Article

INTERVENTIONAL THERAPIES IN FACET SYNDROME

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ABSTRACT

The facet joint syndrome represents a significant cause of chronic low back pain. This study outlines the available interventional treatments, as well as the potential role of ozonotherapy in the management of these patients. Additionally, an initial case series of patients treated with CT-guided intra-articular and deep paravertebral infiltration of an O_2-O_3 mixture is presented.

KEYWORDS: *Facet syndrome, low back pain, ozonotherapy, infiltrations, O_2, O_3*

INTRODUCTION

Low back pain (LBP) is a significant health issue that affects a large portion of the general population; it poses a substantial socio-health problem in Western countries, particularly in light of the progressive aging of the population. Lumbar facet joint syndrome represents a common cause of low back pain, which is often underdiagnosed and improperly treated. Some studies have shown a prevalence of 27-40% of pain arising from the facet joints in patients with LBP. This results in costs for society due to a lack of accurate diagnosis, excessive requests for radiological examinations, unnecessary surgeries, and loss of work capacity, making it the most significant source of healthcare expenditure in industrialized countries.

It is defined as unilateral or bilateral low back pain that radiates to the buttocks, groin region, and thighs up to the knee. The most common etiology is osteoarthritis (1, 2).

Many spinal structures can be responsible for pain; some conditions, such as herniated and protruded discs, can be easily diagnosed with neuroimaging studies; however, other conditions, including facet joint syndrome, are difficult to evaluate with diagnostic imaging alone. Although various diagnostic techniques exist, there is no effective correlation between clinical symptoms and the degree of spinal degeneration. Therefore, clinical evaluation and identification of painful trigger points remain fundamental for guiding treatment.

Interventional radiological treatments for lumbar facet joint syndrome begin with anesthetic joint blocks and steroid injections at the intra- or periarticular level and may escalate to neurolysis treatments (physical or chemical) (3). Infiltrative treatments with O_2-O_3 have demonstrated good efficacy in the treatment of low back pain over the years (4-8), particularly in cases of protrusions or herniated discs. They can be performed under radiological guidance or using anatomical landmarks. Radiological guidance ensures greater precision in needle placement and allows for assessment of gas distribution once injected, thereby increasing clinical efficacy and reducing the risk of complications in treatment. Furthermore, in conditions affecting the posterior compartment, infiltrative treatment with O_2-O_3 has also shown

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effectiveness in managing patients with LBP; thus, radiologically guided infiltration of O_2-O_3 may constitute a valid supplementary and supportive alternative to other interventional treatments for patients with posterior compartment pathology, especially facet joint syndrome, considering its low cost, minimal complication rate, and ease of application (9, 10).

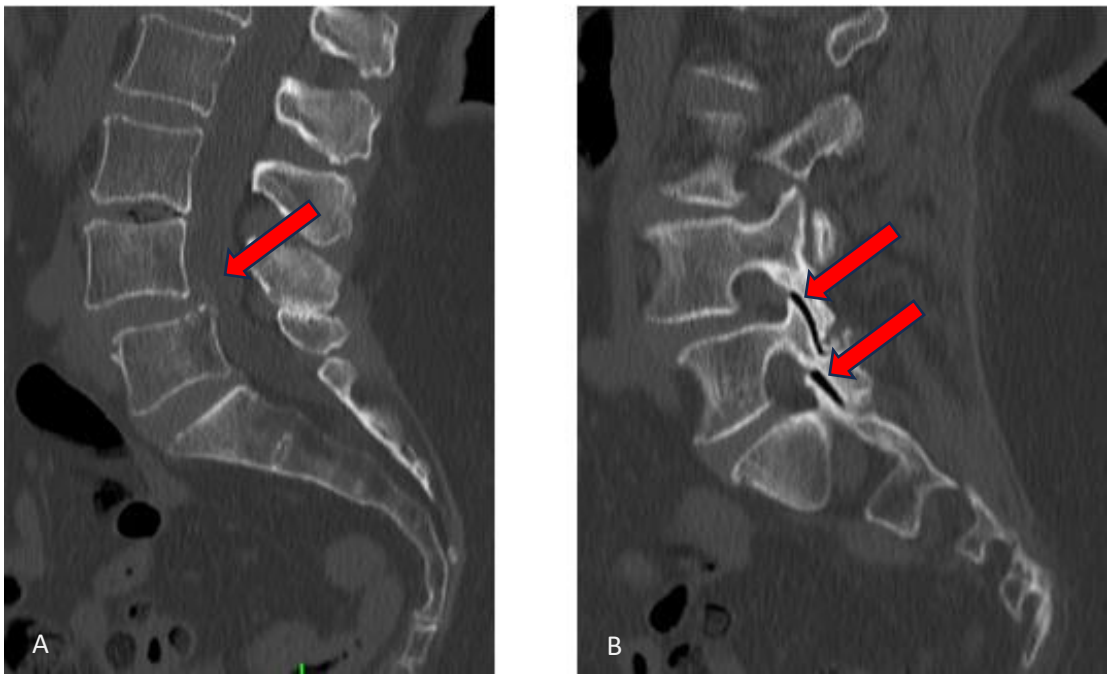
Facet joint syndrome includes localized pain with pseudoradicular irradiation and variability in territorial distribution; it typically involves one or both sides of the gluteal and trochanteric regions (from L4), the groin, and the thighs (L2-L5), terminating above the knee, without neurological deficits. Painful trigger points are often present at the site of interest. The pain is exacerbated during flexion-extension and rotation movements, improves with rest, and worsens in the morning and after periods of inactivity, leading to movement stiffness or after excessive physical exertion; it is aggravated by prolonged standing (11-20).

