



ISCO3 MET/00/04. Paravertebral Ozone Therapy

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ISCO3 MET/00/04 Paravertebral Ozone Therapy

1.1. Brief background

The observation of ozone potent effect on pain relief when applied to the lumbar spine muscles led to its use as an alternative to treat also the conflict between the root and the intervertebral disc. Several mechanisms of action have been proposed to explain the efficacy of ozone therapy, including: analgesic, anti-inflammatory and anti-oxidant effect. These effects seem to be due to its way of acting on diverse targets:

1) Decrease the production of mediators of the inflammation. Induce the inhibition of prostaglandin E2 and phospholipase A2 (like steroids) and other pro-inflammatory cytokines (IL 1, 2, 8, 12, 15 and interferon α).

2) The oxidation (inactivation) of metabolites mediators of pain. Increases the release of immunosuppressive cytokines (IL 10 factor B1) inducing analgesic and anti-inflammatory effect.

3) Increases local microcirculation, reduces venous stasis: analgesic effect.¹

Following Bocci,² paravertebral ozone therapy is administered into a non-toxic concentration ranging from (1 to 40) $\mu\text{g/mL}$ through various percutaneous methods. Jacobs 1982³ reported the results of injections of ozone in various types of spinal diseases demonstrating that intramuscular treatment relieves pain in most patients and lead to an improvement in circulation and absorption of edema with consequent release of mobility. It is worth mentioning that the muscle spasm that is associated to pain tends to push the vertebrae even more thus increasing the protrusion of the disc and the pressure on the root. Muscle spasm relaxation immediately causes a reduction in the volume of the protrusion as seen in image controls. This procedure, virtually free of complications, seeks to address the biochemical and structural changes in the short term and long-term.

1.2. Purpose

The purpose of this SOP is to describe the procedure of the Paravertebral Ozone Therapy, which includes all the elements surrounding the spinal vertebra (disc, foramen, facet, subcutaneous tissues and other elements) and not only the muscles.

1.3. Scope

To specify the use of this infiltration technique, the respective doses, volume of gas and frequency of application.



1.4. Acronyms, abbreviations and definitions

| | |
|------|--------------------------------------------------------------------------------------------------------------------------------------|
| PVOT | Paravertebral Ozone therapy |
| SOP | Standard Operation Procedure |
| TD | Total dose, total amount, in micrograms, of ozone given per session, calculated as volume in mL multiplied by concentration in µg/mL |
| XR | Simple static radiography |
| CT | Computed tomography |
| MRI | Magnetic Resonance Imaging |
| MRLS | MR of lumbosacral spine |
| EMG | Electromyography |
| VAS | Visual Analog Scale |

2. Responsibility

Physician

Assessment of the indication, contraindications
Request the informed consent (ISCO3/QAU/00/21) and the privacy consent
Applications and monitoring
Recording all data on medical records, radiographs and photographs
Prescription of investigations to assess the effectiveness of the treatment
Pain evaluation EVA, ODI, Oswestry Disability Index
Reporting any late complications
Patient follow-up

Anesthesiologist

Venoclises, light sedation

Physiotherapist

Orientation before hospital dismisses for prevention and light exercises.

Nurses

Accommodate the patients
Preparation of the clinical procedure
Supervision of patients and vital signs control
Detects and alert the doctor to anomalies due to possible reactions
Notification of possible complications.



3. Procedure

3.1 Indications of classic intramuscular paravertebral and deep paravertebral injections (facets or perifacet injection).

The classic intramuscular injection was first described by Dr Verga⁴. The deep paravertebral or peri-facet injection was developed by Dr. Scuccimarra.

