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Application of Ozone Therapy at Dubi Point (ST35) in a patient with Gonalgia: Case Study

Aplicação de Ozonoterapia no Ponto Dubi (E35) em paciente com Gonalgia: Estudo de Caso

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Abstract

Introduction: Gonalgia, characterized by knee pain, is a common condition, often associated with inflammatory, degenerative or traumatic processes. Gonarthrosis, a degenerative form of the knee joint, can cause persistent pain and functional impairment. Ozone therapy has been explored as a complementary approach due to its anti-inflammatory, analgesic and regenerative properties. **Methods:** This case study evaluated the effects of ozone therapy on a patient diagnosed with gonarthrosis refractory to conventional treatments. The therapeutic protocol consisted of seven weekly intra-articular ozone applications. The Visual Analog Scale (VAS) and the Lequesne Algofunctional Questionnaire were used as methods of evaluation and analysis. **Results:** A significant improvement in both pain perception and joint functionality was observed over the course of the sessions. The patient reported a progressive reduction in pain and an improvement in general well-being, with no adverse effects. **Conclusion:** Ozone therapy has proven to be a safe and potentially

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effective therapeutic option for the treatment of gonarthrosis-related gonalgia, especially in cases that are difficult to respond to conventional treatments. However, further studies with larger samples and controlled designs are needed to validate these findings.

Keywords: Gonalgia, Gonarthrosis, Ozone Therapy, Knee Joint.

Resumo

Introdução: A gonalgia, caracterizada por dor no joelho, é uma condição comum, frequentemente associada a processos inflamatórios, degenerativos ou traumáticos. A gonartrose, uma forma degenerativa da articulação do joelho, pode causar dor persistente e comprometimento funcional. A ozonioterapia tem sido explorada como uma abordagem complementar devido às suas propriedades anti-inflamatórias, analgésicas e regenerativas. **Métodos:** Este estudo de caso avaliou os efeitos da ozonioterapia em um paciente diagnosticado com gonartrose refratária aos tratamentos convencionais. O protocolo terapêutico consistiu em sete aplicações intra-articulares semanais de ozônio. A Escala Visual Analógica (EVA) e o Questionário Algofuncional de Lequesne foram utilizados como métodos de avaliação e análise. **Resultados:** Observou-se melhora significativa tanto na percepção da dor quanto na funcionalidade articular ao longo das sessões. O paciente relatou redução progressiva da dor e melhora no bem-estar geral, sem efeitos adversos. **Conclusão:** A ozonioterapia mostrou-se uma opção terapêutica segura e potencialmente eficaz para o tratamento da gonalgia relacionada à gonartrose, especialmente em casos de difícil resposta aos tratamentos convencionais. No entanto, são necessários mais estudos, com amostras maiores e desenhos controlados, para validar esses achados.

Palavras-chave: Gonalgia, Gonartrose, Ozonioterapia, Articulação do joelho.

Introduction

Ozone gas (O_3) was discovered in 1840 by Schönbein, who synthesized and named the new gas “ozone”, derived from the Greek word ozein, meaning “to smell”. Ozone therapy (O_3) refers to the use of medical ozone as a therapeutic substance in pathologies associated with chronic hypoxia, inflammation, and redox imbalance, in which ozone has proven to be effective (Sire et al., 2022; Hidalgo-Tallón et al., 2022). This substance is administered as a gaseous mixture of oxygen and ozone (O_2-O_3), capable of stimulating physiological responses, particularly with anti-inflammatory and

analgesic effects (Jeyaraman et al., 2024). The mixture contains between 95% and 99.95% oxygen and 0.05% to 5% ozone, generated from medical oxygen using a certified medical ozone generator (Jeyaraman et al., 2024; ISCO3, 2020). Ozone is a molecule composed of three oxygen atoms (O_3), in contrast to the two atoms present in the oxygen molecule (O_2). Due to its short half-life of only 40 minutes at 20°C, O_3 cannot be stored and must be produced in situ immediately before use (Hidalgo-Tallón et al., 2022).

The therapeutic action of ozone resembles that of a pro-drug, whose activity is mediated by biologically active metabolites generated following chemical interactions with tissues and biological fluids. This process triggers a cascade of endogenous biochemical reactions that modulate cellular pathways and inflammatory processes (Sire et al., 2022). The main mechanism involves improved tissue oxygenation, which is essential for cellular metabolism, promoting tissue regeneration and repair (Jeyaraman et al., 2024).