IMAGING

Pain originating from the zygapophyseal joints, however, is challenging to diagnose based solely on clinical findings, as symptoms and physical examination often lack specificity. This can lead to inefficient use of imaging studies, which may yield incidental findings that may be irrelevant in certain clinical contexts. Moreover, numerous pathological conditions (e.g., vertebral fractures, discopathies, neoplastic lesions) can initially present with overlapping clinical manifestations. Therefore, it is essential to make an appropriate choice of imaging in relation to the clinical context and to establish a clinico-radiological correlation to identify the potential cause of pain in the patient.

X-ray/CT

The initial radiological assessment of a patient with facet joint syndrome includes radiographic studies in the AP, LL, and oblique projections. This can be supplemented by a CT scan, which allows for better evaluation of the anatomy of the joint. Articular degeneration is manifested by narrowing of the joint space, subchondral sclerosis and erosion, the presence of calcifications in the joint capsule, cartilage thickening, hypertrophy of the articular processes and the yellow ligament, and osteophytes. Secondary signs include the presence of intra-articular gas degeneration, joint effusion, and degenerative spondylolisthesis. Synovial cysts may extend posteriorly but, in some cases, also anteriorly, involving the spinal canal or the neural foramen (Fig. 1. A-D).



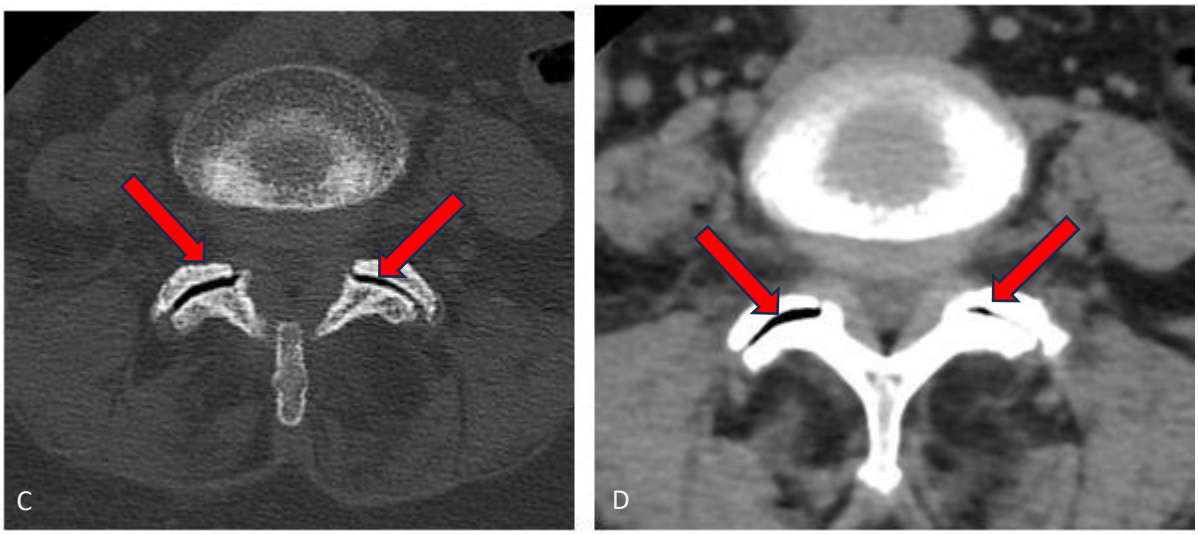


Fig. 1. ***A-B**: **A**): spondylolisthesis L4-L5; **B**): facet joint hypertrophy and sclerosis; **C**): axial CT with the bone algorithm: vacuolar degeneration of the facet joint; **D**): axial CT with soft tissue algorithm: ligamentum flavum hypertrophy.*

MRI

