Review

OZONE THERAPY IN THE TREATMENT OF CHRONIC LOW BACK PAIN: A LITERATURE REVIEW

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ABSTRACT

The treatment of low back pain (LBP) represents one of the most common therapeutic challenges in medicine. Various therapeutic modalities have been explored in an attempt to reduce pain and improve the quality of life for patients, including medications, physical therapy, surgical interventions, and minimally invasive treatments. One of the more recent approaches is the use of ozone, a gas with anti-inflammatory and analgesic properties, which is gaining attention as a therapeutic option for LBP. This literature review examines studies investigating the efficacy of ozone in the treatment of LBP, with particular emphasis on biological aspects, mechanisms of action, and clinical outcomes.

KEYWORDS: *ozone therapy, low back pain, lumbar disc herniation, ozone injection, peridural ozone therapy, intradiscal ozone injection, back pain treatment*

INTRODUCTION

Low back pain (LBP) is one of the most common conditions affecting the vertebral column. It represents a health problem that is significant not only from a clinical perspective but also socially and economically. Approximately 70% of the adult population has experienced at least one episode of LBP during their lifetime, with varying levels of severity, and it is the leading cause of absenteeism from work. The incidence of LBP peaks in the third decade of life; its prevalence increases until the ages of 60-65 years, after which it gradually declines (1-8).

In the majority of cases, it is not possible to identify a specific cause of LBP through clinical and radiographic investigations; rather, it is attributed to various issues affecting the musculoskeletal system (4, 7). The pathogenesis of LBP is indeed multifactorial: mechanical-compressive causes on the nerve root are associated with both cell-mediated inflammatory reactions and non-immunological responses secondary to bioumoral factors. Chronic LBP is frequently attributable to degenerative diseases of the bony and ligamentous structures. By the age of 49, approximately 60% of women and 80% of men exhibit osteophytes on radiological examinations and other early signs of spondylosis. By the age of 79, practically the entire population displays radiographic signs of degeneration (1-8).

In 5-15% of cases, LBP is attributable to disc disease. The natural history of a herniated disc is generally favorable: it is common to observe symptom improvement over the months, with many episodes of LBP resolving spontaneously or with conservative therapies. Nevertheless, some studies have shown that LBP persists 12 months after onset in a percentage ranging from 37% to 54% of patients (1-8). In addition to pharmacological therapy and physiotherapeutic rehabilitation, ozone therapy has been proposed as an exclusive treatment or combined with the abovementioned therapies

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(9-22). Although its efficacy has been demonstrated in various clinical settings, ozone therapy remains virtually unknown to most clinicians.

Ozone and low back pain

Ozone is normally present as a gas in the atmosphere and comprises three oxygen atoms structured in a cyclic form. The medical device that generates ozone utilizes a high voltage gradient (5-13 mV) to produce the following reaction: $3O_2$ + 68400 cal → $2O_3$. The gas mixture commonly used in therapeutic applications comprises 95% oxygen and no more than 5% ozone. The mechanisms of action of ozone, specifically when utilized for the treatment of spinal disorders, include:

- intra- and trans-tissue oxygenation of the pathological site, resulting in a reduction of hypoxia and venous stasis;
- inhibition of the production of mediators in the inflammatory cascade and pain transmission;
- a direct effect of fragmentation of the mucopolysaccharides that constitute the nucleus pulposus of the intervertebral disc, facilitated by the rupture of water molecules. This leads to the lysis of the herniated disc and a reduction of symptoms resulting from nerve root compression (9, 15, 17, 19).

In the treatment of chronic LBP, it is advisable to use conservative or minimally invasive treatments as a first line of intervention. More complex procedures, up to surgical intervention, are frequently necessary but often display an unfavorable risk-benefit ratio. There are indeed numerous cases of recurrence post-treatment, which can culminate in Failed Back Surgery Syndrome (FBSS), with an incidence of 15%. Consequently, there has been a drastic reduction in spinal surgeries in recent years (7, 9).

In light of all this, ozone therapy represents an important therapeutic option. It can be employed as a first-line therapy or as an alternative to surgery in cases of conservative treatment failure. The current trend toward the administration of ozone therapy via intramuscular injection minimizes the invasive nature of the therapy, simplifies its management, preserves healthy tissue, and reduces the risk of infectious complications (9-22). Nevertheless, the role of ozone therapy in the treatment of chronic LBP remains a subject of ongoing discussion.

MATERIALS AND METHODS

This review aims to investigate the actual utility of ozone therapy, focusing on both observational and experimental studies in patients suffering from chronic LBP attributable to spinal pathologies. A bibliographic search was conducted in major scientific databases, including PubMed, Cochrane Library, Scopus, and Google Scholar. The search terms used included a combination of the following keywords:

- “ozone therapy”
- “low back pain”
- “lumbar disc herniation”
- “ozone injection”
- “peridural ozone therapy”
- “intradiscal ozone injection”
- “back pain treatment”

The inclusion criteria encompassed studies involving adults with LBP caused by conditions such as disc herniation or protrusion, treated with ozone therapy (either intradiscal or peridural), with primary outcomes being the reduction of pain and improvement in functionality. In the case of meta-analyses, studies that did not report long-term follow-up data (minimum of 3 months) or that exhibited significant methodological limitations were excluded. The search was limited to studies published between 2000 and 2022.

