“Not just herniated disc” back pain: outcome of oxygen-ozone treatment in selected applications

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ABSTRACT

Low back pain and sciatica are highly debilitating conditions affecting all socioeconomic groups at an increasingly early age. They are caused by different often concomitant spinal disorders: disc or facet joint disease, spondylolisthesis (with or without listhesis), vertebral body and interapophyseal arthrosis, spinal stenosis, radicular and synovial cysts and, more rarely, infections and primary or metastatic cancer.

Treatment of low back pain and/or sciatica requires an accurate diagnosis based on thorough history-taking and physical examination followed by appropriate imaging tests, namely computed tomography and/or magnetic resonance scans in addition to standard X-rays of the spine.

In recent years, several reports have demonstrated the utility of oxygen-ozone therapy in reducing the size of herniated discs. The present study reports on the outcome of oxygen-ozone treatment in 416 patients with non-discogenic low back pain caused by degenerative disease of the posterior vertebral compartment (facet synovitis, Baastrup syndrome, spondylolysis and spondylolisthesis, facet degeneration).

Key words
Oxygen-ozone, Ozone therapy, facet synovitis, Baastrup syndrome, Spondylolysis, Spondylolisthesis, Facet degeneration

INTRODUCTION

Oxygen-ozone therapy was first used to treat herniated discs in 1985 (1,2-4,5,6,7-21,22,23). Since then, many literature studies have reported positive outcomes ranging from 75% to almost 90% in patient cohorts treated for low back pain with or without sciatica due to nerve root compression caused by a herniated intervertebral disc (1,2,7-21,26). All the patients included in our study had a congruous correlation between herniated disc and symptomatology. No patients with myofascial syndromes have been included.

Low back pain and sciatica are highly debilitating conditions affecting all socioeconomic groups at an increasingly early age. Onset may be acute following injury or an unusual movement, or slowly progressive with gradually worsening pain. They are caused by different often concomitant spinal disorders: disc or facet joint disease, spondylolysis (with or without listhesis), vertebral body and interapophyseal arthrosis, spinal stenosis, radicular and synovial cysts, myofascial syndrome and, more rarely, infections and primary or metastatic cancer. (27).
Treatment of low back pain and/or sciatica requires an accurate diagnosis based on thorough history-taking and physical examination followed by appropriate imaging tests, namely computed tomography (CT) and/or magnetic resonance (MR) scans in addition to standard X-rays of the spine.

The present study reports on the outcome of oxygen-ozone treatment in 416 selected patients with low back pain and/or sciatica due to causes other than disc herniation or protrusion. We focused on degenerative disease of the posterior vertebral compartment as a possible source of pain.

1) Facet Synovitis
Facet synovitis is an inflammatory disease of the synovial membrane lining the spinal interapophyseal joints, usually caused by injury or recurrent micro traumas over time. The disease may also arise in young adults following excessive stress on the spine, typically induced by extreme sports.

In most cases, onset consists of acute lumbar pain with monolateral symptoms if only one joint is affected or bilateral low back pain in a band-like distribution if both facet joints are involved (28). Our cohort included only patients with post-traumatic conditions, excluding infectious synovitis and possible SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, osteitis) (29,30). Facet synovitis diagnosis is often challenging and spine MR scans with contrast administration are helpful to confirm the diagnosis (28,31,32).

2) Baastrup Syndrome
Baastrup syndrome or “kissing spines” was first described by the Danish radiologist Christian Baastrup in 1933. It is characterized by degenerative changes to the spinous processes of adjoining lumbar vertebrae that form new joints between them, often causing low back pain refractory to conservative anti-inflammatory and analgesic treatment. Women are mostly affected with an F:M ratio of 4:1 and the syndrome is usually diagnosed in the third decade of life.

Diagnosis is radiological: spinal X-ray will depict extreme hyper lordosis of the lumbar spine with degenerative changes and contact between adjacent spinous processes.

The disease has a progressive courses and worsening low back pain is an indication for MR study of the lumber spine. Scans should include fat saturation (Fat/Sat) sequences and possibly IV gadolinium administration to disclose any signs of acute interspinous inflammation (31,32).

3) Spondylolysis and Spondylolisthesis
Spondylolysis is a bony defect of the neural arch. If the defect results in a forward shift of one vertebral body on another, this is called spondylolisthesis (a term coined by Kilian in 1854). The severity of spondylolisthesis is determined by the Meyerding classification in four grades depending on the degree of vertebral body slippage over the vertebra beneath it (Grade I 0-33%, Grade II 34-66%, Grade III 67-99%, Grade IV 100%).

Grade I spondylolysis is often an occasional finding and most patients are asymptomatic. However a small percentage present low back pain with or without sciatica. These cases do not require surgery and treatment mainly involves physiotherapy and exercise. However, symptoms refractory to conservative therapy may warrant spinal stabilization surgery.