MRI serves as a second-level modality in assessing patients with facet joint syndrome; compared to CT imaging, it allows for a better evaluation of the relationship between the joint and neural structures, particularly in cases of radicular compression due to foraminal or canal stenosis. Additionally, MRI facilitates the assessment of the inflammatory processes affecting the joint, including the synovium and adjacent bone, through the use of T2 sequences with fat saturation; subchondral edema is, in fact, present in 14-41% of patients with low back pain. The presence of diffuse joint effusion may suggest instability, although it is not specific to the site of origin of the pain (Fig. 2 A, B).

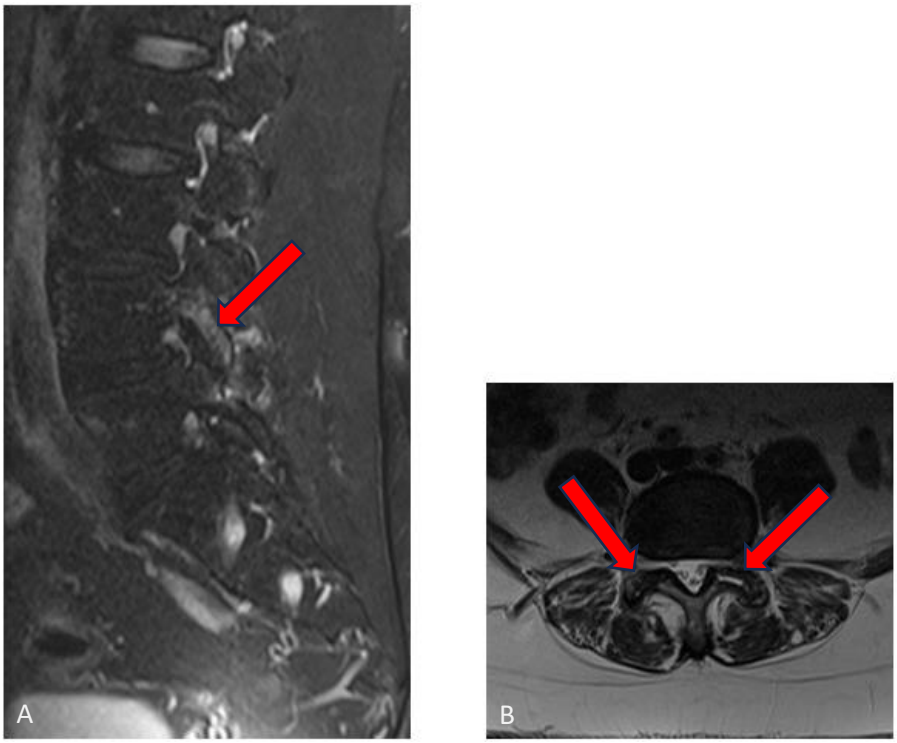


Fig. 2. *A-B: MRI sagittal (**A**), axial (**B**): facet syndrome (**arrows**).*

The study can be enhanced through the injection of a paramagnetic contrast agent with T1-weighted acquisitions with fat saturation (useful for the diagnosis of synovitis); it also allows for a better delineation of the inflammatory status of the degenerative process, thereby aiding in the identification of the therapeutic target for percutaneous treatments. However, administering gadolinium in this context is not routine and is reserved for selected cases.

INTERVENTIONAL TREATMENTS

First-line therapy is conservative, involving pharmacological approaches with the administration of NSAIDs (non-steroidal anti-inflammatory drugs) and muscle relaxants, followed by systemic corticosteroids if necessary. In cases of ineffectiveness, various percutaneous treatments may be implemented, depending on the operator's experience. Imaging-guided techniques enhance technical and clinical efficacy while reducing potential complications, such as hemorrhage, infections, and vasovagal syncope.

