

Applicability of ozone therapy in the treatment of chronic pain: an integrative literature review

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ABSTRACT

This paper aims to present an integrative literature review on the applicability and results of the use of ozone therapy in the treatment of chronic pain. Metodologia: Trata-se de um artigo de revisão integrativa da literatura, utilizando como recorte temporal o período entre 2012 e 2022. Results: The review analyzed 12 articles, according to the inclusion and exclusion criteria. The routes of application found were: rectal, local, paravertebral in its intradiscal, intraforaminal and percutaneous variations. Conclusion: The articles analyzed in this study showed that ozone therapy is considered an effective resource for the treatment of chronic pain, with particularities in the routes of application and in the therapeutic dosages. Ozone therapy is a promising, low-cost, effective therapy for pain relief; however, further studies need to be carried out in order to prove these results.

Keywords: ozone therapy, ozone therapy, integrative therapy, pain treatment, chronic pain.

1 INTRODUCTION

Studies on pain and its interference in the quality of life of the population have been increasingly relevant, since pain is considered one of the great public health problems, becoming more and more a great challenge for health professionals. Furthermore, the aging of the population increases the prevalence of chronic and degenerative diseases¹ and, consequently, the higher incidence of pain that can lead to disability².

Chronic pain is presented as the main complaint of many patients with some clinical impairment, strongly interfering in the quality of life of these individuals³. Recent studies have demonstrated that the prevalence of chronic pain in the elderly varies between 29.7% and 52.8%, occurring more frequently in the lower limbs (34.5%) and in the lumbar region (29.5%), with moderate to intense intensity^{4,5}.

It is also important to differentiate between acute and chronic pain. Acute pain is considered physiological, a warning signal, extremely important for survival. The duration of acute pain is limited in time and space, ceasing with the resolution of the toxic process .⁶

However, chronic pain does not have the biological purpose of warning and survival and it can be said that these truly constitute as a disease⁶ . Regarding the temporal aspect, the definitions of chronic pain vary as to its conceptualization, the duration, whether it is more than three or six months, or even those that persist after the healing of the initial injury. Sometimes it is not possible to reach a causal link, which does not invalidate its diagnosis and its existence .^{5,6}

Treating pain is an instigating process for health professionals, understanding the other's pain is always a challenge, because pain is always subjective, each individual has his own experience and may present a report of pain with or without tissue lesion to justify it. The treatment of pain demands this understanding, in addition to demanding the professional team's experience and even equipment to help in this assessment⁶ .

In developed countries, chronic pain is considered one of the most disabling conditions, but its impact is also believed to be equally important in developing countries⁷ , such as Brazil. The increase in pain intensity generates physical and mental stress, a condition that can considerably decrease a patient's overall quality of life⁸ .

Ozone therapy is a treatment that uses the oxidative potential of ozone and exerts anti-inflammatory, analgesic and antioxidant actions, involving a gaseous mixture of oxygen and ozone, through medical ozone generators^{9, 10} . In order to obtain therapeutic ozone, without the presence of by-products, the conversion of medical oxygen into medical ozone is performed¹⁰ .

Ozone is a molecule formed by three oxygen atoms, characterized as a less stable form of oxygen. The name ozone comes from the Greek word "ozein" (smell), for its strong characteristic odor .^{11,12}

Ozone can be found naturally in the atmosphere in gaseous form, and can be produced in two ways, by the action of ultraviolet rays from the sun, or artificially by a generator, which forms ozone by passing pure oxygen through a high voltage, high frequency electrical discharge. Medical ozone is a mixture of no more than 5% ozone and 95% oxygen. The dose of medical therapeutic ozone used in health care varies between 01 and 100 mg of ozone for each liter of oxygen according to the route of administration and pathology; its half-life is approximately 40 min. at 20° C .¹³

In Brazil, since 2018, ozone therapy is on the list of treatment modalities included by the National Policy of Integrative and Complementary Practices (PNPIC), in the Unified Health System (SUS)^{1,2} . Worldwide, it is a reality in countries like Germany, Cuba, Italy, Switzerland, Austria, Japan, Chile, Peru, United States, Russia, and others^{14,15} .