Gonarthrosis, or knee osteoarthritis, is a progressive degenerative disease affecting joint structures such as cartilage, synovial membrane, and subchondral bone. Its pathophysiology involves inflammatory imbalances mediated by cytokines such as IL-1β, TNF-α, and MMPs, which contribute to the degradation of the cartilage matrix (Sconza et al., 2023). Intra-articular ozone therapy applied to the knee induces controlled micro-oxidation, stimulating antioxidant mechanisms and modulating inflammation (Hidalgo-Tallón et al., 2022; Sire et al., 2022).

From the perspective of Traditional Chinese Medicine (TCM), knee pain is often associated with stagnation of Qi and Xue (energy and blood) in the meridians, especially the Stomach meridian, which passes through the anterior region of the knee. The Dubi point (Stomach 35), located in the lateral depression next to the patella, is classically indicated for the treatment of pain, swelling, and functional limitation in the knee (Deadman et al., 2007). Stimulation of this point has demonstrated analgesic effects, involving neurophysiological mechanisms such as the release of endogenous opioids and the modulation of descending pain pathways (Wang et al., 2008). Administering ozone in this anatomical area may enhance local therapeutic effects by integrating the principles of Traditional Chinese Medicine with the biochemical mechanisms of Western medicine, promoting pain relief and improved functionality.

Therefore, due to the cascade of physiological responses triggered by ozone application, including its anti-inflammatory and analgesic properties, and its potential in

the treatment of musculoskeletal disorders, ozone therapy applied at the Dubi point was selected for this study. The primary objective is to evaluate its application in a patient with gonalgia, to demonstrate the local effects of ozone, analyze its physiological impact on the knee joint, and observe the clinical response after treatment.

Materials and Methods (Case Presentation)

This study consisted of a clinical case conducted between March and May 2025, with the aim of analyzing the effects of seven weekly ozone applications in a patient whose main complaint was gonalgia associated with mobility difficulties. The patient was referred to the rehabilitation clinic “FisicalMira - Wellness and Health” in Odemira.

At the time of assessment, the patient, a 64-year-old male, reported pain with an intensity of “6” on the Visual Analogue Scale (VAS). He presented with bilateral knee pain for several years, with progressive worsening. In 2024, he underwent a total knee arthroplasty on the left side. In the right knee, he experienced disabling pain, more intense at the end of the day, partially relieved by rest.

On physical examination, pain was observed on palpation of the joint lines, with limited range of motion, crepitus during flexion and extension movements, and slight edema. The patient reported partial relief of symptoms with the use of anti-inflammatory medication. A medical diagnosis of grade III gonarthrosis was confirmed, based on the Kellgren-Lawrence classification, as evidenced by imaging tests including computed tomography (CT) and magnetic resonance imaging (MRI). The only identified comorbidity was systemic arterial hypertension (SAH), currently controlled with medication. The patient was taking anti-inflammatory drugs, which provided only partial symptom relief.

Inclusion and Exclusion Criteria

The inclusion criteria adopted in this study included patients over 50 years of age with a history of persistent gonalgia associated with chronic rheumatic pathologies such as gonarthrosis, osteoarthritis, and osteoarthrosis. These degenerative conditions are often accompanied by symptoms such as pain when walking, sitting, or performing physical activities, as well as significant mobility limitations. According to Deadman, Al-Khafaji, and Baker (2007), these clinical manifestations reflect energetic imbalances that may be treated through acupuncture, especially when considering the Traditional Chinese Medicine (TCM) approach to musculoskeletal and joint disorders.

Exclusion criteria included: glucose-6-phosphate dehydrogenase (G6PD) deficiency; use of non-steroidal anti-inflammatory drugs (NSAIDs) within 2 days before the injection; intense physical activity; and severe cardiovascular instability.

For this case study, we selected a 64-year-old male patient who had been referred to the "FisicalMira - Wellness and Health" rehabilitation clinic in Odemira due to gonalgia and difficulty with ambulation. He presented symptoms of chronic pain over several years. A comprehensive anamnesis was carried out, including review of prior medical follow-ups and examination results. This was followed by a physical assessment, with photographic documentation using a mobile phone camera (Figure 1), and palpation of both knees. After the assessment, the patient met all inclusion criteria and was informed about the possibility of participating in this study. On the same day, he signed the informed consent form. Among the several candidates eligible for participation, this individual was selected for the case study because he fulfilled the inclusion criteria most completely.