4) Facet Degeneration
Between 25 and 45% of cases presenting chronic low back pain are due to facet joint syndrome that may be flanked by other conditions, thereby exacerbating the
patient’s pain and disability.
Facet joint syndrome is commonly encountered in elderly patients. It has multiple causes, the most frequent being articular degenerative changes. The condition leads to a reduction or loss of joint cartilage, erosion of the adjacent bone margin, abnormal bone growth of the facet joints and articular processes, and lastly joint instability that may result in degenerative spinal subluxation (pseudospondylolisthesis). Back pain is caused by irritation to the sensory nerve endings in the facet joints and surrounding tissues innervated by the medial ramus of the posterior branch of the spinal nerve. Candidates for interventional treatment are selected on the basis of history-taking and clinical findings supported by diagnostic imaging. Standard X-rays are accompanied by CT scans to disclose the joint relations, growth and deformation of the articular bones and narrowed joint spaces, an indirect index of cartilage rearrangement. MR scans, namely T1 and T2-weighted Fat/Sat sequences with paramagnetic contrast administration, are used to depict the active inflammatory process involving the facet joint and surrounding tissues (28,31,32).

The different treatments proposed to relieve pain caused by facet joint syndrome include intra-articular drug injections, nerve block with anesthetic and radiofrequency ablation.

MATERIALS AND METHODS

We selected 416 patients with different conditions involving the posterior vertebral compartment resulting in low back pain with or without sciatica: 12 had facet synovitis, 16 had Baastrup syndrome, 62 had spondylolisthesis and 326 had facet degeneration. Diagnosis had been confirmed in all cases by MR scans on a Siemens Magnetom AERA 1.5 T system with SYNGO MR D13 software using standard sequences followed by Fat/Sat sequences without and with contrast administration (Table 1). All patients underwent CT-guided targeted injection of an oxygen-ozone gas mixture using the deep paravertebral infiltration technique. Follow-up visit were done at different times in the 4 groups of patients, using the modified Macnab scale to classify results.

Table 1.
MRI scan protocol

<table>
<thead>
<tr>
<th>MRI Type</th>
<th>Protocol Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2 SAG</td>
<td>(Thickness 3 mm, Gap 20%, TR 3500, TE 100, Fov 300 mm, Matrix 384 Pd HF)</td>
</tr>
<tr>
<td>T1 SAG</td>
<td>(Thickness 3 mm, Gap 20%, TR 550, TE 9.7, Fov 300 mm, Matrix 384 Pd HF)</td>
</tr>
<tr>
<td>T2 AX</td>
<td>(Thickness 3 mm, Gap 10%, TR 4280, TE 100, Fov 220 mm, Matrix 384 Pd AP)</td>
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<tr>
<td>T2 SAG pair</td>
<td>(Thickness 3 mm, Gap 20%, TR 3900, TE 100, Fov 300 mm, Matrix 384 Pd HF)</td>
</tr>
<tr>
<td>T1 COR</td>
<td>(Thickness 3 mm, Gap 15%, TR 420, TE 9.1, Fov 300 mm, Matrix 384 Pd RL)</td>
</tr>
<tr>
<td>T1 FS SAG</td>
<td>(Thickness 3 mm, Gap 20%, TR 2500, TE 39, Fov 300 mm, Matrix 384 Pd HF, Fat/Sat)</td>
</tr>
<tr>
<td>T1 FS AX</td>
<td>(Thickness 3 mm, Gap 20%, TR 3500, TE 39, Fov 220 mm, Matrix 384 Pd AP, Fat/Sat)</td>
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INFILTRATION TECHNIQUE

After receiving written informed consent from the patients, the injection level was established on the basis of neuroradiological findings and clinical symptoms. The level was confirmed by preliminary CT scans with patients in a prone position to determine the point of needle entry. The skin was disinfected using a polyvinylpyrrolidone iodine solution after local anesthetic with ethyl chloride spray. CT-guided puncture was then performed using needles with a caliber between 22 G and 25 G. CT guidance also served to check the correct position of the needle in the joint in cases of facet synovitis and degeneration, in the interspinous space in patients with Baastrup syndrome and in the root canal and isthmic lysis points to treat spondylolysis.

An aseptic technique was used to fill a 10 ml polyethylene syringe with a gas mixture of oxygen-ozone at a concentration of 25 µg/ml and between 3 ml and 5 ml was injected depending on the condition to treat, using a microporous filter to minimize the risk of contamination. Further CT scans were done after infiltration to confirm the correct distribution of the gas mixture in the treatment site. Patients were then kept under observation for around 30 min and subsequently discharged.