The regulation of ozone therapy practices by the Professional Boards of Dentistry, Physiotherapy, Pharmacy, Nursing, Veterinary Medicine and Biomedicine, each within their own sphere of action and with

a specific definition on training, contributes to changing once and for all the scenario of Integrative and Complementary Practices in Brazil, bringing more possibilities of treatment and health care to the entire population^{14,15}.

There are several ways of applying medicinal ozone, such as topical, subcutaneous (SC); intramuscular (IM); intradiscal; intracavitary (peritoneal and pleural spaces); intravaginal, intraurethral and vesical applications and ozonated, venous or rectal auto-hemotherapy for the generation of local and systemic effects¹⁰.

Ozone therapy is indicated for a variety of health problems. Its applicability is as a potent antiseptic in the treatment of infectious diseases acting in the activation of the immune system, being able to reverse cases of immunosuppression, improves the delivery of O₂, decreases pain and edema in osteoarticular disorders, presenting a consequent increase in mobility⁹.

Associated with other conservative treatments and percutaneous techniques, ozone therapy has become an important tool to avoid surgical procedures, for example, in the treatment of herniated discs in patients with low back pain. In addition, it prevents complications related to the post-surgical period because it is a minimally invasive technique that has few reports of complications after its use^{9,10}.

The International Scientific Committee for Ozone Therapy (ISCO3), created the "Madrid Declaration on Ozone Therapy". The Madrid Declaration is the guiding document for the work of the ozone therapist, updating the scientific data and making changes whenever necessary, keeping the declaration in line with the scientific research in medical ozone therapy, with studies conducted in different parts of the world. This document considers preclinical, genotoxic, toxicological, pharmacological and clinical studies, evaluation of the application and the harmlessness of this medical therapy broad dose scale.¹⁶

2 OBJECTIVE

The objective of this integrative literature review is to investigate the results of using ozone therapy in the treatment of chronic pain and to present the main routes of application of this therapy.

3 METHODOLOGY

This is an integrative review of the literature on the results of using ozone therapy in the treatment of chronic pain. The evaluation period of the published articles was a ten-year period, from 2012 to 2022. The analysis of the available publications was carried out through the following steps: investigation of the results of the use of ozone therapy in the treatment of chronic pain and identification of the pathologies for which the best results in pain reduction were obtained, as well as the most used routes of application.

The inclusion criteria were complete and available texts describing studies with the use of ozone therapy in the treatment of chronic pain. The exclusion criteria were incomplete texts and studies that did not present the indication for the use of ozone therapy (pathology), in addition to studies published more

than ten years ago. To guide the integrative review, the following question was formulated: What are the results of ozone application in the treatment of chronic pain?

To survey the scientific production, the following databases were searched: Latin American and Caribbean Literature on Health Sciences (LILACS), Medical Literature Analysis and Retrieval System on-line (MEDLINE), Scielo and the *National Library of Medicine's* PubMed search service. The *Medical Subject Headings* (MeSH) and Decs descriptors and the Boolean operator AND were used, resulting in the following combinations: ozone therapy and pain; ozone therapy and chronic pain; pain and treatment. For the analysis of the articles, those written in Portuguese, English and Spanish were considered.

4 RESULTS AND DISCUSSION

In the database search, 254 (two hundred and fifty-four) articles were located. After reading the titles and abstracts, 227 (two hundred and twenty-seven) were excluded for being repeated and/or not answering the research questions. Thus, 27 articles were selected for reading in full, and of these, 15 studies were excluded for not meeting the inclusion criteria and/or not being available in full. Twelve articles were analyzed and selected for the research.

Figure 1. Selection and analysis of the articles



Figure 2. Description of the pathologies where ozone therapy was applied to obtain analgesia.