Treatment Protocol

The patient underwent a treatment protocol consisting of one 40-minute session per week, with a six-day interval between sessions, over an approximate period of three months, for a total of seven sessions. In each session, the patient completed a questionnaire, the target joint was visually assessed, all necessary materials were prepared, and intra-articular ozone therapy was administered to the right knee. For this procedure, the "Ozonotte" device was used (Figure 2), which generates ozone (O_3) from medical oxygen (O_2), producing a gas mixture containing 95%-99.95% oxygen and 0.05%-5% ozone. This mixture is intended to increase microcirculation, reduce inflammation, and relieve local pain. The applications were carried out using a 20 mL syringe with a 27G needle containing the ozone gas (O_3).

According to the Madrid Declaration, ozone therapy should be administered at a concentration of 2-10-20 µg/NmL. The initial volume used should be 10 mL, gradually increased by 5 µg/NmL in subsequent sessions (ISCO3, 2020).

The application was performed in the anterolateral region of the knee, i.e., via intra-articular injection (see Figure 1). The ozone was introduced in a single injection to minimize patient discomfort, with the needle slowly withdrawn to ensure full dispersion of the gas throughout the joint. The injection was administered at a slow pace to allow

the gas to expand evenly within the joint space, avoiding pain and thereby improving joint mobility and, consequently, the patient's ability to perform daily activities.

Throughout the treatment, the patient's pain was continuously assessed using the Visual Analogue Scale (VAS). Muscle strength and quality of life were evaluated using the Lequesne Algofunctional Questionnaire.

Figure 1 - Intra-articular application of ozone in the right knee

Source: Personal Archive

Figure 2 - Ozonette Sedecal - Medical Ozone Generator

Source: Personal Archive

The Visual Analogue Scale (VAS) is a pain assessment tool that measures pain

subjectively and is commonly used for both acute and chronic pain (Figure 3). Scores are based on patients' self-reported symptoms, recorded by marking a single point along a 10 cm horizontal line that represents a continuum between two extremes, 'no pain' at the left end (0 cm) and 'worst possible pain' at the right end (10 cm). The measurement is taken from the left end of the line to the patient's mark, recorded in centimetres, and interpreted as an indicator of the patient's pain intensity. These values can also be used to monitor changes in pain over time (Delgado et al., 2018). In this study, the VAS was administered at three time points: initially during the baseline assessment, again during the fifth session, and finally in the seventh session.

Figure 3 - Visual Analogue Scale (VAS)

Source: Leão MGdS, et al., (2016). Análise comparativa da dor em pacientes submetidos à artroplastia total do joelho em relação aos níveis pressóricos do torniquete pneumático. Rev Bras Ortop. http://dx.doi.org/10.1016/j.rbo.2016.02.002

The Lequesne Algofunctional Questionnaire was developed in France in the 1970s and first published in the 1980s. This assessment tool includes three levels of questions. The first level comprises 11 questions addressing pain and discomfort, along with one question regarding the ability to rise from a chair. The second level contains nine questions related to walking ability and distance covered, while the third level includes four questions concerning activities of daily living. Scores range from 0 to 24, where 0 indicates no impairment and 24 indicates extremely severe impairment, thus allowing for the evaluation of both symptoms and physical disability (Marx et al., 2006). For this study, the questionnaire was administered at three stages: during the initial assessment, again in the fifth session, and finally in the seventh session.

Ethical Considerations

All study objectives, expected outcomes, and follow-up procedures were clearly explained to the participant, and confidentiality of personal data was assured. The patient underwent a total of seven sessions of intra-articular ozone therapy. In addition, the patient's medical history and previously prescribed medications were reviewed.

Based on the exclusion criteria, previous medications were discontinued, and paracetamol was the only permitted analgesic in case of pain. Written informed consent was provided, read, and signed by the participant, who was also informed of their right to withdraw from the study at any time. This study was approved within the postgraduate course in medical ozone therapy, conducted by the Egas Moniz School of Health & Science in collaboration with 2M Pharma.

Results

The results showed improvements in pain reduction, particularly in the areas of greatest discomfort. Pain levels, as measured by the Visual Analogue Scale (VAS), exhibited a significant decrease, confirming the clinical efficacy of ozone therapy in reducing pain associated with gonalgia. Furthermore, the progressive and consistent improvement in the overall score on the Lequesne Questionnaire throughout the course of treatment is noteworthy, as shown in Graphs 2 and 3.

Regarding muscle tone, no changes were observed, as this type of treatment does not aim to strengthen muscle. However, a clear improvement in muscle relaxation and gait was noted.