RESULTS

Ozone therapy has generated increasing interest in the management of LBP, particularly in patients with disc herniation or refractory chronic pain. Although numerous studies have suggested the efficacy of this treatment, the scientific evidence remains partial and presents significant methodological limitations. Below, each study included in the review is discussed in detail, highlighting strengths, weaknesses, and implications for clinical practice.

Andreula et al. (9) compared the effects of ozone therapy as a sole treatment or in combination with local injections of corticosteroids and anesthetics. The study included 600 patients with clinical symptoms arising from sciatic nerve compression and radiological evidence (CT or MRI) of disc herniation. 300 patients received intradiscal (4 mL)

and periganglionic (8 mL) injections of an O_2-O_3 mixture with an ozone concentration of 27 µg/mL. The therapeutic outcome was assessed at 6 months using a modified MacNab method. In the patients treated with ozone therapy, good symptom control was recorded in 70.3% of cases. The sequential administration of steroids and anesthetic increased the response rate to 78.3%. The difference between the two groups is statistically significant, highlighting that the primary impact on the outcome is attributable to ozone therapy.

Bonetti et al. (10) studied a sample of 306 subjects suffering from chronic low back or sciatic pain, with 166 cases attributed to discopathy and 140 to other causes. The sample was divided into two groups, which received either a CT-guided intraforaminal injection of an O_2-O_3 mixture or a periradicular steroid injection. Follow-up assessments were conducted in one week and six months to evaluate the short- and long-term effectiveness of the treatment. At the first follow-up, most subjects reported benefit, regardless of the treatment received. However, at six months, a statistically significant difference favoring ozone therapy was observed only in subjects with discopathy. Among those not affected by discopathy, therapeutic failure was reported in only 8.6% of subjects treated with ozone therapy, compared to 21.4% of those treated with steroids.

Gallucci et al. (11) compared the efficacy of intraforaminal and intradiscal administration of steroid, local anesthetic, and an O_2-O_3 mixture with injections of only steroids and anesthetic in subjects with sciatica due to disc herniation. In this randomized controlled study, 159 patients of both sexes across a wide age range (18-71 years) were investigated. The outcome was assessed using the Oswestry Disability Index (ODI), administered to patients prior to treatment and after 6 months. At follow-up, 74% of subjects who received ozone therapy in conjunction with steroid and anesthetic showed clinical improvement versus 47% among those who only received the two drugs.

Zambello et al. (12) conducted a randomized study involving 351 subjects suffering from chronic LBP. Subjects were treated with ozone therapy or epidural steroid injections. The study included a cross-over between the two therapies in case of therapeutic failure after 4 weeks of treatment. The therapeutic response was optimal or good in 47.3% of patients undergoing steroid treatment compared to 77.1% of subjects receiving ozone therapy. Only 11 subjects initially assigned to ozone therapy required therapeutic crossover compared to 38 initially treated with steroids. Among subjects receiving steroid therapy as a second-line treatment, only 36.4% reported symptomatic improvement compared to 70.8% of subjects who received ozone therapy after the failure of steroid treatment.

An important multicentric, double-blind, randomized study conducted in 2009 by Paoloni et al. (13) examined the efficacy of ozone therapy versus placebo. The control group received a simulated intramuscular paravertebral injection via skin puncture and manual pressure application at the lumbar level. Patients receiving ozone therapy showed a significant improvement in symptoms, as evaluated by the visual analog scale for pain (VAS), with an average score of 0.66 compared to 4.00 in the control group. Furthermore, 61% of treated patients reported long-term maintenance of analgesia (6 months) against 33% in the control group. The use of ozone therapy also resulted in a significant reduction in non-steroidal anti-inflammatory drug usage and an improvement in disability.

Zhang et al. (14) prospectively evaluated the efficacy of ozone therapy in a sample of 172 subjects with low back and sciatica pain. The sample was divided into two groups: the first received intradiscal and intraforaminal injections of O_2-O_3, while the second received the same therapy combined with 1 mL of betamethasone. Symptom evaluation was conducted via VAS and JOA score (Japanese Orthopedic Association LBP evaluation system) at three weeks, six months, and twelve months after treatment commencement. Favorable results were obtained in both groups, with a VAS score reduction from 7.68 to 2.17 in the first group and from 7.49 to 2.23 in the second. No statistically significant differences between the two groups were recorded. This study suggests that ozone therapy, associated with minimal side effects, could be proposed as a valid alternative to both surgical intervention and steroid therapy.