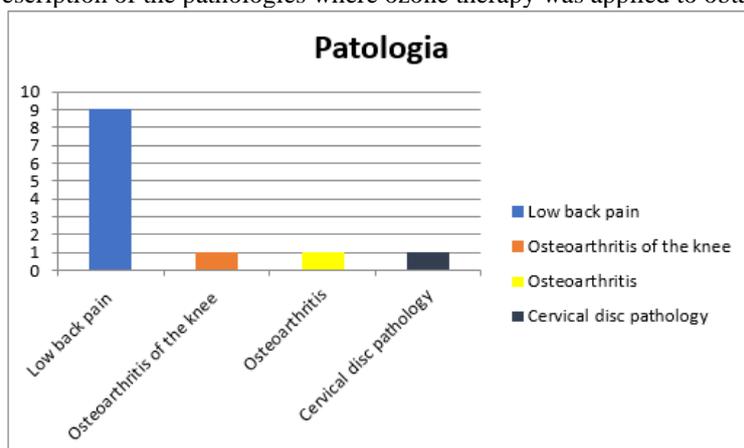


Table 1. Applicability of ozone therapy in the treatment of chronic pain: an integrative literature review

AUTHORS	STUDY OBJECTIVES	DETAILS	APPLICATION ROUTES AND PATHOLOGY
Jesus <i>et al.</i> , 2017 ¹⁷	To determine the effectiveness of ozone therapy in the treatment of Osteoarthritis.	There was a significant reduction in pain and return of joint function in patients receiving medical ozone compared to the placebo group after 08 weeks of treatment. The results of the study showed that administration of 20µg/ml medicinal ozone for 08 consecutive weeks improves joint function and reduces pain in patients with knee osteoarthritis.	Intra-articular. Osteoarthritis of the knee.
Dall'Olio <i>et al.</i> , 2014 ¹⁸	To evaluate the results of using ozone therapy for lumbar disc herniation in patients with subacute partial motor weakness due to nerve root compression.	This article reported the efficacy of ozone therapy associated with anti-inflammatory foraminal injection in 13 patients with low back and sciatic pain and subacute partial motor weakness caused by nerve root compression unresponsive to conventional medical treatment. The results of the study were promising, as 100% of the patients experienced resolution of motor weakness, while 84.6% experienced complete pain relief. The results demonstrate that ozone therapy can be considered an important and effective treatment option for pain relief in patients with lumbar disc herniation	Intradiscal. Lumbar disc herniation.
De Andrade <i>et al.</i> , 2019 ¹⁹	To determine the effectiveness of ozone therapy for the relief of low back pain in adult patients when compared to other therapies.	This study used randomized clinical trials to compare the effectiveness of ozone and other therapies for the relief of low back pain in adults. Six clinical trials were selected, in these, 779 articles identified, showed that the ozone group is more effective for the relief of low back pain, however, they were mostly classified with high or uncertain risk of bias. The systematic review concluded that ozone therapy used for six months for low back pain relief is more effective than other therapies. However, this result is not definitive, since data from studies with moderate to high risk of bias were used, suggesting that better-designed studies should be conducted to prove the therapeutic results of ozone therapy.	The routes of application used in the studies were not described. Low back pain.
Rodriguez <i>et al.</i> , 2019 ²⁰	The purpose of this study was to characterize the response in pain relief in a neurosurgery center.	The results of the study showed pain relief in most patients who received the treatment, with a decrease in the degree of pain in 80.7% of patients after ozone therapy. This study did not describe the therapeutic dose used in the treatment, making it difficult to replicate the method.	Paravertebral. Pathology of the lumbar spine.
Barbosa <i>et al.</i> , 2020 ²¹	To evaluate the effects of using ozone therapy in the treatment of low back pain, focusing on its beneficial and adverse effects in a cross-sectional literature survey.	The procedure with ozone applications through percutaneous injections for the treatment of low back pain has been shown to be safe, especially when compared to surgery and use of medications, as long as strict criteria are followed.	Paravertebral. Pathology of the lumbar spine.
Biazzo <i>et al.</i> , 2018 ²²	To present the results of using paravertebral injections of medicinal ozone in the treatment of low back pain.	Intramuscular lumbar paravertebral ozone injections due to low back pain were applied to 109 patients, of these, 42 discontinued treatment with an average of 5.4 injections and were excluded from the study. Of the remaining 67 patients, only 24 continued in the study. Local and radiating pain, perceived functional status, and disability were assessed before treatment and one month after the last ozone therapy application. As a result, there was a reduction in pain and a reduction in disability, and no complications were reported with the use of ozone therapy. The study concluded that lumbar paravertebral ozone injections are minimally invasive, safe, and less expensive than most of the drugs used in this type of treatment, as well as being effective in relieving pain and disability.	Paravertebral. Pathology of the lumbar spine.