Medial branch blocks

Since it is often not entirely clear whether a facet joint is painful or not based on clinical assessment or imaging, a controlled nerve block can assist in the etiological diagnosis of low back pain. However, it does not address the pathogenesis of the pain.

There are several open questions:

- *degree of response:* authors do not fully agree on the clinical criteria for response to nerve blocks; some consider a response positive if there is a complete reduction of pain, while others do so for partial reduction;
- *target of the block:* it is currently believed that blocking the medial branch is more specific than intra-articular injections, and this target is thus utilized in selecting patients who are candidates for neurolysis;
- *number of blocks and levels:* various authors suggest performing blocks in two different sessions. Additionally, due to the dual innervation of the facet joint, the diagnostic block should be performed at a minimum of two levels per single block;
- *type of drug to be injected and volume:* diagnostic blocks include local anesthetics (lidocaine and/or bupivacaine); some authors find it advantageous also to combine steroids. There is no consensus on the volume of anesthetic to be injected, with recommendations varying from 0.25 ml to 0.5 ml per single block. However, there are potential false positives for various reasons: placebo effect, diffusion of the injected drug to other structures that may also be responsible for pain, and excessive administration of local anesthetic.

Articular steroid injections

The infiltrations of the articular facets include long-acting steroids and local anesthetic. They can be performed intra-articularly, periarticularly, or along the medial branch of the dorsal ramus, using radiographic, CT, or ultrasound guidance (Fig. 3 A, B).

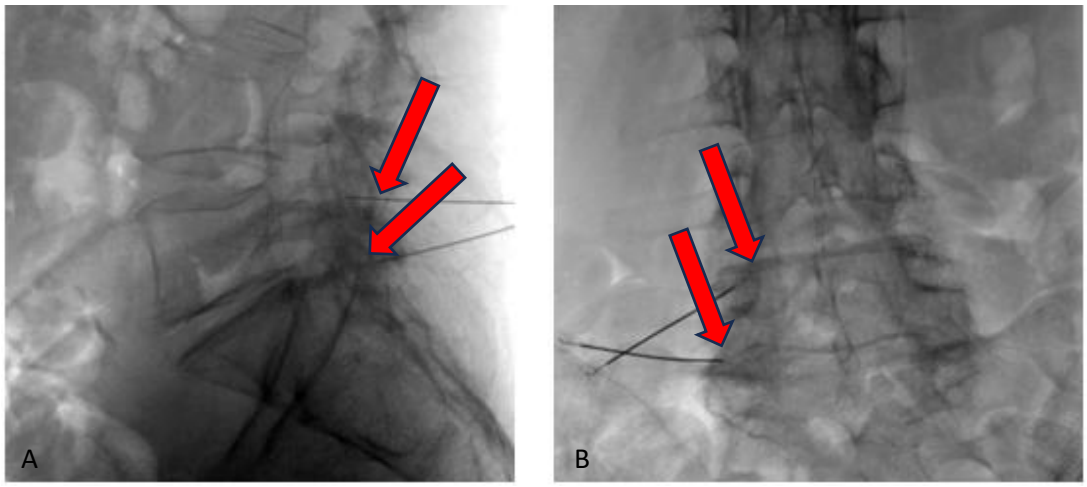


Fig. 3. *LL X-ray (**A**) and AP X-ray (**B**): assessment of proper needle positioning for treatment of the facet joints (**arrows**).*

Steroids allow for the interruption of nociceptive inputs at both central and peripheral levels and reduce the pro-inflammatory environment present in the affected joint; a short- to medium-term reduction in pain can be achieved with these treatments (4). Multilevel injections have demonstrated greater efficacy compared to single injections; however, the long-term efficacy is limited. No significant differences exist in the treatment site, as no real difference in outcomes has been observed between intra-articular and periarticular injections.

