ORIGINAL ARTICLE

Clinical and imaging selection criteria treating lumbar disk herniations by oxygen-ozone therapy, corticosteroid and local anaesthetic.

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ABSTRACT

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Abstract
Radicular lumbar back pain is an important public health problem not already provided with an unequivocal treatment approach. Medical and physical therapies represent the first solution, however when these are not successful, the second therapeutic step is still controversial and mini-invasive treatment may play an important role. In these cases, oxygen-ozone therapy has been proved to be a very safe and effective option that is widely used with different modalities.
This paper, by reviewing oxygen-ozone therapy literature data, aims to propose an effective procedural technique and to clarify patient's selection criteria; furthermore, complications and follow-up management are also considered.

1.Introduction

Low back pain (LBP) is one of the most common and important clinical, social, economic, and public health problems affecting the human population worldwide **(1)**. In 1,6% to 43% of the cases there are sciatic symptoms associated **(1, 2)** which, in 90% of the times, are generated by disk herniation (DH). **(3)**
The mechanism of radicular pain in the lumbar region is not fully understood but is likely due to mechanical and/or inflammatory factors. There is a component of direct compression of the nerve root or dorsal root ganglion, and indirect compression on perineural vessels. Once the disk gets injured, facet capsule, epidural tissue surrounding the nerve root and the nerve root itself get inflamed with production of a cascade of inflammatory mediators, all of which activate afferents, sensitize nociceptors and make the nerve exquisitely sensitive to pressure generating pain with either gentle manipulation or pressure **(3, 4, 5, 6)**. For this, the inflammatory component of radicular pain allows that a bulging or protruding disk generates pain without a necessary root compression.
The natural history of DH tends to be favourable. Spontaneous regression of DH is seen in two thirds of the cases (7), and a spontaneous resolution of pain within the acute phase (from 6 to 12 weeks after pain onset) in 60-80% of patients **(2)**. Nevertheless, the 1-year recurrence rate is significant and approximately 37-54% of patients maintain the pain after long periods of time (at least 12 months) **(1)**.
Ozone (O3) is a strongly oxidant gas with antiseptic, immunomodulating, analgesic and anti-inflammatory properties **(9)**. Oxygen-ozone gas mixture (O2O3) is commonly used in the clinical practice, mostly in Europe and Asia, in the treatment of nociceptive-neuropathic pain, in inflammatory and degenerative processes of the muscle-skeletal system and especially in degenerative disc disease and DH **(8)**. O3 is administered in the form of O2O3 at nontoxic concentrations ranging from 1 to 40 μg of O3 per mL of oxygen, using various percutaneous methods **(1)**.

The biological action of medical ozone is not fully understood but some mechanisms of action were proposed to explain its efficacy in DH treatment:
a) reduction of the inflammatory components: O3 interrupts the self sustained cycle of the inflammatory cascade by altering the breakdown of arachidonic acid to inflammatory prostaglandins;
b) hyper-oxygenation of the interested area: DH impinge on the venous and arterial flow causing phlebostasis and arteriostenosis which lead to hypoxemia of the tissues; by applying O2O3 to the herniated site, oxygen concentration increases;
c) diminishing the size of the herniation: O3 breaks down the glycosaminoglycans chains in the nucleus pulposus and reduces their ability to hold water, thereby shrinking the nucleus and subsequently reducing intradiscal and perirradicular pressure;
d) stimulation of repair process: O3 promotes the fibroblastic activity inducing the collagen deposition **(10)**;
e) placebo effect: In a lesser proportion, there is a simultaneous psychogenic stimulation of the central analgesic system induced by the gas injection, somehow creating a placebo effect **(11)**.

2. Procedural technique

The first therapeutic approach to lumbar DH must be conservative with pharmacological, physical and cognitive-behavioural therapy **(8)**. In case of failure, the choice and indication for the appropriate therapy remain unclear. In fact, before recurring to surgical treatment many interventional techniques should be considered.
Percutaneous techniques minimize the invasive nature of surgery, rendering administration more straightforward and faster while sparing healthy tissue and minimizing surgery's complications **(1)**. Many common minimally invasive treatments **(6)**, rely on the removal of disc material or on the fibrosis of the disc to reduce pressure on the ganglion nerve root. The size of the needles used in these procedures range from 8-17 gauge (G) and, sometimes, is difficult to reach safely into the disc. O2O3 nucleolysis instead is performed through a 20-22 G needle and is often combined with perirradicular administration of steroids and local anaesthesia **(6, 12)**.
There is not a standard protocol and every operator developed his own technique on the basis of experience and resources availability. In our department, patients do not routinely receive any pre or post-operation medications; we do not perform local anaesthesia. Working in sterile condition is essential. Fluoro or CT-guidance are both feasible depending on operator preference. The patient lies in a prone position, a pillow can be placed under the abdomen to increase the lumbosacral angle. The approach with the patient lying laterally on the healthy site is also described **(13, 14)**.
Disc access is gained with a postero-lateral extrapedicular approach on the symptomatic side at the level of the DH. The puncture site is 6-10 cm away from the vertebral midline using a 15 cm needle 19-22 G, depending on the patient build, with an angle of about 40-45°. When the needle enters the disc, a soft resistance is felt.