Sucuoğlu <i>et al.</i> , 2021 ²³	To investigate the effects of paravertebral ozone injections in the treatment of low back pain and physical activity in subjects with acute lumbar disc herniation as an add-on treatment.	Thirty-eight patients were distributed into two groups: ozone therapy group (OT), with twenty subjects and 18 subjects in the control group (PC). Both groups received two sessions per week, with a total of 08 sessions of lumbar ozone therapy application. The ozone concentrations were 20-25 µg/ml (30 ml) and 0.1 µg/ml (30 ml), administered to the OT and PC groups, respectively. Patients were evaluated before treatment, 15 and 30 days after the start of treatment, and one month after the end of treatment. As a result, there was a significant improvement in low back pain in the ozone therapy group in all evaluation periods, with the most significant improvement in the evaluation after 30 days of treatment. As a conclusion, treatment with lumbar ozone therapy can decrease pain and disability in patients with acute low back pain.	Paravertebral. Pathology of the lumbar spine.
Uçar D <i>et al.</i> , 2020 ²⁴	The purpose of this study was to obtain pain scores for patients undergoing paravertebral ozone injections for neck pain caused by cervical disc disease.	Intramuscular injections of ozone therapy were applied to treat cervical pain in 72 patients in a multicenter study. Patients received ozone therapy injections with 30 mL of 20 µg/mL of O3/O2 gas (in the paravertebral space). Subjects were treated once a week for 06 weeks. Assessments were performed before (pre-injection) and after treatment (i.e. at 2 and 6 months). Significant improvements were observed at both 02 and 06 months compared to pre-injection scores. As a result, paravertebral ozone injection was shown to be effective in treating cervical pain caused by cervical disc disease.	Paravertebral. Cervical disc pathology.
Niu <i>et al.</i> , 2018 ²⁵	This study investigated the therapeutic effect of low, medium and high concentrations of medicinal ozone on trauma-induced lumbar disc herniation.	A total of 80 patients were divided into a control "low dose medicinal ozone group" (20 µg/ml), a "medium dose medicinal ozone group" (40 µg/ml), and a "high dose medicinal ozone group" (60 µg/ml). The patients were evaluated upon admission, at 6 and 12 months after treatment. As results, all patients showed disc retraction at 06 and 12 months of follow-up; while patients in the medium-dose medicinal ozone group (40 µg/ml) showed the highest disc retraction rate. Low concentrations of medicinal ozone (20 µg/ml and 40 µg/ml) reduced serum IL-6, IgG, and IgM expression, presenting as analgesic and anti-inflammatory effects, while high concentrations of medicinal ozone (60 µg/ml) increased serum IL-6, IgG, IgM expression, presenting effective in reducing pain and inflammation.	Paravertebral. Lumbar disc herniation.
Sampaio <i>et al.</i> , 2018 ²⁶	The aim of this study is to validate the relevance of ozone therapy in clinical practice, and to emphasize its possible use in physical therapy for patients with lumbar disc herniation.	A systematic review was carried out, with the selection of 20 articles, but only 4 met the inclusion criteria. Each of the articles was described individually, using the PICOS flowchart (population, intervention, comparison, outcome, and type of study). After the analyses, all the authors confirmed the efficiency of ozone therapy as a therapeutic method in reversing the pain symptomatology in patients with lumbar disc herniation. The study concluded that ozone therapy is an effective therapeutic option for patients with low back pain associated with lumbar disc herniation.	Paravertebral. Lumbar disc herniation.
De Oliveira <i>et al.</i> , 2012 ²⁷	Conducting a literature review regarding the use of ozone therapy in the treatment of low back pain and lumbosciatalgia was the goal of this 2012 study.	Fifty-four articles were selected, of these, two were multicenter randomized studies, four were systematic reviews, one was a meta-analysis with more than 8,000 patients in multiple centers, one was an Italian national consensus, several double-blind studies, some with control groups, and many studies were observational. The degree of evidence to support a stronger recommendation is still considered low for intradiscal, intramuscular paravertebral, or intraforaminal administration, but this picture seems dynamic and trending in favor of the indication of ozone therapy. As a conclusion of the study, ozone therapy proved to be effective in the treatment of low back pain with or	Intradiscal, paravertebral intramuscular or intraforaminal Low back pain and lumbosciatalgia