Neurolysis

It is performed on patients who have had a positive response in cases of anesthetic nerve block. When conducted after proper patient selection, it allows for pain reduction, improvement in disability, and decreased reliance on analgesics. However, regardless of the technique employed, it does not provide a definitive resolution of pain, as the damaged nerve may potentially regenerate. Two main techniques of physical neurolysis are primarily utilized:

- *radiofrequency:* this technique involves positioning an electrode under radiological guidance, followed by releasing a sinusoidal current. It can be performed as either ablative or pulsed radiofrequency, the latter allowing the avoidance of any potentially damaging effects on the nerve roots and possible spinal instability due to muscle denervation. Literature data demonstrate a significant reduction in pain in approximately 90% of patients with a duration of effect lasting up to 12 months. Potential complications include painful dysesthesia or cutaneous hyperesthesia, formation of neuromas, deafferentation pain, and accidental damage to the nerve root;
- *cryoneurolysis:* this technique consists of applying cold to the nerve to induce denaturation through the rapid decompression of a gas released at the tip of the needle. An ice ball is formed at the needle tip, which leads to a conduction block. Similar to radiofrequency, the success of the treatment relies on appropriate indication and patient selection. It shows results that are substantially comparable to those of radiofrequency. The advantages include being reversible, repeatable, and having a lower incidence of complications.

Surgery

There is no compelling evidence regarding the role of surgery in degenerative facet joint pain. In cases of spondylolisthesis, surgical intervention may be warranted if interventional therapies have failed, utilizing treatments such as lumbar decompressive laminectomy and arthrodesis. Other surgical treatments include endoscopic neurotomy.

OZONE THERAPY

Ozone therapy has progressively established itself in the treatment of spinal pain, primarily for cases of low back pain and sciatica due to herniated or protruded discs; the first use in this clinical field dates back to 1985, subsequently confirmed by numerous clinical studies that have supported its effectiveness both in alleviating symptoms and in progressively reducing the size of herniated disc tissue in follow-up imaging. The efficacy of the treatment has also progressively emerged in the management of non-discogenic pain caused by pathologies of the posterior compartment.

Over the years, infiltration treatments with O_2-O_3 have been performed with or without radiological control; in the former case, the gas injection is performed into the paravertebral musculature using anatomical landmarks, while in the latter case, radiographic, CT, or ultrasound guidance is employed to assess the correct positioning of the needle. A meta-analysis from 2021 showed that imaging-guided techniques provided a better reduction in pain compared to unguided methods, allowing for more accurate and deeper positioning of the needle; particularly, a greater difference in outcomes was noted in older patients, presumably due to anatomical changes related to osteoarthritis, scoliosis, vertebral collapse, etc., which may occur and thus make needle positioning even less accurate in unguided procedures.

Bonetti and colleagues (2, 4), demonstrated the efficacy of O_2-O_3 treatment in a cohort of 416 patients with pathologies of the posterior compartment, including facet joint synovitis, Baastrup's syndrome, spondylolysis, spondylolisthesis, and degenerative pathology of the facet joints, who were selected through accurate clinical and imaging evaluation. The subgroup of 326 patients with facet joint syndrome showed a significant reduction in initial pain in 74.5% of cases, even after a single treatment under CT guidance; in cases with insufficient reduction, a second infiltration further increased the percentage of clinical success, thus suggesting oxygen-ozone treatment as a valid alternative to other interventional and conservative treatments, given the minimal complication rate, low cost, and no exclusion for subsequent treatments such as steroid injections, radiofrequency, or surgical interventions.

Mechanism of action

The osteoarthritic degeneration of the facet joints begins at the level of the cartilage, leading to subsequent reduction of the joint space and increased vascularization, with multiple inflammatory mediators involved. In the late stages, this process culminates in articular hypertrophy, osteophyte formation, and progressive thickening of the subchondral bone tissue, resulting in sclerosis and erosion.

Various studies have demonstrated an increase in the infiltration of immune system cells and pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, and prostaglandins) as well as enzymes contributing to cartilage degradation. In addition, anti-inflammatory cytokines and inhibitors of the aforementioned enzymes are upregulated in an attempt to generate a

reparative response. Angiogenic factors are also present, which contribute to inflammation by enhancing the local influx of inflammatory cells and promoting neurogenesis.