Data analysis was carried out through questionnaires completed by the patient at the beginning of each session, evaluating pain relief, knee mobility, and overall perception following ozone (O_3) application.

According to VAS assessments, the patient reported a pain level of “6” in the first session, which decreased to “4” in the fifth session, and “2” by the seventh. In other words, the patient’s pain consistently reduced from 6 to 2 over the course of the seven sessions, indicating a significant and sustained improvement. This outcome supports the effectiveness of ozone therapy in this clinical case, as illustrated in Graph 1.

The analysis of the Lequesne Algofunctional Questionnaire - Knee demonstrated that intra-articular ozone therapy provided a significant clinical benefit for the patient with advanced gonarthrosis (Kellgren-Lawrence grade III), with a 63% reduction in the Lequesne score after seven weeks of treatment, as shown in Graphs 2 and 3. The evolution of the total score indicates a progressive and consistent improvement throughout the treatment period:

- Weeks 1-2: 17.5 points (very severe impairment);
- Week 3: 16.5 points (early therapeutic response);

- Week 4: 13.0 points (notable reduction);
- Week 5: 10.0 points (transition to moderate impairment);
- Week 6: 8.5 points (continued improvement);
- Week 7: 6.5 points (mild to moderate impairment).

The total reduction of 11 points (representing 63% improvement) evidences the clinical response associated with the effects of ozone therapy.

Domain-Specific Analysis - Domains with Most Pronounced Improvement:

- Maximum walking distance: Improved from 5 to 2 points (60% improvement), indicating a significant increase in locomotion capacity;
- Night pain: Completely resolved (from 2 to 0 points), suggesting enhanced sleep quality;
- Squatting: Improved from 2 to 0 points (100% improvement), reflecting important functional gains;
- Walking on uneven ground: Improved from 1 to 0 points (100%), facilitating ambulation in varied environments.

Domains with Partial Response:

- Pain while walking: Reduced from 2 to 1 point (50% improvement);
- Morning stiffness: Decreased from 2 to 1 point (50% improvement);
- Descending stairs: Improved from 1.5 to 1 point (33% improvement).

Temporal Response Pattern:

- Initial phase (Weeks 1-2): Symptom stability, with no significant changes;
- Intermediate phase (Weeks 3-4): Onset of therapeutic response, mainly in walking distance and night pain;
- Advanced phase (Weeks 5-7): Consolidation of clinical gains and continuous improvement in all domains;

Clinical-Functional Correlation: The patient's progression in the Lequesne questionnaire is clinically consistent with grade III gonarthrosis treated with intra-articular ozone therapy, highlighting:

I. Analgesic Response: Reduction in pain (nighttime, during walking, and standing up) suggests an anti-inflammatory effect of ozone therapy, with a positive impact on quality of life;

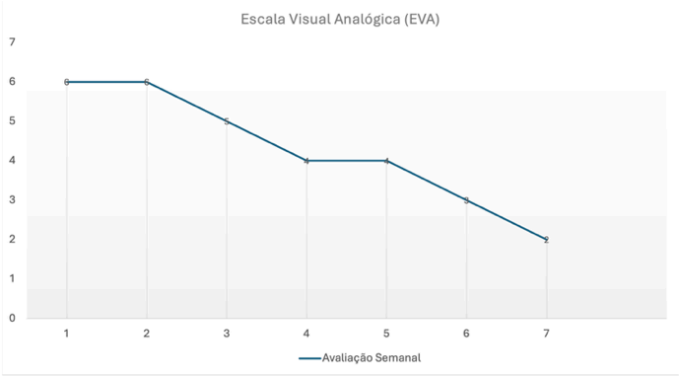
II. Functional Gains: Improvement in squatting, walking capacity, and mobility over uneven terrain indicate partial restoration of joint functionality;

III. Temporal Pattern: Gradual and progressive response, with more significant improvement observed after the 3rd week, suggesting a cumulative effect of the ozone sessions;

IV. Domain-Specific Impact: Greater effect observed in pain-related parameters, and lower effect in more complex functional tasks (e.g., stair descent), reflecting structural limitations of the joint in advanced osteoarthritis.

