Original article

CT-guided ozone mixture injection in treatment of symptomatic lumbar facet synovial cysts

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Abstract. *Background and aim:* To evaluate the clinical and radiological outcomes, in terms of safety and efficacy, of a new treatment method for symptomatic lumbar facet synovial cysts (LFSC), based on ozone injection inside the cyst. *Methods:* We retrospectively reviewed clinical records and imaging studies of 77 patients who underwent CT-guided ozone treatment of symptomatic facet joint synovial cysts in our department over a 5-year span. Clinical outcome was assessed with Numerical Rating Scale (NRS) and Oswestry Disability Index (ODI) evaluations, obtained prior to the intervention and at 1-, 3-, 6- and 12-months follow-up. Follow-up MRI imaging at 6 and 12 months were obtained and confronted with the pre-procedural MRI to analyse cyst modification after the intervention. *Results:* Ozone administration was technically successful in 100% of procedures; no immediate complications occurred. At 1 month evaluation, 92% of the patients referred partial or complete symptomatic response; 86% of patients at 3 months and 84% at 6 months confirmed symptoms improvement; final assessment, at 12 months after intervention, outlined overall significant clinical improvement in 81% of patients. During the 12 months of follow-up only 3 patients had a relapse of the cyst (at 6 months) that were retreated with a 100% success. *Conclusions:* CT-guided ozone therapy for symptomatic LFSC is a safe and innovative treatment option, with good clinical results at 12 months follow-up in a significative percentage of patients, thus reducing the need for invasive surgical interventions. (www.actabiomedica.it)

Key words: Ozone injection; lumbar facet synovial cysts; radiculopathy; low-back pain

Introduction

Lumbar facet synovial cysts

Lumbar facet synovial cysts (LFSCs) are round, fluid-containing lesions arising from the capsule anywhere around the facet joint. They occur most often in the lumbar spine, with prevalence of the L5-S1 segment, as the lumbar spine moves more and is more prone to instability, but can also occur, even if rarely, in the thoracic and cervical spine (1, 2).

The next most common level for synovial cyst occurrence is L4-L5, followed by L3–4, followed by L2–3. (3)

LFSCs are most frequent in people with an average age of around 60 years. (4)

They are common to find in spine imaging, with an estimated prevalence of 1 in 15, and they are linked with aging and degenerative spine disease. (5) Therefore, synovial cysts are associated with degenerated facet joints and may arise from periarticular tissues. (6)

Although the pathogenesis of facet-joint synovial cysts remains unclear, they are widely regarded as part of a spinal degenerative process, commonly caused by conditions such as spinal instability and trauma (7). Recently, it has been reported that a large proportion are not synovial in derivation but result from pseudocystic degeneration of the ligament flavum. (8)

Regarding their clinical presentation, it is variable and depends on their location, size, and relation to adjacent neural structures. Although clinically silent, mainly when they have an extracanal location, in a relatively small percentage of the population, synovial cysts can become symptomatic when they have an intracanal location, presenting with lumbar pain, ipsilateral radiculopathy or, more rarely, cauda syndrome secondary to contact with nerve roots and their inflammation. (9, 10) They are present in as much as 10% of patients with lumbar pain or radicular pain. (11)

Imaging

The imaging appearance of facet joint cysts can be variable on both MRI and CT.

On CT scan, they may have varying densities depending on the composition of the cyst. Simple fluid density suggests a serous type of synovial fluid with increasing density suggestive of inspissation, hemorrhage, or increased protein or calcium content. Air density within the cyst can result from a negative pressure void allowing for dissolved nitrogen in fluid to sublimate into a gaseous state. (12)

MRI is the imaging modality of choice for the diagnosis of synovial cysts. The appearance on MRI can also vary with a predominantly serous fluid containing cyst demonstrating a well-defined hypo-intense rim with characteristic hyper-intense fluid signal on T2 weighted imaging and hypo-intensity on T1 weighted imaging. Increased signal on T1 weighted sequences may herald the presence of haemorrhage or increased protein content, while markedly diminished signal intensity on all pulse sequences may reflect the presence of hemosiderin, calcification, or nitrogen gas within the cyst. (13)

Treatment

Treatment for lumbar facet joint synovial cysts includes both conservative and surgical treatment. (3)

Conservative options include bed rest, physical therapy, acupuncture, oral analgesics and anti-inflammatories, and percutaneous injection and aspiration.