Moreover, the development and progression of osteoarthritis are associated with an increase in oxidative stress and overproduction of reactive oxygen species (ROS). In normal cartilage, chondrocytes produce low levels of ROS, maintaining a balance with the body's physiological antioxidant systems, thus contributing to the maintenance of cartilage homeostasis, modulating the aging and apoptosis of chondrocytes, as well as the synthesis of the extracellular matrix. In osteoarthritic cartilage, abnormally high levels of ROS are produced in response to increased mechanical stress, fluctuations in the partial pressure of oxygen, and immunomodulatory mediators; concurrently, a reduction in antioxidant enzymes is observed. The increase in oxidative stress subsequently leads to apoptosis and premature aging of chondrocytes and synoviocytes. It also causes the activation of NF-kB, which contributes to the increase of pro-inflammatory factors. Ozone therapy acts through various mechanisms:

- activation of cellular metabolism;
- reduction of the synthesis of pro-inflammatory cytokines and prostaglandins;
- increase in immunosuppressive cytokines;
- reduction of oxidative stress in response to chronic oxidative stress;
- improvement of oxygen supply to tissues.

In the clinical context of osteoarthritis, it acts as a regulator of the inflammatory response, enhancing the synthesis of TNF-β and reducing pro-inflammatory cytokines (TNF-α and IL-8). Furthermore, it intervenes in the regulation of the NF-kB pathway, through which the production of pro-inflammatory cytokines is favored, implicating the inhibition of extracellular matrix synthesis and resulting in cartilage damage, alterations in the cartilage matrix, and apoptosis. The NF-kB pathway is directly activated by ROS or through pro-inflammatory mediators such as TNF-α. O_2-O_3 directly reduces the production of ROS or indirectly inhibits TNF-α, thereby blocking the NF-kB pathway.

The administration of low doses of O_2-O_3 also stimulates the organism's response by inducing the production of antioxidant enzymes, enabling the organism to adapt to chronic oxidative stress, and normalizing the redox balance. Finally, it enhances the effective utilization of oxygen in the mitochondrial respiratory chain, stimulating glycolysis in damaged cells and thus preventing cellular death.

PRELIMINARY EXPERIENCE

We present a preliminary experience involving 11 patients with a clinical and radiological diagnosis of low back pain due to facet joint syndrome, treated with CT-guided deep periarticular and paravertebral injections of O_2-O_3.

Technique

- an anamnesis interview is conducted with the patient, highlighting any contraindications to treatment that may be present in the medical history (remote pathological anamnesis);
- the evaluation of the medical history is then performed (recent medical history), with particular attention to the onset of symptoms, location and characteristics of the pain, and any previous treatments (conservative or minimally invasive) undertaken;
- an assessment of the radiological documentation is necessary, including an MRI study of the lumbar spine or, if contraindicated or not feasible for other reasons, a CT study. The patient is informed about the mechanism of action and effects of the treatment with O_2-O_3, including the efficacy rate and possible rare side effects;
- informed consent is obtained through the patient's signature;
- the patient is then accompanied to the CT room, positioned in the prone position on the table;
- preliminary low-dose scans are obtained to determine the correct centration of the level of interest and measurement of the injection site (Fig. 5).

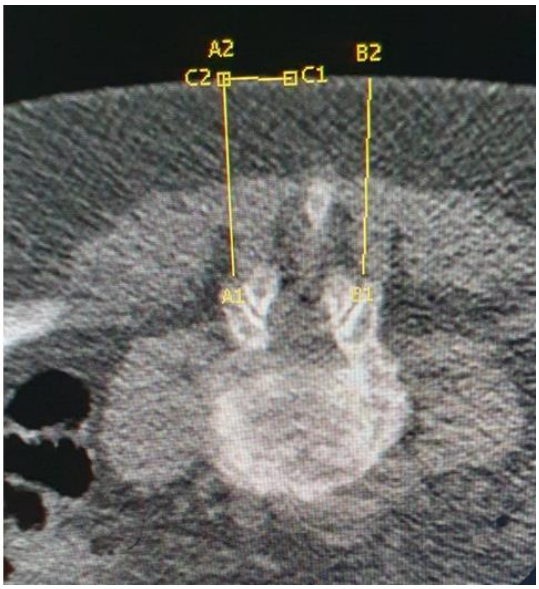


Fig. 5. *Preliminary CT scan prior to treatment.*

- marking on the patient's skin to identify the entry point based on the measurements taken, followed by disinfection of the skin with povidone-iodine and superficial anesthesia using ethyl chloride spray;
- placement of the needles (Fig. 6).