		without sciatic pain, and was associated with few adverse events.	
Cedeño, <i>et al.</i> , 2020 ²⁸	To evaluate the results of rectal ozone therapy in patients with osteoarthritis.	A prospective descriptive study was conducted at the Rheumatology Service in a hospital in Spain from July 2017 to February 2019. The study population consisted of 101 patients. The study sample was 60 patients, selected according to simple random sampling. As a result, the use of ozone therapy in patients with functional disability due to osteoarthritis treated with ozone therapy by transrectal route, presented therapeutic effect was very positive, there was a decrease in pain and the use of analgesics, improving the quality of life of these patients.	Rectal. Oesthesarthritis.

5 LITERATURE REVIEW

A randomized, double-blind, controlled study¹⁷ aimed at determining the efficacy of ozone therapy in the treatment of osteoarthritis was conducted and showed satisfactory results. In the study, elderly people between 60 and 85 years old were divided into two groups: experimental group for those who received treatment with medicinal ozone control group for those who received placebo. As a result, there was significant pain reduction and return of joint function in the patients who received the medicinal ozone when compared to the placebo group, after 08 weeks of treatment. The results of the study showed that weekly administration of 20µg/ml medicinal ozone for 08 weeks, improves joint function and reduces pain in patients with knee osteoarthritis.

Authors¹⁸ evaluated the results of using ozone therapy for lumbar disc herniation in patients with subacute partial motor weakness due to nerve root compression. This study reported the efficacy of ozone therapy associated with anti-inflammatory foraminal injection in 13 patients with low back and sciatica pain and subacute partial motor weakness caused by nerve root compression unresponsive to conventional medical treatment. The results of the study were promising, as 100% of the patients experienced resolution of motor weakness, while 84.6% experienced complete pain relief. The results demonstrate that ozone therapy can be considered an important and effective treatment option for pain relief in patients with lumbar disc herniation.

The purpose of a 2019 study¹⁹ was to determine the effectiveness of ozone therapy for low back pain relief in adult patients when compared to other therapies. Randomized clinical trials were used to compare the effectiveness of ozone and other therapies for the relief of low back pain in adults. Six clinical trials were selected, in these, 779 articles identified, showed that the ozone group is more effective for the relief of low back pain, however, they were mostly classified with high or uncertain risk of bias, another important aspect is that the study also denoted greater effectiveness at six months of the ozone group compared to other therapies (steroid and placebo). The systematic review concluded that ozone therapy used for six months for low back pain relief is more effective than other therapies. However, this result is not definitive, since data from studies with moderate to high risk of bias were used, suggesting that better designed studies should be conducted in order to prove the therapeutic results of ozone therapy.

According to the results indicated in a 2019 study²⁰ the use of paravertebral ozone therapy is a conservative therapeutic resource that aids in pain relief, providing an improvement in the quality of life of patients presenting with clinical pictures of spinal pathologies. In this study, 78 patients with spinal diseases underwent ten sessions of paravertebral ozone therapy over a period of two weeks. The objective of this study was to characterize the response in pain relief in a neurosurgery center. The results of the study showed pain relief in the majority of patients who received the treatment, with a decrease in the degree of pain in 80.7% of patients after ozone therapy. This study did not describe the therapeutic dose used in the treatment, making it difficult to replicate the method.