The indications for this procedure are:

1. Patients that failed with medical treatment and physiotherapy for an initial period of three weeks to three months.
2. As a second option in the Progressive Treatment Scale for Pain in the Spine.⁵ Patients are offered this option as an alternative to relieve pain and stop the continued use of medications, aiming facilitate the activity and thus avoid surgery.
3. Patient with back and cervical pain and lumbar sciatica, and brachialgia with and without disc protrusion (bulging discs), disc subligament herniation and disc extrusion.
4. Fibromialgia
5. Contractures
6. Mio-fascial Syndromes
7. Degenerative disc disease (DDD)
8. Grade I symptomatic spondylolisthesis
9. Spondylopathy
10. Facet joint disease
11. Facet joint osteoarthritis
12. Lumbar spinal stenosis
13. Others less frequent indications are active spondylodiscitis.

Dr. Albert HB, Rollason J, Lambert P *et al.* published the paper: Is the herniated nucleus material in lumbar disc herniation infected with bacteria, and does the infection cause Modic changes in the vertebral space?⁶ In his papers published recently there is no doubt that degenerative changes (Modic 1) and back pain is related most of the times with infection by slow proliferating bacteria and that it could be treated by ozone therapy.

The physician must have a deep knowledge on the anatomy and of the listed above pathologies.⁷

3.2 Clinical evaluation

1. All patients undergo clinical examination on admission.
2. Undergo differential diagnose
3. A clinical, laboratory and image evaluation is necessary to establish a precise diagnosis and to permit comparisons between the patient's status before, during and after ozone therapy.
4. All patients also undergo imaging studies such as: Simple static radiography (XR), computed tomography (CT) and / or MRI of the lumbosacral spine (RMLS) and electromyography (EMG) for diagnosis.



5. Patients using steroid injections are discontinued in its use before the procedure.
6. All patients must sign an informed consent.

3.3 Contraindications

Absolute contraindication:

Favism: Glucose-6-phosphatedehydrogenase deficiency (favism, acute hemolytic anemia).*

Relative contraindications / special situations:

- ✓ Uncompensated diabetes
- ✓ Pregnancy, especially in the first 3 months
- ✓ Uncompensated toxic hyperthyroidism - Basedow Graves status
- ✓ Thrombocytopenia less than 50.000 and serious coagulation disorders
- ✓ Severe Cardiovascular instability
- ✓ Acute alcohol intoxication
- ✓ Acute infarction of myocardium
- ✓ Massive and acute hemorrhage
- ✓ During convulsive states
- ✓ Hemochromatosis
- ✓ Patients receiving treatment with copper or iron.

Contraindication for intramuscular injection:

1. Patients with massive disc herniation occupying more than 50% of the spinal canal,
2. Patients with evident motor or sphincter neurological deficit, patients with painful symptoms over six months duration and
3. Patient with calcified disc herniation. This patient has to be referred for surgery and excluded from group to be treated with ozone.
4. Herniated disc with a free fragment.

* The prevalence of Glucose 6 phosphate dehydrogenase (G6PD) deficiency varies among ethnic groups with overall lower frequency in the Americas (3.4%), Europe (3.9%), and the Pacific (2.9%) as compared to sub-Saharan Africa (7.5%), the Middle East (6.0%), and Asia (4.7%).⁸ Test of G6PD is recommended prior to O₃ therapy in order to avoid complications.

3.4 Recommended doses intervals, anatomical point of reference

Paravertebral classic injection

The method used for application is done on ambulatory basis with the patient in prono with or without (optional) local anesthesia: (0.5-1.0) mL procaine or lidocaine 2% per point.

For cervical and dorsal spine pain. Classical paravertebral infiltration is performed by locating the upper part of the spinous process and injecting the cervical and dorsal column with 5 mL of ozone at (10-20) µg/mL, 1.5 cm laterally from the spine/column, with a (0.8 x 40) mm needle. Treat satellite points of pain, especially in cervical pathology, where there are very common in the form of mio-fascial syndromes. In these cases, inject ozone in the points of pain in small amount (2-3) mL at (10-15) µg/mL.

The infiltration for lumbar spine is made 2.0 cm from the spinous process, and 10 mL at (10-15) µg/mL concentration. The distribution of the needles is always bilateral, lateral or 2 cm above and



2 cm below the hernia. A depth from 2 to 4 cm should be considered when taking into account the patient's constitution and/or the area to be treated (smaller in thin patients and in the dorsal region, and greater in obese patients and in the lumbar region). The recommended needle sizes for this procedure are 27G (0.4 x 40) mm to 30 G (0.3 mm) x 1½" (40 mm). In some cases and with expert hands, longer needles may be used. Inject slowly and aspirating all the time to avoid a possible embolus.