Various options are currently adopted for symptomatic LFSCs treatment when conservative therapy is not sufficient, starting with mini-invasive interventions such as image-guided aspiration and injections of steroids, that have shown good short-term benefits, but high rates of clinical recurrence. (14)

Surgical intervention is most effective when the entire cyst is excised. It leads to high resolution rates, with very rare instances of recurrence, but requires a more invasive approach, and it is not without inherent risks. Typically, surgical treatment requires laminectomy and/or facetectomy and now includes a minimally invasive endoscopic/microscopic approach. Common surgical risks include spinal instability, dural tear, neurologic injury, epidural haemorrhage and haematoma.

Surgical treatment is typically recommended as soon as conservative measures fail to alleviate symptoms. Percutaneous interventions are usually indicated in elderly or high-risk patients. (15,16)

Ozone

The aim of this study is to report the clinical and imaging outcomes for symptomatic LFSCs, treated with a novel mini-invasive image guided approach, based on ozone intracystic injections.

Ozone is an important oxidant gas. When in contact with biological fluids or cells it forms various reactive oxygen species (ROS) from O3. In this way Ozone causes an increase of oxidative damage, but cells respond with the activation of many transcriptional factor, such us “nuclear factor-erythroid 2-related factor 2” (NRF2). The increased expression of these transcriptional factor causes an important release of antioxidant enzymes and in that way a huge antioxidant response. Some of the antioxidants produced are glutathione S-transferase (GST), catalase

(CAT), heme oxygenase (HO)-1, superoxide dismutase, glutathione peroxidase, heat shock proteins and quinone-oxidoreductase, that play a role as free radical scavengers (6). Secondary the exposition to O3 cause an increase of IL8, and many growths factor as Platelet-derived Growth Factor (PDGF), Transforming Growth Factor-Beta (TGF-B) and other fundamental for the process of tissue remodelling (17).

O3 injected into the middle of the disc through the conventional posterior lateral route had produced the desired result for small or medium size disc herniations (18). Ozone in that approach cause the oxidation of nucleus pulposus that reduce its dimension. The reduction of disk size may cause a reduction of nerve roots compression. (19)

Moreover, ozone inhibits production of bradykinin and other allogenic molecules and pro-inflammatory cytokine. Finally, ROS and LOP produced by ozone, cause an increase of local microcirculation that increase the O2 supply and reduce the venous stasis caused by disk compression of venous vases (20,21).

So, ozone is a powerful gas with anti-inflammatory and anti-septic properties. It is preferable to cortisone, which may cause arachnoiditis and hasn't any antiseptic properties.

Methods and materials

Study design

We performed a detailed review of medical charts and imaging studies of all patients who underwent mini-invasive CT-guided intracystic ozone injection for symptomatic LFSCs at our Institution in a 5-year period from 2016 to 2020. Cyst were directly filled with ozone, without aspiration, using an ozone machine. Treatment with ozone was routinely performed in our department since ozone is widely used for peri-radicular and intra-articular treatment.

Clinical outcome was evaluated using the Numerical Rates Scaling (NRS) and Oswestry Disability Index (ODI), obtained before treatment and at the programmed follow-ups at 1, 3, 6 and 12 months.

Follow-up lumbar spine imaging was obtained with an MRI without contrast performed at 6 and 12 months, in order to review and compare with preoperative imaging. MRI sequences consist of: T1 in the sagittal plane; T2 in the axial, coronal and sagittal planes; T2-STIR in the sagittal plane.