In the studies that used the variations of the paravertebral oxygen-ozone pathway, it was demonstrated that it is safer and easier to administer, because it is not necessary to use anesthetics, sedation or radiology, showing that this therapeutic resource is efficient in reducing pain²¹⁻²⁵.

Authors²¹ evaluated the effects of the use of ozone therapy in the treatment of low back pain, focusing on its beneficial and adverse effects in a cross-sectional bibliographic research. The conclusion of the study is that the procedure is effective and has a favorable analgesic profile, however, it is necessary to have medical orientation and dose control, in addition to the evaluation of specific tests that will help in its control and safety of use of this therapy. According to the study, in clinical practice, the procedure with ozone applications through percutaneous injections for the treatment of low back pain is safe, especially when compared to surgery and the use of medication, as long as strict criteria are followed.

A study²² presented the results of using paravertebral injections of medicinal ozone to treat low back pain. In this study, 109 patients underwent intramuscular injections of lumbar paravertebral ozone due to low back pain. Of these, 42 discontinued treatment with an average of 5.4 injections and were excluded from the study. Of the 67 remaining patients, only 24 had continued in the study to the end. Local and radiating pain was assessed using a Visual Analog Scale (VAS). Perceived functional status and disability were assessed using the Oswestry Disability Index, administered before treatment and one month after the last ozone therapy application. As a result, a reduction in pain, as measured by the VAS, was observed in 23 of 29 cycles (79%) of ozone therapy. Regarding the evaluation of pain-related disability, the reduction of the Oswestry Disability Index score was evaluated in all patients except one. There were no complications with the use of ozone therapy. The study concluded that lumbar paravertebral ozone injections are minimally invasive, safe, cost less than most drugs used in this type of treatment, and are effective in relieving pain as well as disability. This technique is easy to perform, does not require CT scans or anesthesiological support.

A 2021 study²³, investigated the effects of paravertebral ozone injections for the treatment of low back pain and physical activity in subjects with acute lumbar disc herniation as an additional treatment. Thirty-eight patients were distributed into: ozone therapy (OT) group with twenty subjects and 18 subjects in the control group (CP). Both groups received two sessions per week, with a total of 08 sessions of lumbar

ozone therapy application. The ozone concentrations were 20-25 µg/ml (30 ml) and 0.1 µg/ml (30 ml), administered to the OT and PC groups, respectively. Patients were evaluated using the visual analog scale (VAS) and the Oswestry Disability Index (ODI) before treatment (V1), 15 (V2) and 30 (V3) days after the start of treatment, and one month (V4) after the end of treatment. As a result, there was a significant improvement in low back pain in the ozone therapy group in all evaluation periods, with significant improvement in the evaluation after 30 days of treatment. As a conclusion, treatment with lumbar ozone therapy can decrease pain and disability in patients with acute low back pain.

Intramuscular ozone therapy injections were applied to treat cervical pain in 72 patients in a multicenter study²⁴. Patients received ozone therapy injections with 30 mL of 20 µg/mL ozone (in the paravertebral space). Subjects were treated once a week for 06 weeks. Assessments were performed before (pre-injection) and after treatment (i.e. at 02 and 06 months). Significant improvements were observed at both 02 and 06 months compared to pre-injection scores. As a result, paravertebral ozone injection was shown to be effective in treating cervical pain caused by cervical disc disease.