The needle position in the center of the disc must confirmed by fluoroscopy or CT images, and the ideal needle position is considered to be at the junction between the posterior and the middle third of the disc (Figures 1 - 2).

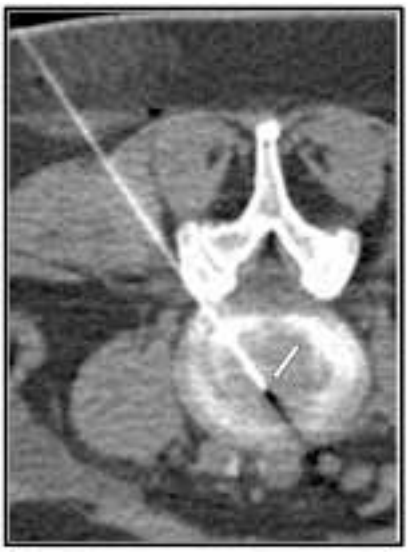

Figure 1. CT-guided positioning of a spinal needle into the nucleus pulposus (arrow).

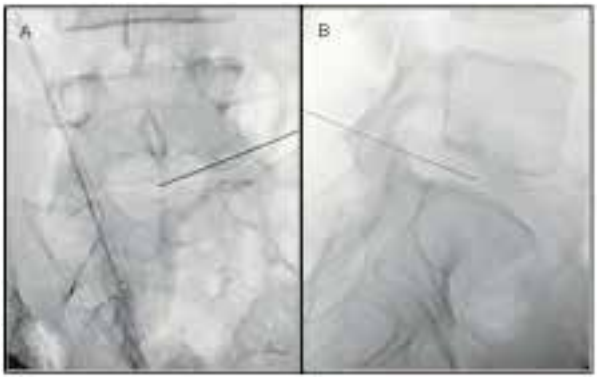

Figure 2. Anteroposterior (A) and lateral (B) views of lumbar intersomatic disc puncture under fluoroscopy guidance.

1-3 mL of gas mixture, 2% ozone (30-40 µg/mL) in 98% oxygen, are injected into the disc. Then the needle tip is withdrawn into the intervertebral foramen (where the operator feels minor resistance) and other 10 mL of O2O3 and 2 mL of corticosteroid/local anaesthetic (1/1) are injected. Under CT-guidance the distribution of the O2O3 in the disc, foramen and epidural spaces can be observed (Figure 3).

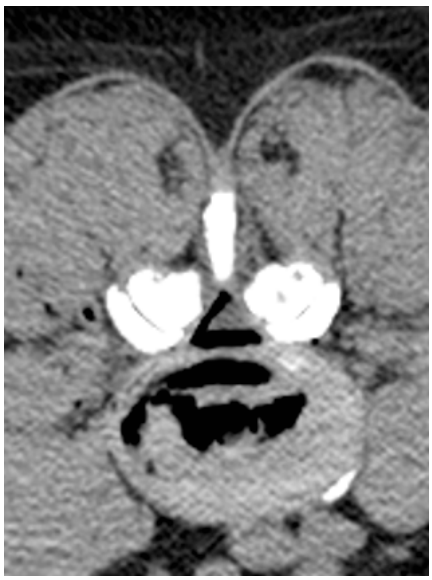

Figure 3. Ozone–oxygen mixture diffusion into the disc and the spinal canal

Finally, the needle is removed and the patient is required to lie in the bed (in a supine position) for 1 hour before being dismissed to home. Heavy activity must be avoided for the following 2 weeks.
If the postero-lateral approach at L5-S1 level is unfeasible due to a high position of the iliac crests, a translaminar approach can be considered. In this case, CT-guidance is advised because it allows the visualization of the dural sac. The puncture site is 2 cm away from the diseased spinal process in the intervertebral space, the needle is advanced stepwise into the hernia through the space between the medial border of the articular process and the lateral border of the dural sac; the ideal position of the needle tip is inside the herniated portion of the disc. Before slowly inject O2O3 (5-6 mL) one must retrieve a little bit the syringe piston to make sure that is not in a blood or cerebrospinal fluid containing space.