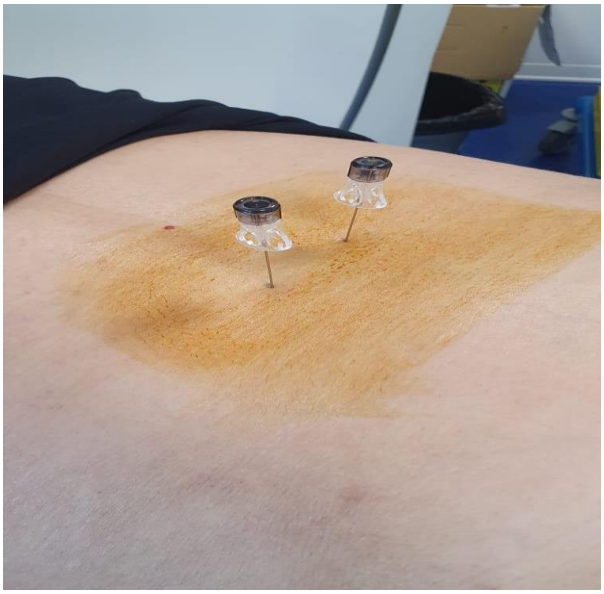


Fig.6. *Placement of the needles*

- verification of the correct positioning of the needle at the level of the joint interline through targeted CT scanning (Fig. 7).

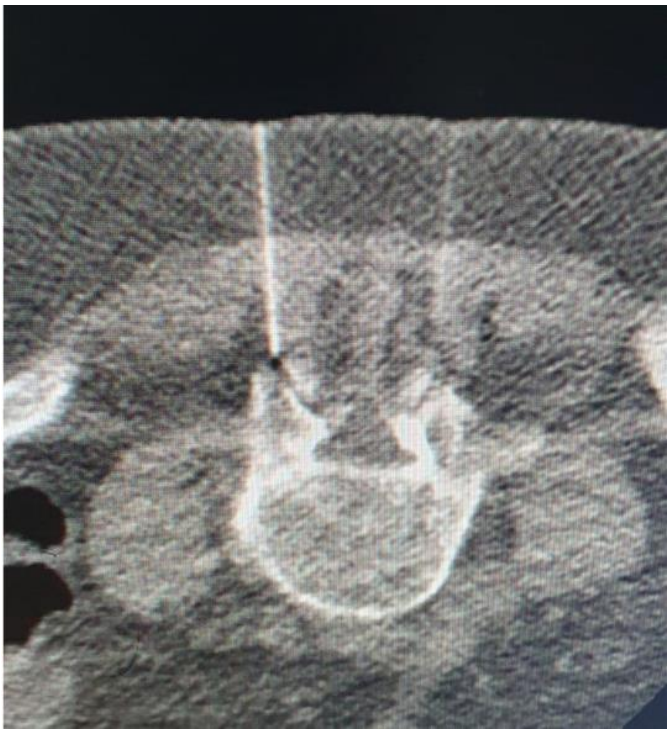


Fig. 7. *CT control of needle positioning.*

- repositioning if necessary;
- using a sterile 20 ml syringe, inject 2-3 ml into the intra- and periarticular sites and 4-5 ml into the deep paravertebral site of a mixture of O_2-O_3 at a concentration of 25 µg/ml;
- withdrawal of the needle with compression;
- control with CT scans to verify the correct distribution of the gas (Fig. 8);

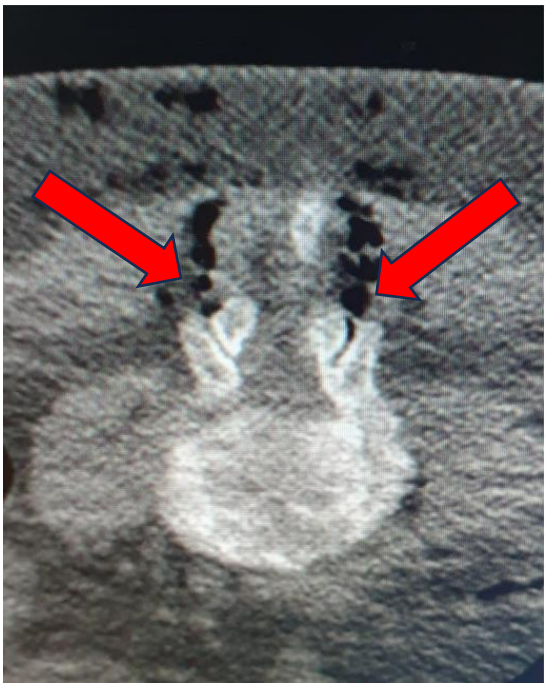


Fig. 8. *CT control of the distribution of the gaseous mixture O_2-O_3 (**arrows**).*

- implementation of physiotherapy treatment using a diamagnetic pump (CTU) or laser;
- clinical assessment of the patient's condition and discharge.