Facet Synovitis

Most of the 12 patients treated with oxygen-ozone therapy for facet synovitis were relatively young (75% were under 40) aged between 17 and 56 years. In all cases, the onset of acute lumbar pain was linked to injury and the side of facet synovitis correlated with the side of the patient's clinical symptoms. No signs of ongoing infection were present. MR scans with Fat/Sat sequences after paramagnetic contrast (gadolinium) administration confirmed the diagnosis (Fig.1).

Figure 1
T1 Fat/Sat axial MR scan after gadolinium administration: bilateral post-traumatic facet synovitis (arrows).
**Baastrup Syndrome**

Sixteen patients with Baastrup syndrome (11F-4M, aged range 51/78 years) were treated. In all cases, MR scans depicted inflammation in the interspinous ligament and perispinal soft tissues (Fig. 2A).

![Figure 2 (A, B) T1 Fat/Sat axial MR scan after gadolinium administration: A) Before treatment contrast uptake is visible in the interspinous ligament and paraspinal soft tissues. B) After treatment there is a marked reduction of inflammatory contrast uptake in the paraspinal soft tissues.](image)

Patients presented pain in the medio-inferior dorsal and lumbosacral spine where degenerative changes were most evident, and all had an associated antalgic contracture of the paraspinal muscles. Four cc of the oxygen-ozone gas mixture were injected into the inflamed interspinous ligaments depicted on the MR scan using 23G needles followed by infiltrations into the paraspinal muscles affected by antalgic contracture.

**Spondylolysis and Spondylolisthesis**

Given the widely acknowledged success of oxygen-ozone therapy for nerve root compression caused by herniated disc, we administered oxygen-ozone to 62 patients (19F-43M, aged range 21/58 years) with Grade I spondylolysthesis (44 with L5 over S1 and 18 with L4 over L5) with bilateral isthmic lysis and associated disc disease (45 bilateral median-paramedian protrusions and 17 contained lateral disc herniations) and low back pain with or without sciatica. Seventeen patients also presented associated disc herniation. Diagnosis was confirmed in all cases by standard X-ray with morphodynamic (flexion-extension) tests and CT scan of the lumbosacral spine. Treatment was administered by CT-guided bilateral periganglionic ozone infiltration and injection of the gas mixture in close proximity to the lysis points in the neural arch (Figs 3,4).
Facet Degeneration
We selected 326 patients with facet joint syndrome (185M-141F, aged between 58 and 91 years, average age 73.2 years) for oxygen-ozone therapy. The clinical diagnosis was based on patient reports of pain during daily activities and following certain passive and active movements designed to mobilize the facet joints. The main symptoms are listed in Table 2.
Table 2.
Main symptoms in facet degeneration
• Deep-seated low back pain, usually prevailing on one side
• Pain in the groin, thigh, buttock and iliac crest
• Pain applying finger pressure over the facet joints
• Worsening of pain induced by extension of the spine (back arching)
• Pain on rotating the trunk towards the affected side
• Worsening of pain after prolonged standing (++) and sitting (+)
• Improvement with bed rest
• Spinal rigidity
• Absence of lower extremity motor-sensory neurological deficits
• Typical features of facet degeneration disclosed by standard X-rays, CT and MR scans.

All patients were treated by CT-guided injection of 2-3cc of the oxygen-ozone gas mixture into or around the facet joint using a 22G needle. One level was treated in 184 patients (56.4%) of whom 71 (38.6%) only on the side of pain. Different levels were treated in the remaining 142 patients.

RESULTS

Facet Synovitis
Eight (66.7%) of the 12 patients treated had an almost complete resolution of pain after just one oxygen-ozone infiltration so no further injections were administered. The remaining four patients (33.3%) underwent a second infiltration ten days after the first treatment.
A multidisciplinary approach was adopted for this set of patients and a physiatrist devised a physiotherapy program for each case based on postural re-education. Five patients (41.6%) also underwent associated Tecar therapy. Physiotherapy treatments were performed after ozone therapy and were useful in maintaining good long-term clinical outcome.

Baasstrup Syndrome
All 16 patients treated reported a clear-cut improvement in pain one week after oxygen-ozone therapy, but all had a partial return of pain six months later. A second infiltration was performed in seven cases (43.75%) again with a marked reduction of pain and a decrease in perispinal contrast uptake at MR follow-up (Fig. 2B, page 5). All patients underwent a physiotherapy and exercise program to prevent relapse (in five cases the physiatrist prescribed cycles of mud balneotherapy every 6-12 months).