Technique

All CT-guided interventions were performed at our out-patient clinic by a single interventional radiologist with a 25 years' experience in spine disease and treatments.

Patient was placed in the prone position, with a support under the belly in order to prevent excessive back lordosis. Low-dose CT scan of the lumbar region was performed.

Following the conclusion of procedural planning, sterile disinfection of the lumbar region was obtained. Local anaesthesia was routinely not performed.

The LFSC was accessed with a 22G Chiba needle, via a transforaminal approach for foraminal cysts, and ipsilateral or contralateral translaminar approach for medially placed lesions.

Additional low dose CT scans were performed to guide needle positioning until the cyst was entered; aspiration of the cyst was then performed followed by injection of 1-2 mL of gas mixture (2% O3, 98% O2). Final CT scan was then performed to confirm cyst rupture and gas leakage in the epidural space and facet joint (Figure 1 and 2).

When a transforaminal access was used, additional administration of 8 mL of ozone gas mixture and 2 mL of corticosteroid/local anaesthetic was performed after withdrawal of the needle into the foraminal space.

Patients were then discharged after a brief observation interval of 2 hours and referred for follow-up assessment.

Statistical analysis

All continuous numerical data were evaluated as mean ± standard deviation (SD). *Student t* was used for continuous variables. The statistical significance of the differences between pre- and post-operative data was defined by a *P-value* < 0.05.

All statistical data were processed using *GraphPad* software (Prism, La Jolla, US).