3. Indications: clinical and radiological

LBP syndrome represents a complex nosological entity and it is not a simple task to differentiate the source of the pain. So clinical evaluation and selection of patients for O2O3 therapy can be extremely challenging. The main objective in patient evaluation is to identify the source of the pain by performing a complete history and physical examination, supplemented with appropriate imaging studies. It must be ensured that a conservative approach has already been tried with pharmacological and physical therapy for at least 4-6 weeks **(15)**. The best clinical indications for O2O3 is radicular pain more important than low back pain; the patient must refer pain in a well-discriminated and constant cutaneous dermatome with positive Lasègue test; the pain should score 5 or more on the visual analogue scale. There should not be a neurological motor deficit, or cauda equina syndrome **(2)**. Suspected infectious/inflammatory or neoplastic bone

lesions must be excluded **(3, 5, 14)**.
In case of suspicious facet syndrome, a facet infiltration with steroid and local anaesthetic is suggested as diagnostic test before oxygen ozone treatment.
The clinical evaluation must be in accordance with imaging studies, which must demonstrate lumbar herniation/protrusion congruent with the clinical symptoms; significant structural deformity of spine, severe vertebral osteoarthrosis, fractures or calcified hernia should not be present **(1, 15)**. Recently came to light some studies referring that disk decreased ADC index on MRI prior to the treatment show poor improvement of clinical symptoms **(12)**.
It is important to refer that imaging by itself is not a sufficient indication to treatment, remind that disc bulging is present in 52% of the population and disc herniation is present in around 20-28% of asymptomatic subjects.
Absolute contra-indication to the procedure is referred allergy to proposed drugs **(15)**. Relative contra-indications to the procedure are: bleeding disorder, pregnancy, G6PD deficiency, hyperthyroidism, severe anaemia, severe myasthenia, recent myocardial infarction and history of mental disease.
Although the treatment with O2O3 has many advantages, the patient's selection criteria are the key points to a successful clinical result.

4. Complications

Ozone therapy for lumbar DH is a procedure with very low or no adverse effects at the concentrations between 10-40 µg/mL. Most of the studies report no complications, being the overall complications rate estimated under 0.1% **(1, 13)**.
In literature there have been reported: bilateral vitreo-retinal haemorrhages; thunderclap headache after O2O3 therapy related to pneumoencephalus as a consequence of inadvertent intrathecal puncture; paraesthesias on the anterolateral portion of the left leg and foot, suggesting nerve injury; few temporaries episodes of impaired sensitivity; one case of vertebrobasilar stroke and a subcutaneous haematoma at the puncture site **(1)**.
On the infectious field it was described a case of L5-S1 discitis **(8)** and a case of fatal septicaemia. O3 has disinfecting proprieties, it is not likely for the gas mixture to be infected **(15)**, most likely these complications are due to inadequate asepsis and iatrogenic inoculation of the bacteria during the injection **(1)**.

5. Follow-up

One month clinical follow-up should be made in the most objective and quantitative way recurring to tools (Visual Analog scale (VAS), Oswestry Disability Index (ODI) or the Modified MacNab criteria) to access patient pain and function before and after treatment.
In the appropriate clinical/imaging context, intradiscal injection of O2O3 has a reported success rate that reaches 90% at short-term follow-up (6 months) **(13)** and a 75-82% success rate at long- term follow-up (12 months) with no major or minor side effects **(1)**. Around 73% of the patients who went through O2O3 therapy are still better at 5 and 10 years **(4)**. An average reduction in pain intensity in VAS from 7.58 before treatment to 2.64 two years after treatment has been reported with similar results in ODI classification **(5)**.
At 6 months MR follow-up, approximately 75%-96% of patients has a significant herniation volume reduction, with the higher reduction observed in larger disks **(9, 12, 16)**; it has been recently reported that the T2 shine through effect increases already two months after O2O3 nucleolysis which, in the future, may be used to predict shrinkage of lumbar disc herniation **(16, 17)**. Furthermore, the high negative predictive value of DWI-ADC analysis could be useful to select those patients who will require further treatment with ozone **(15)**.

Finally, starting a rehabilitation programme is extremely important **(3, 5, 13)**.

6. Conclusions

O2O3 therapy is a safe and cost-effective approach to patients with sciatica refractive to conservative therapy, having demonstrated good short and long term results, significantly shorter recovery time compared to the alternative treatments **(9)**, and reducing the need for surgery. Moreover, it must be considered also that patients without a good response to O2O3 therapy may still undergo surgical discectomy **(4, 13)**.

Conflict of Interest: The authors declare that they have no conflict of interest.
For this type of study formal consent is not required.