RESULTS

From January to May 2024, 11 patients (7 females and 4 males) with a clinical diagnosis of lumbar facet joint syndrome were treated. All patients underwent MRI or, if contraindicated or unavailable, CT imaging, which demonstrated radiological evidence of periarticular bone edema or other signs of joint overload. The treatment site was determined through clinical evaluation that identified a painful trigger point correlated with radiological findings; treatments were administered in a single session across a minimum of 1 level to a maximum of 3 levels.

Patients underwent a minimum of 2 to a maximum of 4 injections, with the treatment proposed at time 0, after 7-10 days, after an additional 15-20 days, and the last one after 20-30 days, within a total timeframe of approximately 2 months; in some patients, due to organizational reasons, the treatment intervals were extended beyond the initially agreed schedule.

In 8 out of 11 patients (72%), a reduction in pain of varying degrees was reported during the treatment, with the most significant improvement observed between the second and third injections, resulting in an overall subjective clinical improvement compared to the initial condition, a partial resumption of physical activity (commensurate with the patient's age), and a reported decrease in analgesic consumption. The total number of procedures was agreed upon with the patient based on clinical response.

The three cases of clinical failure were characterized as follows:

- a patient with a neurological condition, with a long history of low back pain and multiple prior treatments, underwent bilateral injection at 3 levels (L3-L4, L4-L5, and L5-S1); after the first treatment, there was a worsening of symptoms in the 5 days following;
- a patient with a depressive syndrome, suffering from chronic pain for years, received 2 injections without clinical benefit, after which she chose to discontinue treatment;
- a patient with chronic pain for years experienced mild improvement after the first 2 treatments; however, following physical exertion, symptoms recurred during the execution of the third injection, which proved to be ineffective. The scheduled fourth injection was canceled and replaced with a periarticular steroid injection.

No significant post-procedural complications were observed.

DISCUSSION

The data present in the literature support the possibility of using infiltrative treatments under radiological control with O_2-O_3 in patients with lumbar facet joint syndrome. CT guidance ensures correct positioning and identification of the injection site, as well as verification of the distribution of the medical gas, increasing the treatment efficacy rate while minimizing the risks of accidental puncture of neural or vascular structures and the rate of complications. The use of a low-dose scanning protocol significantly reduces the risk associated with the administration of ionizing radiation, which is considerably lower than the safety benefits provided by radiological guidance for the procedure.

Deep periarticular and paravertebral infiltration guided by CT has proven to be easily and swiftly applicable and has not shown technical issues compared to other infiltrative procedures such as medial branch blocks or corticosteroid injections; intraarticular injection in some patients has proven challenging due to the presence of osteophytes that hindered access to the joint space, as well as due to the presence of joint sclerosis, which prevented direct injection or minimized the quantity injected.

Given the progressive improvement observed with subsequent infiltrations, it may be advisable to propose to the patient a guided CT treatment cycle consisting of a minimum of two sessions and a maximum of four, as the most significant results have been noted between the second and third treatments. To reduce the risk of post-treatment pain, particularly in cases of multiple injections across several levels, it may be prudent, especially during the first treatment session, to reduce the injection volumes.

CONCLUSIONS

The limited follow-up period did not allow for the evaluation of medium- and long-term effects of the treatment and the potential need for a repetition of the infiltration cycles. Despite the low number of patients treated and the short

follow-up duration, considering the preliminary results achievable with this methodology and the extremely low complication rate, it can be suggested that O_2-O_3 infiltrations guided by CT, both peri- and intra-articular, be used as a first-line therapy in patients diagnosed with facet joint syndrome who are poorly responsive to medical therapy. In particular, compared to intra-articular treatment with corticosteroids combined with anesthetic injections, O_2-O_3 does not present systemic side effects (e.g., hypertension, elevated blood glucose levels, etc.) or local effects (such as periarticular accumulation and calcifications) and has no risk of allergic reactions; compared to neurolysis procedures, it also offers the advantages of reduced costs, the possibility of outpatient treatment, and speed of execution.

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