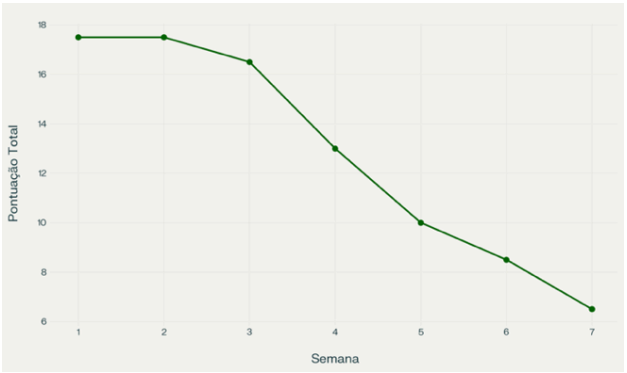
Conclusion and Clinical Relevance: The favorable evolution across multiple functional and pain-related domains suggests that this therapeutic approach may represent a valid conservative management option for gonarthrosis, particularly in patients with poor response to conventional anti-inflammatory drugs and those wishing to delay more invasive surgical interventions.

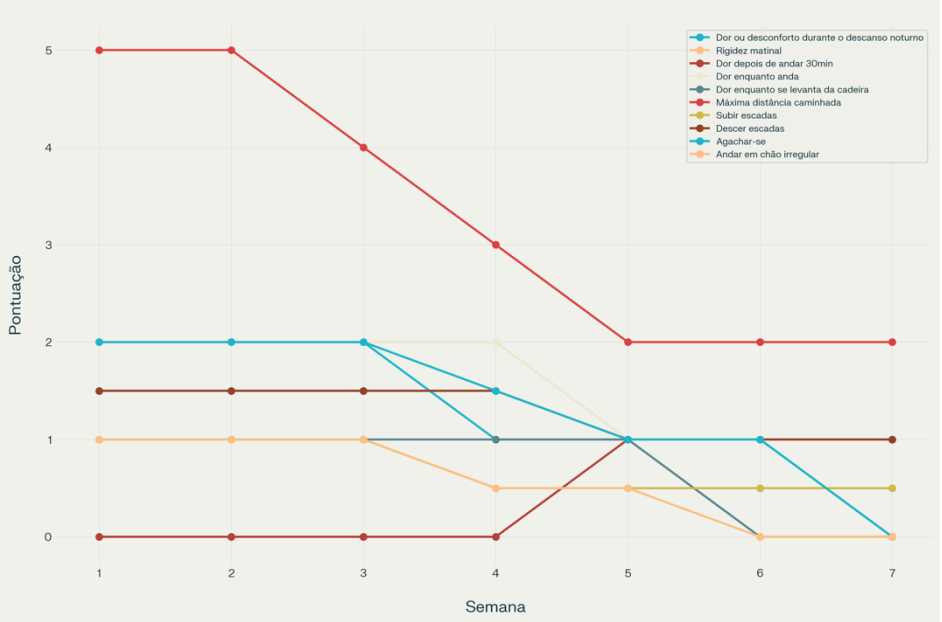
Graph 1 - Pain Index by VAS



Source: Personal Archive

Graphs 2 and 3 - Strength Analysis by the Lequesne Questionnaire





Source: Personal Archive

Discussion

According to Bocci (2011), ozone therapy is currently widely used in orthopedic contexts of human medicine, being applied in cases of knee and lumbar spine pain, among others, through the injection of ozone into paravertebral muscles and soft tissues, a technique the author refers to as “chemical acupuncture.” The author explains that ozone acts directly on nociceptors, triggering an anti-nociceptive response that is effective in approximately two-thirds of patients through the release of chemical mediators.

However, Bocci (2011) emphasizes that the practice of ozone therapy remains controversial, mainly due to its misuse by unqualified professionals. He warns of the risks associated with improper ozone concentrations and volumes, which can lead to adverse effects such as acute pain and, in more severe cases, vagal hypertonia and even cardiac arrest. Therefore, the slow and careful administration of the gas, in compliance with recommended clinical parameters, is essential.

Knee osteoarthritis (gonarthrosis) is a multifactorial and progressive clinical condition that significantly impacts patient functionality and quality of life. The progressive degradation of articular cartilage, accompanied by bone and synovial changes, reflects a complex pathophysiological process in which local inflammation and oxidative stress play central roles (Goldring & Goldring, 2007; Raeissadat et al., 2021). The predominance of mechanical pain with inflammatory features, often exacerbated by

peripheral and central sensitization, renders osteoarthritic pain a multidimensional phenomenon, requiring therapeutic approaches that go beyond mere symptomatic control (Woolf, 2011; Felson, 2009).