A prospective study by Melchionda et al. (15) compared the efficacy of ozone therapy (administered via paravertebral intramuscular injection) with conservative treatment based on non-steroidal anti-inflammatory drugs in patients with acute L5-S1 radiculopathy. 38 subjects were divided into two groups and clinically and neurologically examined after one, two, and four weeks, as well as after three and six months. MRI and electromyographic studies were conducted at baseline and after six months. Pain intensity and degree of disability were assessed using VAS and ODI scales, respectively. A statistically significant difference between the two groups was detected starting from the second week of treatment: 50% of subjects treated with ozone therapy reported freedom from pain symptoms compared to only 16.6% of subjects undergoing anti-inflammatory treatment. This trend was confirmed at the six-month follow-up (80% vs. 50%). No side effects were noted in the administration of ozone therapy in this study.

Rimeika et al. focused on the efficacy and safety of treatment with an oxygen-ozone mixture for LBP, particularly in the management of conditions like disc herniation (21). The meta-analysis included 45 articles comparing the efficacy of imaging-guided injection techniques with non-guided techniques. Parameters considered included pain reduction (measured using the VAS), improvements in functionality (using the Oswestry Disability Index - ODI), and the safety of

treatment by evaluating the presence of side effects. In all 45 articles included in the meta-analysis, ozone was administered as a gaseous mixture of O_2-O_3 with a concentration varying between 10 and 40 µg/ml; the injection of O_2-O_3 was paired with steroids in 8.3% of cases, anti-inflammatories in 2.2% of cases, and anesthetics in 13% of cases, while in 6.5% of cases, it was coupled with other techniques (radiofrequency thermocoagulation, collagen injection, bioresonance magnetotherapy, and/or electrical stimulation).

The imaging guidance used predominantly involved CT or fluoroscopy, with a single prospective study based on ultrasound guidance. Non-imaging-guided techniques were based on paravertebral-intramuscular injections using anatomical landmarks. The meta-analysis showed that both injection methods (with and without imaging guidance) led to significant improvements in the management of LBP. However, the analysis also revealed that imaging-guided techniques tend to yield better results, both in terms of pain reduction and functional improvement, compared to non-guided techniques.

In particular, patients treated with imaging-guided injections demonstrated greater precision in administering the oxygen-ozone mix, reducing the risk of improper administration and enhancing the drug distribution in the target area. Despite the superior efficacy of imaging-guided techniques, the overall findings suggest that non-guided injections can also represent a valid therapeutic option with a good safety profile but greater variability in results. The analysis also indicated that both methods are associated with fewer side effects compared to other invasive treatments such as surgery.

The article by Clavo et al. (22) presents a randomized, double-blind, controlled clinical study comparing the efficacy of ozone therapy to surgery for treating lumbar disc herniation. The study involved patients with symptoms refractory to conservative treatment for at least six weeks. Participants were randomized into two groups: one received intradiscal and paravertebral ozone therapy, while the other underwent standard surgical intervention for disc decompression. The evaluation of outcomes was based on pain measurement scales (e.g., VAS scale) and functional disability indices (e.g., Oswestry Disability Index) with regular follow-up intervals. The analysis showed that ozone therapy resulted in a significant reduction in pain and functional improvement comparable to those achieved with surgery but with lower associated risks and shorter recovery times. The percentage of patients reporting significant clinical improvement was similar in both groups. Furthermore, the complication rate was lower in the ozone-treated group compared to the surgical group.

DISCUSSION

Ozone therapy has been successfully utilized in recent years for the treatment of chronic low back pain originating from discopathy or other causes. In patients with herniated discs, ozone therapy has proven effective in reducing pain even after the failure of other conservative therapies. The cost-benefit ratio of this therapy is significantly favorable in light of its efficacy, low incidence of side effects, and the high prevalence of chronic low back pain in the general population. Consistent with the prevalence of specific pathologies, the majority of studies include patients suffering from chronic lumbosacral pain secondary to herniated discs. Other considered causes include spinal canal stenosis, facet joint osteoarthritis, disc protrusions with vertebral instability, and intervertebral osteochondrosis, among others.

As previously described, ozone is a strong oxidizing agent that contributes to the reduction of the herniated nucleus pulposus by acting on the proteoglycans that make up this structure. This suggests that the dimensional reduction effect may positively impact pain symptoms by alleviating compressive symptoms across various pathological contexts. This review confirms the substantial absence of side effects from the treatment thanks to the ozone concentrations used in therapeutic settings and the recent trend to prefer intramuscular injections over riskier transforaminal and intradiscal injections.

Moreover, injections can be repeated after a certain period on the same site. Adding to this is a positive economic consideration, as ozone therapy involves significantly lower costs compared to surgical treatment or prolonged pharmacological therapy. Therefore, ozone therapy can be considered a valid therapeutic option for the treatment of chronic low back pain in numerous pathological contexts, both as a first-line treatment and as an alternative to surgery in case of failure of other conservative strategies.

CONCLUSIONS

In conclusion, scientific evidence suggests that ozone therapy represents an effective therapeutic option for the treatment of chronic low back pain, particularly in patients with discopathy. This literature review indicates that ozone therapy can significantly contribute to pain reduction and improvement of patients' functionality, thereby enhancing their quality of life.

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