

## Guest Editorial

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# Oxygen-ozone therapy for musculoskeletal pain in rehabilitation: Evidence and future perspectives

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Dear colleagues,

Musculoskeletal pain is a common issue in several pathological conditions like osteoarthritis and low back pain, with relevant negative implications in terms of chronic pain development, disability and increased sanitary costs worldwide [?]. As the search for minimally invasive treatment options intensifies, oxygen-ozone therapy has emerged as a promising intervention and its anti-inflammatory and tissue-regenerative properties makes it as a viable alternative to more conventional treatments like corticosteroid injections [?,?].

This editorial focusses on the current evidence supporting oxygen-ozone therapy, in particular in osteoarthritis and low back pain treatment, and explores its potential integration with other therapeutic strategies like physical rehabilitation interventions.

Recent studies highlighted the role of oxygen-ozone therapy in the management of knee [?,?,?,?], hip [?], and trapeziometacarpal [?] osteoarthritis, three condi-

tions affecting millions of individuals globally, with detrimental effects on pain and functioning.

A recent randomized controlled trial published in the *Journal of Back and Musculoskeletal Rehabilitation* (JBMR) [?] compared the efficacy of ultrasound-guided oxygen-ozone therapy injections and corticosteroid injections for knee osteoarthritis, showing similar improvements on pain relief and functional outcomes over 12 weeks in both groups. These results suggest that oxygen-ozone therapy offers a comparable, non-invasive alternative to corticosteroids injective treatment, especially for patients who wish to avoid the potential risks of repeated steroid use. However, the comprehensive osteoarthritis management requires to address both the structural and functional aspects of joint health. Accordingly, another study on advanced knee osteoarthritis [?] showed that patients who underwent a combination of arthroscopic debridement and functional exercise experienced greater pain relief, improved joint function, and better inflammatory marker outcomes than those who only received debridement treatment. These results suggest that oxygen-ozone therapy could be integrated in the rehabilitation framework of joint pathologies in order to target both the inflammatory pathway and joint mechanics to enhance recovery.

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Similar to osteoarthritis, low back pain (LBP) is another highly prevalent musculoskeletal disorder where oxygen-ozone therapy has recently shown some significant potential therapeutic indications [?]. LBP, and in particular chronic low back pain, can be worsened by several factors such as lifestyle, central sensitization (where the central nervous system becomes hypersensitive to pain), and individual pain experiences [?, ?].

A recent cross-sectional study conducted in Japan [?] revealed that central sensitization, age, and past pain experiences are key contributors to the chronic progression of LBP, particularly in caregivers. The study underscores the importance of early therapeutic interventions to prevent the shift of acute LBP into a chronic condition. Given the crucial role of central sensitization in the chronicization process of LBP, therapies that can reduce inflammation and modulate nociceptive pathways – like oxygen-ozone therapy – could be effective therapeutic solutions. Indeed, oxygen-ozone therapy can decrease inflammatory mediators and improve oxygen delivery to tissues, thus interrupting the transition from acute to chronic pain, especially in vulnerable populations like older adults and caregivers.

In conjunction with oxygen-ozone therapy, self-managed exercise interventions, such as the Self-Natural Posture Exercise (SNPE) program, have demonstrated positive effects to improve the management of chronic LBP. Son et al. in a recent randomized study published in *JBMR* [?] evaluated the feasibility and efficacy of face-to-face and virtual SNPE programs among individuals with chronic LBP. Both groups showed improvements in pain levels, along with enhancements in HrQoL. The findings of this study suggest that the combination of physical exercise with oxygen-ozone therapy could provide greater benefits for chronic pain management in LBP patients. This multimodal approach could target both mechanical and biochemical contributors to pain, resulting in better pain relief and enhanced physical function and HrQoL. Given the success of the virtual SNPE program, tele-rehabilitation could be a promising tool to implement oxygen-ozone therapy protocols into broader treatment plans, improving the access to care for a larger part of the population.

In addition to the therapeutic interventions, the ability to predict and prevent the progression of chronic pain is crucial in order to optimize long-term outcomes. Indeed, a recent study using data from the Korean National Health and Nutrition Examination Survey developed machine learning models to predict LBP occurrence based on demographic and lifestyle factors [?].

Such predictive models could enable clinicians to implement early preventative strategies, such as oxygen-ozone therapy or exercise interventions, in high-risk populations.

Another important factor in the complex management of chronic LBP is social support. A recent study on exercise adherence [?] found a positive relationship between perceived social support and the number of exercise sessions completed by individuals with chronic LBP. While social support did not directly influence exercise self-efficacy, it played a crucial role in maintaining regular physical activity levels, a crucial aspect in the correct management of chronic pain conditions. The integration of social support interventions in rehabilitation programs, particularly those integrating oxygen-ozone therapy or tele-rehabilitation, could further enhance the adherence and improve the long-term outcomes in these patients.

The integration of oxygen-ozone therapy with other therapeutic strategies, such as exercise programs like SNPE and predictive models, presents a comprehensive approach to managing chronic musculoskeletal pain. Moreover, the growing use of tele-rehabilitation platforms, as demonstrated in the virtual SNPE program, opens new avenues for expanding access to effective pain management strategies.

Oxygen-ozone therapy offers an effective and minimally invasive option to treat chronic musculoskeletal pain, specifically in conditions like osteoarthritis and LBP. When combined with physical rehabilitation strategies and supported by predictive models and social support interventions, oxygen-ozone therapy could have the potential to provide comprehensive pain relief and improved functional outcomes in these patients [?, ?].

Future research is needed to better define standardized oxygen-ozone therapy protocols, including optimal ozone concentrations and injection frequencies, across different musculoskeletal conditions. Larger randomized controlled trials are highly recommended in order to explore the long-term efficacy of oxygen-ozone therapy in preventing chronic pain, particularly in cases involving central sensitization. Furthermore, the integration of social support and predictive models into rehabilitation plans could improve patient outcomes by addressing both the physical and psychological aspects of chronic pain.

The current issue of *JBMR* deals with these aspects, and it is with great pleasure that the Editor's Choice is awarded to Aslan et al. [?], who highlighted the efficacy of ultrasonography-guided oxygen-ozone therapy com-

pared to corticosteroids in terms of Western Ontario and McMaster Universities Osteoarthritis (WOMAC) scores modifications between baseline and 12-weeks post-injection in a large sample of patients affected by knee osteoarthritis. Their paper has been made freely available for you to read, download, and share.

In conclusion, we could suggest that oxygen-ozone therapy is a novel, safe, and effective intervention rehabilitative approach to treat musculoskeletal pain and could be implemented in the complex rehabilitation framework of several highly prevalent musculoskeletal conditions like osteoarthritis and LBP. Quality of evidence should further increase in the future to reach a higher scientific consensus on the efficacy oxygen-ozone therapy for the complex treatment of musculoskeletal disorders.

On behalf of the editorial team of JBMR, we hope you enjoy reading this last issue of 2024!

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### Conflict of interest

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### Ethical approval

As this is an editorial, there was no need for ethics approval or consent to participate.

### Author contributions

Study conceptualization: MI, AdS; Methodology: MI, AdS; Investigation: MI, AdS; Writing – Original Draft Preparation: MI; Writing – Review and Editing: AdS; Study supervision: MI, AdS Both authors have read and agreed to the published version of the manuscript.

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