References

1. De Oliveira Magalhaes F, Dotta L, Sasse A, Teixeira MJ, Fonoff ET. Ozone Therapy as a Treatment for Low Back Pain Secondary to Herniated Disc: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Pain Physician. 2012 Mar-Apr;15(2):E115-E129.
2. Apuzzo D, Giotti C, Pasqualetti C, Ferrazza P, Soldati P, Zucco G. An observational retrospective/horizontal study to compare oxygen-ozone therapy and/or global postural re-education in complicated chronic low back pain. Funct Neurol. 2014 Jan-Mar; 29(1):31-39.
3. Crockett MT, Moynagh M, Long N, Kilcoyne A, Dicker P, Synnott K, Eustace SJ. Ozone-augmented percutaneous discectomy: A novel treatment option for refractory discogenic sciatica. Clin Radiol. 2014;69:1280-1286.
4. Buric J, Rigobello L, Hooper D. Five and Ten Year Follow-up on Intradiscal Ozone Injection for Disc Herniation. Int J Spine Surg. 2014;8:17.
5. Li B, Xu X, Du Y, Yang HF, Li Y, Zhang Q, Huang YY, Meng J. CT-Guided Chemonucleolysis Combined with Psoas Compartment Block in Lumbar Disc Herniation: A Randomized Controlled Study. Pain Medicine. 2014;15(9):1470–1476.
6. Murphy K, Muto M, Steppan J, Meaders T, Boxley C. Treatment of contained herniated lumbar discs with ozone and corticosteroids: a pilot clinical study. CAR Journal. 2015;66(4):337-384.
7. Splendiani A, Perri M, Conchiglia A, Fasano F, Di Egidio G, Masciocchi C, Gallucci M. MR Assessment of Lumbar Disk Herniation Treated with Oxygen-Ozone Discolysis: The Role of DWI and Related ADC versus Intervertebral Disk Volumetric Analysis for Detecting Treatment Respons. Neuroradiol J. 2013 Jun;26(3):347-356.
8. Vanni D, Galzio R, Kazakova A, Pantalone A, Sparvieri A, Salini V, Magliani V. Intraforaminal ozone therapy and particular side effects: preliminary results and early warning. Acta Neurochir. 2015 Aug 21 (Epub ahead of print).
9. Lehnert T, Naguib N, Wutzler S, Nour-Eldin A., Bauer RF, Kerl JM, Vogl TJ, Balzer JO. Analysis of Disk Volume before and after CT-guided Intradiscal and Periganglionic Ozone–Oxygen Injection for the Treatment of Lumbar Disk Herniation. J Vasc Interv Radiol. 2012;23:1430–1436.
10. Rahimi-Movaghar V, Eslami V. The Major Efficient Mechanisms of Ozone Therapy are Obtained in Intradiscal Procedures. Pain Physician. 2012;15(6):E1007-E1010.
11. Borrelli E. Mechanism of action of oxygen ozone therapy in the treatment of disc herniation and low back pain. Acta Neurochir Suppl. 2011;108:123-125.
12. Niu XK, Bhetuwal A, Yang HF. Diffusion-Weighted Imaging for Pretreatment Evaluation and Prediction of Treatment Effect in Patients Undergoing CT-Guided

Injection for Lumbar Disc Herniation. Korean J Radiol. 2015 Jul;16(4):874-880.
13. Dall'Olio M, Princiotta C, Cirillo L, Budai C, De Santis F, Bartolini S, Serchi E, Leonardi M. Oxygen-Ozone Therapy for Herniated Lumbar Disc in Patients with Subacute Partial Motor Weakness Due to Nerve Root Compression. Intervent. Neuroradiol. 2014 Oct;20(5):547-554.
14. Lu W, Li YH, He X.Treatment of large lumbar disc herniation with percutaneous ozone injection via the posterior-lateral route and inner margin of the facet joint. World J Radiol. 2010 March 28;2(3):109-112.
15. Zhang Y, Ma Y, Jiang J, Ding T, Wang J. Treatment of the lumbar disc herniation with intradiscal and intraforaminal injection of oxygen-ozone. J Back Musculoskelet Rehabil. 2013;26(3):317–322.
16. Perri M, Grattacaso G, Di Tunno V, Marsecano C, Di Cesare C, Splendiani G and Gallucci M. MRI DWI/ADC signal predicts shrinkage of lumbar disc herniation after O2–O3 discolysis. Neuroradiol J. 2015 Apr;28(2):198–204.
17. Perri M, Grattacaso G, Di Tunno V, Marsecano C, Gennarelli A, Splendiani A, Di Cesare E, Masciocchi C, Gallucci M. T2 shine through phenomena in diffusion weighted MR imaging of lumbar discs after oxygen–ozone discolysis: a randomized, double blind trial with steroid and O2–O3 discolysis versus steroid only. Radiol Med. 2015;120(10):941-950.