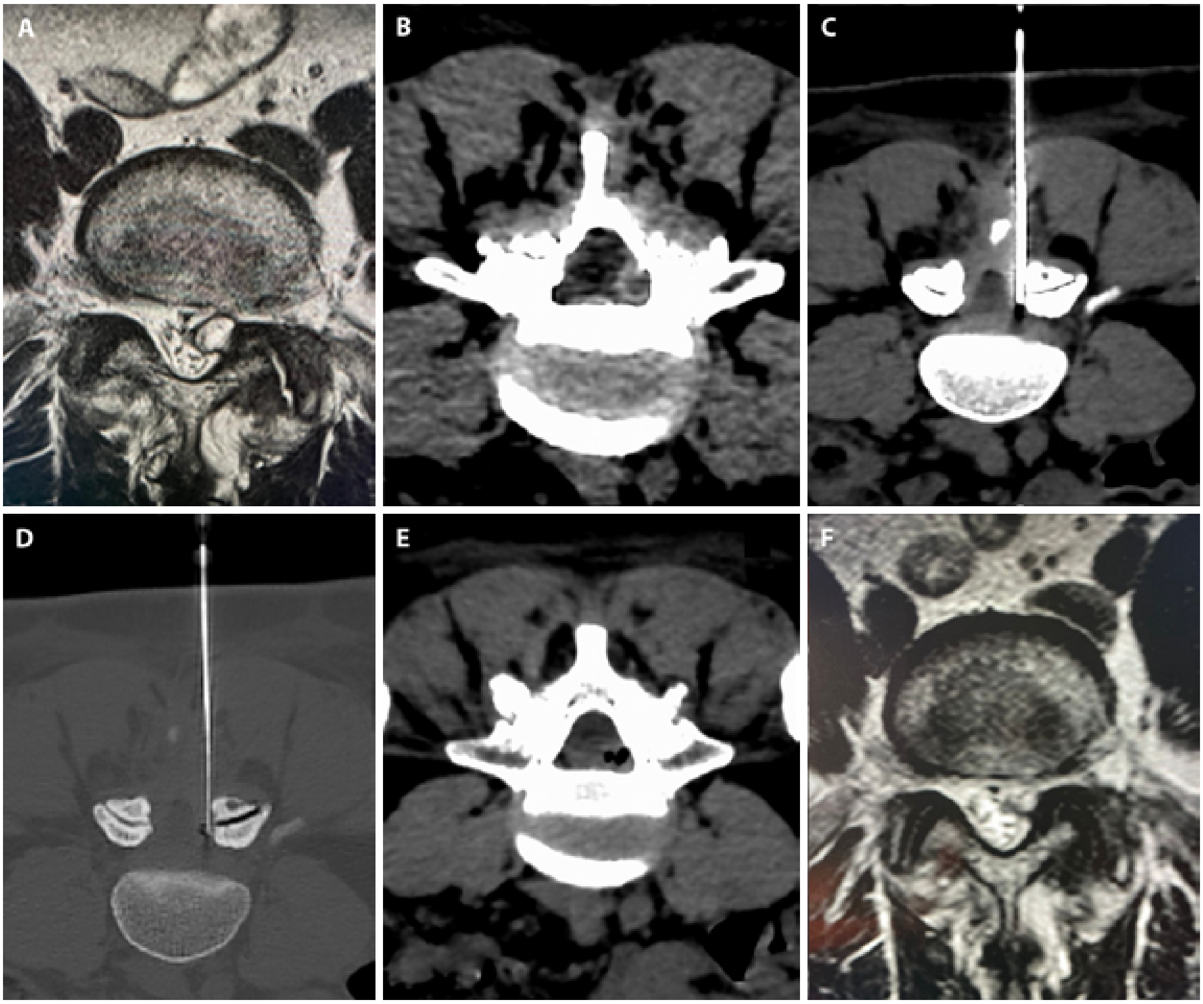

Figure 1. A: MRI T2W axial plane showed a large synovial cyst on the left zygapophyseal joint. B: Axial CT scan of the same cyst, with thickened walls, due to chronic nature of the pathology. C-D: Intra-procedural CT scan showed the correct positioning of the 22G needle inside the cyst. E: CT control scan after O2\O3 injection; the leakage of the gaseous mixture outside the cyst is noticeable. F: control MRI images demonstrate a shrinkage, with significant reduction of painful symptoms.

Results

Over a 5 years span, 77 patients underwent CT-guided intrasynovial ozone administration for symptomatic LFSC.

The study included 35 men and 42 women, with a mean age of 66 years (range 38-88y).

The most common clinical presentation was simultaneous presence of radiculopathy and low-back pain (63%); the remaining population only reported radiculopathy.

Mean LFSC size was 9mm (6-18mm); most common treated level was L5-S1 (53%), followed by L4-L5 (35%) and L3-L4 (12%).

Technical success intended as cyst injection and rupture was obtained in all cases (100%).

In 43 cases (56%) we opted for an ipsilateral translaminar approach, while in 11 cases (14%) a contralateral translaminar approach was used, and the remaining 23 cases (30%) were performed with an ipsilateral transforaminal approach.

No patients were lost during follow-up.

Figure 2. A-B: MRI and CT imaging of zygapophyseal arthrogenic synovial cyst at L4-L5 level in patient with acute onset of back pain and radiculopathy. MRI allowed to point out the signal and homogeneity of the synovial fluid due to the chronic nature of the pathology. CT demonstrated cystic wall thickening and arthropathic changes of the bone surfaces of the joint. On the superior border of the volume acquired, the radiopaque functional grid lays to precisely aim the entry and landing point of the needle. C-D: CT imaging demonstrated the needle tip perforation of the superior cystic wall with subsequent synovial fluid aspiration and sudden relief of the painful symptomatology. E: CT imaging of ozone diffusion in and outside the cyst after cystic burst, within the articular surfaces and periarticular muscles and other soft tissue.

Baseline NRS and ODI values for study population were respectively 7.2 ± 0.9 and 74.9 ± 1.8.

At 1 month follow-up, 92% of patients referred partial or complete resolution of symptoms; registered mean values for the complete cohort were 3.1 ± 0.7 for NRS and 35.3 ± 2.7 for ODI evaluation ($p<0.05$).

No procedure related complications were reported; some patients presented a relapse of symptoms.