Authors²⁵ investigated the therapeutic effect of low, medium, and high concentrations of medicinal ozone on trauma-induced lumbar disc herniation. A total of 80 patients were divided into a control group, a low dose medicinal ozone group (20 µg/ml), a medium dose medicinal ozone group (40 µg/ml), and a high dose medicinal ozone group (60 µg/ml). CT scans and enzyme-linked immunosorbent assay (ELISA) were performed to detect IL-6 level, SOD activity, IgM, and IgG levels at the time of admission and at 6 and 12 months after follow-up. As results, all patients showed disc retraction at 06 and 12 months of follow-up; while patients in the medical ozone group with medium dose (40 µg/ml) showed the highest disc retraction rate. Low concentrations of medicinal ozone (20 µg/ml and 40 µg/ml) reduced serum IL-6, IgG, and IgM expression, presenting as analgesic and anti-inflammatory effects, while high concentrations of medicinal ozone (60 µg/ml) increased serum IL-6, IgG, IgM expression, presenting effective in reducing pain and inflammation.

A systematic review was conducted²⁶ with the objective of validating the relevance of ozone therapy in clinical practice and emphasizing its possible use in physical therapy. A total of 20 articles were selected, but only 04 met the inclusion criteria. Each of the articles was individually described, using the PICOS flowchart (population, intervention, comparison, outcome and type of study). After the analyses, all the authors confirmed the efficiency of ozone therapy as a therapeutic method in reversing the pain symptoms in patients with lumbar disc herniation. The study concluded that ozone therapy is an effective therapeutic option for patients with low back pain associated with lumbar disc herniation.

Authors²⁷ conducted a literature review regarding the use of ozone therapy in the treatment of low back pain and lumbosciatalgia. Fifty-four articles were selected, of these, two were multicenter randomized studies, four were systematic reviews, one was a meta-analysis with more than 8,000 patients in multiple centers, one was an Italian national consensus, several double-blind studies, some

with control groups, and many studies were observational. The degree of evidence to support a stronger recommendation is still considered low for intradiscal, intramuscular paravertebral, or intraforaminal administration, but this picture seems dynamic and trending in favor of the indication of ozone therapy. As a conclusion of the study, ozone therapy proved to be effective in the treatment of low back pain with or without sciatic pain, and was associated with few adverse events.

A prospective descriptive study²⁸ was conducted at the Rheumatology Service of a hospital in Spain from July 2017 to February 2019 to evaluate the results of using rectal ozone therapy in patients with osteoarthritis. The study population consisted of 60 patients, selected according to simple random sampling. According to the authors, the most affected joint was the knee in 100% of the patients studied. As a result, the use of ozone therapy in patients with functional disability due to osteoarthritis treated with transrectal ozone therapy had a very positive therapeutic effect, with a decrease in pain and in the use of analgesics at the end of the treatment. Most of these patients had moderate physical disability (53.3%) at the beginning of the treatment, and after 3 months of using ozone therapy there was a predominance of mild disability (26.6%), showing that ozone therapy was beneficial for reducing pain, improving mobility, and reducing the use of analgesics in patients with osteoarthritis.

6 CONCLUDING REMARKS

The articles analyzed in this study demonstrated that ozone therapy is a resource considered effective in the treatment of chronic pain. The main pathology described in the studies was low back pain, and the routes of application described in the studies varied and were performed via paravertebral and rectal application. The rectal and paravertebral routes were shown to be effective, prevalent, and of safe execution for the application of ozone therapy. The other routes, such as the intradiscal, require more medical support and have a higher risk of complications, being less used in the clinical practice of health professionals. The interventions in the ozone therapy practice should be necessary, safe and effective; therefore, a careful evaluation of each patient by the health professional is important, in order to select, within his/her attributions and competencies, the best way of ozone application to be adopted in the treatment. Although ozone therapy needs higher levels of scientific evidence to clarify some standardization doubts, which routes present the best results and which doses are the safest, the technique has studies that show that this therapeutic resource is promising, presenting very satisfactory and effective results in the treatment of pain in several pathologies, regardless of the routes of application. Studies with a more homogeneous population, with a more detailed description of the dosages and routes used, as well as which pathologies were treated, are necessary for this therapeutic resource to show its clinical efficacy and for professionals to be safer in its clinical management. According to the studies analyzed, ozone therapy proved to be a promising therapeutic resource for the treatment of pain.

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