Frequency of treatment. Two times a week up to 15 procedures. These can be shortened once the symptoms have disappeared.

Paravertebral deep injection (Peri-facet injection). The method used for application is done on ambulatory basis with the patient in prono with or without (optional) local anaesthesia: (0.5-1.0) mL procaine or lidocaine 2% per point.

Cervical / dorsal hernias: For this procedure use the same 27 G 0.4 x 40 mm needle. Concentration (10-20) µg/mL, volume (3-5) mL, Distance: 1.5 cm from the spinous process.

Lumbar hernias: For this injection it is necessary to use a longer needle, 0.4 mm or 0.5 mm x 90 mm spinal needle to inject over the *laminae*, close to the foramen, or around the *facet* joint. Concentration (10-20) µg/mL, and a volume of (7-10) mL Distance: 2.0 cm from the spinous process.

It is advisable to accompany the infiltrations with a systemic administration of the ozone, because, these injections do not reach the appropriate doses or frequency to achieve the pre-conditioning effect at the cellular level, with the synthesis of the anti-oxidant enzymes and the generation of gifted erythrocytes, with the improvement of the oxygenation of the tissues. This effect is only achieved with 15-20 sessions of ozone at systemic level (systemic route) at appropriated doses.⁹

These procedures are in line with the Madrid Declaration (ISCO3/QAU/01/03).¹⁰

3.5 Alternatives

Guidelines and Assessments

After the procedure, the patients rest for 15 min and are oriented to physiotherapy and to progressively reduce the use of analgesics and anti-inflammatory drugs. During the infiltration processes the patient is instructed not to exert heavy tasks, but he can continue with his daily life. Once finished the protocol the patients is instructed to return to their activities and to restart the physiotherapy prevention program with stretching and strengthening exercises.

3.6 Frequent side effects

Pain, risk of local hematoma, risk of infection if unappropriated asepsis is done.

In case of other side effects follow the instructions of ISCO3/CLI/00/01 "First Aids in Ozone Therapy - Inhalator exposition and accidental over dose" and report the side effect using ISCO3/REC/00/03 "The ISCO3 Safety Information and Adverse Event Reporting Program Form".



3.7 Warning

Avoid

Injection should not be made under pressure, in order to avoid unnecessary risks. **Under any sign of bleeding, mainly at cervical region and other places, the injection should NOT be done.**

3.8 Patients Follow-up

Patients may be followed and re-evaluated from time to time, from the clinical / subjective point of view and/or with laboratory and/or image examinations.

The item pain is assessed using the Visual Analog Scale (VAS 1) before and immediately after (VAS 2) the procedure, and at 1, 3, 6, 12 and 24 months. The difference between VAS1 - VAS2 is considered an index of analgesic effect. This difference is calculated as a percentage to allow direct visualization of the results. The statistical analysis frequently used is the Excel Statistical System.

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4.1 SOP References

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- ISCO3/DEV/00/01 Guidelines and Recommendations for Medical Professionals Planning to Acquire a Medical Ozone Generator.
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5. Documentation and Attachments

5.1 List of recommended medical disposables

Asepsis kit and surgical drapes. Spinal Needles 22G 9 cm for lumbar and sacral spine and 24G 9 cm for cervical and thoracic spine.

6. Change History

| SOP no. | Effective Date | Significant Changes | Previous SOP no. |
|-----------------|----------------|---------------------|------------------|
| ISCO3/MET/00/04 | 30/05/2016 | Draft. | First version |
| | 26/11/2016 | Draft 2 | |
| | 30/01/2017 | Version 1 | |

7. Document Records

| | Name | Title | Signature | Date |
|------------------------------|--------------------------------------------------------------------------------------------------------|--------------|-----------|------------|
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