At 3 months, 86% of the population confirmed a partial or complete resolution of symptoms; mean NRS values of 3.2 ± 1.1 and ODI values of 37.0 ± 3.4 ($p<0.05$).

At 6 months evaluation, 84% of the study population described a good clinical outcome with mean NRS values of 3.7 ± 1.3 and ODI values of 38.5 ± 3.1 ($p<0.05$).

3 patients underwent a second ozone injection for LFSCs relapse, documented by MRI scan, with a 100% response.

At 12 months follow-up, 62 patients (81%) confirmed primary complete or partial response of treatment with a good functional outcome; mean NRS values of 4.4 ± 1.7 and ODI values of 41 ± 5.3 ($p<0.05$) (Figure 3).

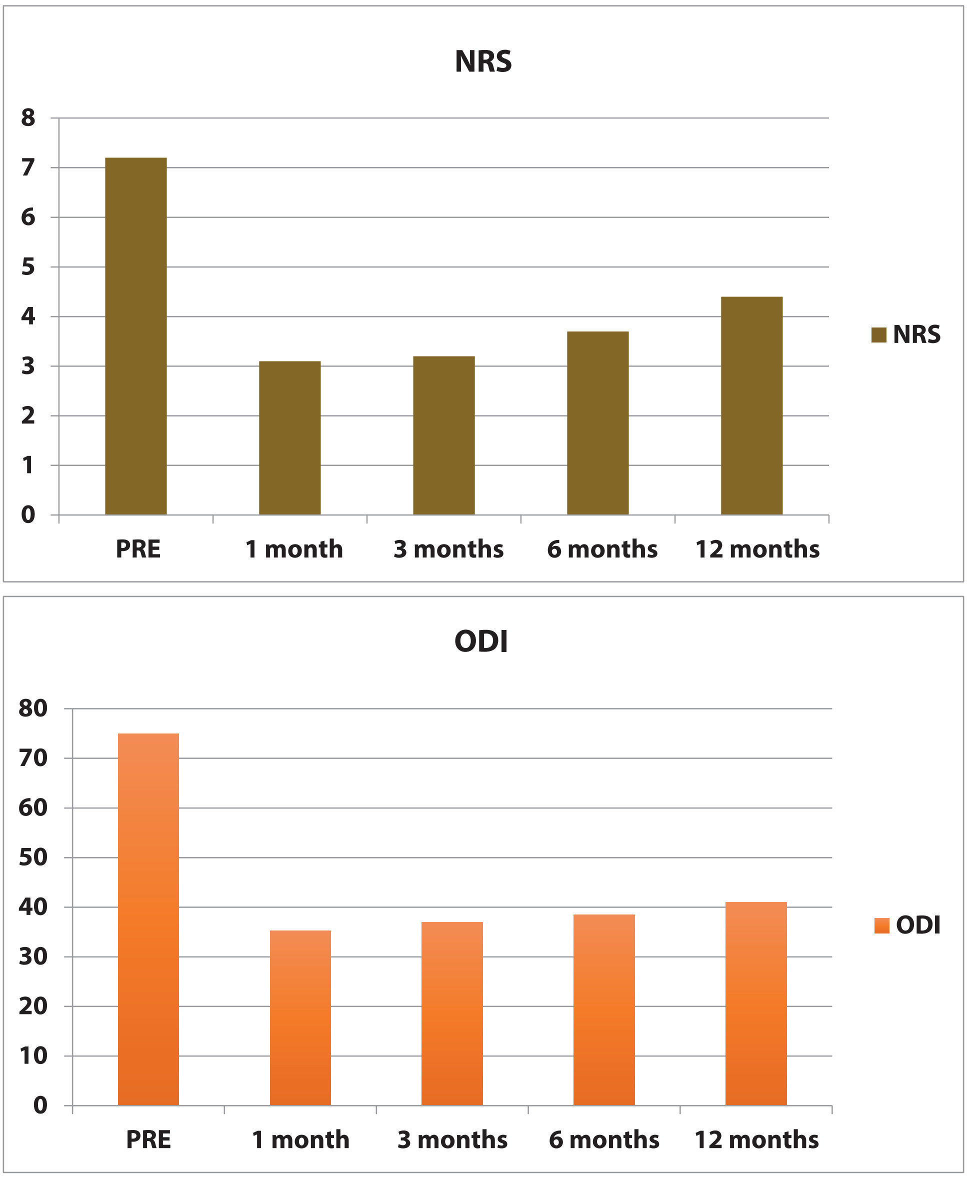

Figure 3. NRS and ODI scale pre-operative and at 1, 3, 6 and 12 months.

At the end of the follow-up period, 7 patients (9%) had a relapse of the LFSC and 8 (10%) had poor response to treatment. Therefore, they were referred to neurosurgical evaluation due to poor response from mini-invasive treatment, both for relapse of LFSCs and radiculopathy/low-back pain.

MRI examination without contrast was performed in all patients at 6- and 12-months distance from the intervention.

At 6 months, 3 patients (4%) that had an evident volume reduction in the previous MRI studies, documented a recurrence. Therefore, they have been retreated, with a 100% success.

At 12 months, control imaging showed reduction or disappearance of the treated cyst in 59 patients (77%); in 11 patients (14%) the target LFSCs was mostly unchanged relative to baseline evaluation in every control; a fissuration of the cyst's wall occurred in 5 of them, while in 7 patients (9%) the treated cyst was increased in size.

Mean LFSCs size, measured on axial and sagittal plane by the same radiologist, was 4 mm at 6 months and 5 mm at 12 months ($p<0.05$).

Discussion

Treatment with ozone of LFSC has never been described previously; ozone is commonly used in spinal intervention for disc disease and nerve root inflammation to achieve longer lasting results compared to simple steroid/anesthetic injections. (22)

In this paper, we aim to describe a novel technique for treatment of symptomatic LFSC and, in particular, to assess its long-term efficacy compared to conventional mini-invasive treatments.

