertebral disc, nerve roots, epidural space, or paravertebral muscles. It is considered a minimally invasive interventional procedure, usually performed in an outpatient setting under imaging guidance .

Patient selection is essential and is based on a combination of clinical assessment and imaging findings, most commonly magnetic resonance imaging (MRI). Imaging is essential to confirm structural abnormalities such as lumbar disc herniation and helps exclude conditions requiring urgent surgical management, including progressive neurological deficits, spinal infections, or severe spinal instability. Standard procedural precautions include strict aseptic technique, coagulation assessment, and appropriate management of anticoagulant or antiplatelet therapy.

Ozone is generated immediately before administration from medical-grade oxygen using a dedicated generator that ensures precise control of concentration. Because ozone is highly unstable and has a short half-life, the gas mixture must be administered immediately after generation [35].

Several administration techniques have been described according to the clinical indication .

Intradiscal injection is the most commonly used approach for lumbar disc herniation associated with radicular pain. Its primary objective is biochemical disc decompression through oxidation of proteoglycans within the nucleus pulposus, resulting in disc dehydration, reduction of intradiscal pressure, and indirect nerve root decompression [36].

Transforaminal or periradicular injection targets the affected nerve root within the epidural space and is often combined with local anesthetics or corticosteroids to enhance anti-inflammatory effects .

Caudal epidural injection is mainly used in patients with lumbar spinal stenosis or diffuse epidural inflammation .

Epiduroscopy-guided ozone administration is typically reserved for patients with persistent pain related to epidural fibrosis, especially following spinal surgery .

Paravertebral intramuscular injections represent a simpler technique mainly used in mechanical low back pain or early degenerative disc disease .

Most procedures are performed under fluoroscopic or computed tomography guidance, although ultrasound may be used for selected approaches [37].

Despite increasing clinical use, treatment protocols remain heterogeneous. Ozone concentrations generally range from 10 to 40 μg/mL depending on the target tissue and the technique employed. Further research is needed to standardize treatment protocols and better define optimal indications for each approach [38].

From a rehabilitation perspective, ozone therapy should not be considered a stand-alone intervention. Optimal outcomes are likely achieved when the procedure is integrated into a multidisciplinary management strategy that includes therapeutic exercise, patient education, maintenance of physical activity, and functional rehabilitation.

3.4. Limitations of Current Evidence

Despite growing interest in ozone therapy, several limitations of the current evidence should be acknowledged. First, substantial heterogeneity exists across studies regarding ozone concentrations, injection techniques, treatment protocols, and the number of sessions performed. Second, patient selection criteria vary considerably between studies, limiting the generalizability of reported outcomes. Third, many available studies present a moderate to high risk of bias and lack long-term follow-up data [39].

The absence of universally accepted treatment protocols further complicates the interpretation of results and contributes to uncertainty regarding the optimal concentration, route of administration, and treatment schedule. In addition, most studies involve relatively small sample sizes and heterogeneous comparator interventions, making direct comparisons difficult [40], [41].

Finally, direct comparisons with other minimally invasive interventions remain limited. These limitations highlight the need for well-designed randomized controlled trials using standardized methodologies, clearer patient stratification,

and longer follow-up periods in order to better define the role of ozone therapy within contemporary spine care and rehabilitation pathways .

4. Conclusion

Ozone therapy has emerged as a promising minimally invasive therapeutic option in the management of patients with lumbar disc herniation and radicular symptoms refractory to conservative treatment. By targeting both the mechanical and inflammatory components of the disease process, ozone therapy may contribute to pain relief, functional recovery, and improved participation in rehabilitation programs.

Current evidence suggests favorable short- and medium-term outcomes, particularly in carefully selected patients with disc-related radicular symptoms. However, substantial heterogeneity persists regarding treatment protocols, routes of administration, ozone concentrations, and patient selection criteria, limiting the strength of current recommendations.

From a Physical and Rehabilitation Medicine perspective, ozone therapy should not be considered a stand-alone treatment, but rather an adjunctive intervention integrated within a comprehensive management strategy combining therapeutic exercise, patient education, pharmacological treatment when indicated, and functional rehabilitation.

Future research should focus on well-designed randomized controlled trials, standardized procedural protocols, and long-term follow-up in order to better define the optimal indications, comparative effectiveness, and precise role of ozone therapy within contemporary spine care pathways.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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