Spondylolysis and Spondylolisthesis
All 62 patients treated by oxygen-ozone therapy were followed up at one, three and six months after treatment using a modified MacNab scale. A complete resolution of pain was obtained in 38 patients (61.3%) after the first infiltration and clinical wellbeing persisted at six months follow-up. The remaining 24 patients (38.7%) had only a partial remission of pain and the treatment was repeated after the first follow-up. 8 patients (12.5%) had a partial benefit from the second infiltration at the three-month follow-up after which they underwent a third oxygen-ozone injection.
The 24 patients with partial pain remission at six-month follow-up were referred for neurosurgical assessment and five (7.8 %) underwent spinal stabilization surgery,
while the remaining 19 received only rehabilitation with a physiotherapy and exercise program.

Among the 17 patients (27.4%) with herniated disc associated with spondylolisthesis, follow-up CT scan demonstrated complete dehydration of the herniated disc in eight cases (47%), obviously with no change in the listhes grade (Fig. 5).

![Figure 5 (A, B)](image)

**Figure 5 (A, B)**
T2 sagittal MR scan before and after oxygen-ozone therapy in a patients with Meyerding Grade I spondylolysis and spondylolisthesis:
A) Herniated disc in L5-S1 before treatment.
B) Complete dehydration of the herniated disc at long-term follow-up after treatment.

**Facet Degeneration**
At clinical follow-up ten days after oxygen-ozone infiltration in the 326 treated patients, 243 (74.5%) reported a major reduction of pain. The remaining 83 patients (25.5%) had an unsatisfactory therapeutic outcome. They declined further oxygen-ozone therapy and were referred to a physiatrist.

Of the 243 with an excellent or good initial outcome, 116 underwent clinical follow-up after three months. Of these, 83 (71.5%) reported a persistent good outcome, whereas the remaining 33 (28.5%) complained of symptom recurrence and underwent a second infiltration; 26 of these cases (78.8%) again had an excellent therapeutic outcome with an almost total resolution of pain.
DISCUSSION

The well-known mechanisms of action of oxygen-ozone infiltration are responsible for the excellent therapeutic outcome obtained in our cohort of patients with facet synovitis, Baastrup syndrome or facet degeneration. An oxygen-ozone gas mixture injected into the site of inflammation exerts a strong anti-inflammatory and analgesic effect. This is ascribed to the capacity of ozone to normalize the cytokine and prostanglandin levels, increase superoxide dismutase, minimize reactive oxidant species and improve local periganglionic circulation with a eutrophic effect.

In patients with post-traumatic facet synovitis the effect of oxygen-ozone infiltration is almost immediate and a single injection may be sufficient to resolve the condition. Instead, in patients with Baastrup syndrome the treatment proved effective in resolving pain with a secondary effect on muscle tone, reducing the antalgic contracture of the paraspinal muscles. This group of patients obtained a clinical benefit after just one targeted oxygen-ozone infiltration.

In line with the scientific literature, facet joint syndrome was the commonest cause of non-discogenic back pain in our cohort of patients (78.4%). Facet degeneration is currently treated by infiltration of drugs or using highly effective radiofrequency techniques. We substituted targeted infiltration of steroids and anesthetic with injection of an oxygen-ozone gas mixture (Fig.6) obtaining a positive outcome in over 70% of cases, reserving radiofrequency ablation for patients failing to respond to ozone therapy.

Figure 6

Intraprocedural CT scan in a patient with facet degeneration: control of the correct needle position in the facet joint interline and regular distribution of the gas oxygen-ozone gas mixture in and around the joint.

Oxygen-ozone infiltration yielded pain relief in 38 of our patients (61.3%) with spondylolisthesis and spondylolysis. In the light of this, ozone therapy could be proposed to treat patients with Grade I listhesis, although a good outcome requires a multidisciplinary approach and the support of a physiatrist for postural re-education after oxygen-ozone infiltration to ensure long-term benefit. In addition to physiatry referral, patients failing to respond to ozone therapy should be assessed by a neurosurgeon for possible spinal stabilization surgery.
CONCLUSIONS

In recent years, the application of MR scans with fat saturation sequences and gadolinium administration in routine diagnostic imaging has helped clinicians establish and confirm the diagnosis in patients with degenerative disease of the lumbar spine and low back pain, leading to targeted treatment strategies. In patients with non-radicular low back pain, symptoms often stem from disease or degenerative changes in the posterior elements of the lumbar spine (“the posterior vertebral compartment”). Appropriate patient selection for oxygen-ozone therapy and the choice of the best targeted treatment yield good clinical results in most cases. This was demonstrated by the successful treatment outcomes in between 61% and 74.5% of our cohort. The rapid resolution of pain with no complications, the ease of performing the technique and CT-guided control of infiltration suggest oxygen-ozone administration is a viable alternative to conservative therapies and probably the first choice treatment for disorders of the posterior vertebral compartment. In addition, oxygen-ozone therapy does not preclude subsequent infiltration or surgical treatment.

References