Minimally invasive options have already been described for LFSCs treatment. The earliest treatment consists of fluoroscopically guided facet joints injections with 1-3 mL of anesthetic/steroids mixture along iodinated contrast medium, aimed to over-distend the joint and eventually to cause an indirect rupture of the cyst with extravasation of the solution in epidural space.

These studies report good initial clinical response with significant recurrence rates at long-term follow-up, with a favorable outcome as low as 33% at 12 months post-intervention. (23, 24, 25)

Also, CT-guided cyst treatment techniques, with direct puncture of LFSCs, have been described.

These studies report increased interventional technical success compared to the previous technique; long-term follow-up have shown variable results with clinical success rates of 75% at 12 months, but with more patients who needed a new treatment (21% vs 4% of our study). (26, 27)

A novel work by *Shah et al.* (28) describes the *"fenestration technique"*, consisting of repetitive back and forward needle movement inside the cyst, followed by cyst aspiration, in order to create multiple holes in the lesion wall, with reported satisfying long-term results.

Compared to existing literature, our study confirms the good clinical results of the minimally invasive treatments for symptomatic LFSCs in the short term.

Most importantly, our project suggests that LFSCs treatment with ozone solution leads to better results in the long-term follow-up with an overall clinical success of 81%. It's an important result, considering that it allows to reduce the need for invasive surgical interventions.

At the 12-months from the intervention, the MRI examination without contrast showed reduction or disappearance of the treated cyst in most cases. The increasing in size happened in only 7 patients, but dimensional criteria is not reliable; a cyst of the same dimension but with a fissurated wall does not cause the same insult since it's not anymore a closed system, thus exerting less pression on nearby structures. This is also proved by the patient's clinical improvement, mostly stable over time.

This study has some limitations, mainly its retrospective nature and the lack of a control group. Albeit the reported results are encouraging, further studies are needed to confirm their reliability.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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