In this context, ozone therapy has emerged as a minimally invasive therapeutic alternative, with well-established mechanisms of action in controlling inflammation and oxidative stress. According to the Madrid Declaration (ISCO3, 2020), this therapeutic modality is considered safe, with specific protocols for intra-articular administration. Its clinical efficacy is supported by trials demonstrating significant improvements in pain, stiffness, and functionality parameters (Sconza et al., 2023; Jeyaraman et al., 2024).

From a biochemical perspective, ozone contributes to the modulation of the inflammatory intra-articular environment of the knee joint, while the process of "controlled micro-oxidation," as described by Hidalgo-Tallón et al., (2022) and Sire et al., (2022), induces a cellular preconditioning effect, stimulating adaptive protective responses.

While hyaluronic acid and platelet-rich plasma (PRP) remain widely used in the treatment of osteoarthritis, comparative studies indicate that ozone therapy may offer equivalent or complementary effects, particularly in reducing inflammatory biomarkers such as IL-6 and MMP-13 (Sconza et al., 2023). Although some studies, such as that by Raeissadat et al., (2021), report superior functional outcomes with PRP compared to ozone, both therapies demonstrate efficacy in pain relief, reinforcing the importance of individualized approaches in the management of gonarthrosis.

In addition to its local effects, ozone therapy also has systemic potential, acting on central mechanisms of chronic pain and sensitization, as described in studies by Sire et al., (2022) and Hidalgo-Tallón et al., (2022). This makes it particularly appealing for patients with refractory pain or contraindications to nonsteroidal anti-inflammatory drugs (NSAIDs).

Therefore, considering current evidence, the integration of ozone therapy into the treatment of knee osteoarthritis appears to be a promising strategy, supported by robust pathophysiological mechanisms and consistent clinical outcomes. Its use may be considered both as a primary therapy in early and moderate stages of the disease, and as an adjunct in multimodal therapeutic plans, especially when other options have failed or are contraindicated.

Moreover, the analgesic effects observed with intra-articular ozone therapy can, in part, be compared to the neurophysiological mechanisms involved in traditional

acupuncture. According to Wang et al., (2008), acupuncture modulates nociceptive pathways in the central and peripheral nervous systems, promoting the release of neurotransmitters such as endorphins, serotonin, and norepinephrine, which results in decreased pain perception. Similarly, ozone therapy appears to activate anti-nociceptive responses through the stimulation of peripheral receptors and neurochemical regulation of the pain-inflammation axis, supporting its utility as a complementary or alternative approach to other non-pharmacological neuromodulation techniques.

In this context, the description of the "chemical acupuncture" technique, as initially mentioned by Deadman et al., (2007) and later expanded upon by Bocci (2011), contributes to a broader understanding of ozone therapy as an intervention that transcends classical pharmacology. The controlled insertion of ozone gas into specific anatomical points, such as joints or paravertebral muscles, can be understood as a therapeutic stimulus like traditional needling, but enhanced by the gas's biochemical action. This analogy reinforces the hypothesis that the clinical success of ozone therapy in cases of chronic pain, such as advanced gonarthrosis, may stem both from its direct biochemical effects and from the activation of sensory and reflex pathways associated with acupuncture-induced analgesia.

Conclusion

Considering the clinical and pathophysiological evidence reviewed, ozone therapy emerges as a promising therapeutic alternative in the management of knee osteoarthritis, particularly in refractory cases or those with contraindications to prolonged use of anti-inflammatories. Its analgesic and anti-inflammatory effects, together with its ability to modulate oxidative stress and stimulate local and systemic adaptive responses, underscore its relevance both as a primary therapy and as an adjunct in multimodal approaches.

In summary, intra-articular ozone therapy proved effective in relieving pain and improving joint function in a patient with advanced gonarthrosis (Kellgren-Lawrence grade III), resulting in a 63% reduction in the Lequesne Questionnaire score after seven weeks of treatment. These findings reinforce its clinical potential, especially when ozone therapy is administered accurately and safely, following established protocols.

The analogy with traditional acupuncture, supported by the concept of "chemical acupuncture," expands the understanding of ozone therapy as an integrative technique that acts not only through local biochemical mechanisms but also via

neurophysiological pathways involved in pain neuromodulation. Nevertheless, its efficacy is directly linked to proper clinical application and the training of healthcare professionals involved, as emphasized by Bocci (2011).

Thus, considering the positive clinical outcomes observed in this case study and supported by the current literature, the cautious inclusion of intra-articular ozone therapy is recommended as part of gonarthrosis treatment strategies. Further research, particularly randomized clinical trials with larger samples, is essential to consolidate its therapeutic role and to define its efficacy and safety parameters with greater precision.

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