International Scientific Committee of Ozone Therapy ISCO3

ISCO3 MVE/00/05. Paravertebral Ozone Therapy in Small Animals

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ISCO3 MVE/00/05. Paravertebral Ozone Therapy in Small Animals

Index

ISCO3 MET/00/05 Paravertebral Ozone Therapy in Small Animals.......................................................... 3
  1.1. Brief background ........................................................................................................................... 3
  1.2. Purpose .......................................................................................................................................... 3
  1.3. Scope ............................................................................................................................................ 3
  1.4. Acronyms, abbreviations and definitions ....................................................................................... 3

  2. Responsibility of the veterinarian towards the animals and towards the owner .................................. 4

  3. Procedure ......................................................................................................................................... 4
     3.1 Indications .................................................................................................................................... 4
          3.1.1 High cervical disc disease C1-C5 ...................................................................................... 5
          3.1.2 C6-T2 low cervical disc disease ....................................................................................... 5
          3.1.3 T3-L3 thoracolumbar disc disease ..................................................................................... 5
          3.1.4 L4-S2 lumbosacral disc disease ......................................................................................... 5

  3.2 Contraindications ........................................................................................................................... 6

  3.3 Mechanism of action ....................................................................................................................... 6
     3.3.1 Why does ozone work in herniated discs? ............................................................................. 6

  3.4 Application form ............................................................................................................................... 7

  3.5 Dosage ........................................................................................................................................... 7

  3.6 Materials ........................................................................................................................................ 7

  3.7 Method .......................................................................................................................................... 7
     3.7.1 Cervical spine .......................................................................................................................... 7
     3.7.2 Thoracolumbar spine .............................................................................................................. 8
     3.7.3 Lumbosacral spine .................................................................................................................. 8

  4. Side effects and precautions ............................................................................................................ 8
     4.1 Sedation protocol for aggressive animals .................................................................................. 9
          4.1.1 Dogs ....................................................................................................................................... 9
          4.1.2 Cats ....................................................................................................................................... 9

  5. Warning, Contingencies, Corrective Actions .................................................................................... 9

  6. References ........................................................................................................................................ 9
     6.1 SOP References ............................................................................................................................ 9
     6.2 References .................................................................................................................................... 10

  7. Change History ................................................................................................................................. 11

  8. Document Records .......................................................................................................................... 11
ISCO3 MET/00/05 Paravertebral Ozone Therapy in Small Animals

1.1. Brief background

For the most frequent pathologies in the spine, paravertebral intramuscular infiltration is, among all types of therapeutic applications with medical ozone, the first in chronological order of appearance. C. Verga, in 1989, was the first to describe the applications of intramuscular ozone, at the paravertebral level and at trigger points, in patients with chronic low back pain. Later, in the 90s, its use is extended to treat acute and chronic polyarthritis (hip, knee, sacroiliac joint, interphalangeal), tendinitis, epicondylitis, carpal tunnel syndrome and myofascial pain.

In veterinary medicine, herniated discs are one of the most diagnosed neurological pathologies. Clinical signs can range from episodes of pain (cervical, thoracolumbar and / or lumbo-sacrum) to paralysis of the extremities, which can affect dogs of any breed, morphology, age and, although less frequently, also cats.

Paravertebral infiltration in animals is carried out, after hair removal and disinfection of the skin, by locating the upper part of the spinous process, 0.5-3 cm (depending on the size of the animal) lateral to it. Infiltrations will always be bilateral on both sides of the spine.

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; in small animals.

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

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>ATV</td>
<td>Veterinary Technical Assistant</td>
</tr>
<tr>
<td>b.w.</td>
<td>body weight</td>
</tr>
<tr>
<td>CT</td>
<td>Computer Tomography Scan</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>FTC-β</td>
<td>Transforming Growth Factor beta</td>
</tr>
<tr>
<td>IFN-α</td>
<td>Interferon alpha</td>
</tr>
<tr>
<td>IL</td>
<td>Interleukin</td>
</tr>
<tr>
<td>MAH</td>
<td>Mayor auto emo therapy</td>
</tr>
<tr>
<td>MiAH</td>
<td>Minor auto emo therapy</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>OS</td>
<td>Oxidative Stress</td>
</tr>
<tr>
<td>RIO3</td>
<td>Rectal insufflation of ozone</td>
</tr>
<tr>
<td>SOP</td>
<td>Standard operating procedure</td>
</tr>
</tbody>
</table>
2. Responsibility of the veterinarian towards the animals and towards the owner

It is essential that the guardian/owner of the animal is fully informed in advance by the veterinarian about the method itself, about all the steps of the procedure, about the desired effects and also about possible unwanted side effects.

A session of paravertebral intramuscular infiltration of ozone should be performed by a medical veterinarian properly trained in ozone therapy. A trained and trusted ATV can assist in performing the procedure:
- Requesting the signature of the Informed Consent to the guardian of the animal
- Accommodating the animal in the consultation room
- Controlling vital signs (temperature, tension, etc.)
- Depilating and disinfecting the skin area to be treated
- Detecting and alerting the veterinarian to anomalies and / or possible adverse reactions.
- Follow-up of the patient, contacting the animal’s tutor, one day after the session, to check that there has been no late complication.

It is the responsibility of the clinical veterinarian to see that all steps of the procedure are performed correctly to avoid errors and prevent accidents.

3. Procedure

3.1 Indications

These procedures are in line with the Madrid Declaration (Table 1) (ISCO3/QAU/01/03).9

Table 1. General guide line of the use of ozone in the treatment of hernial disc in small animals.10-15

<table>
<thead>
<tr>
<th>PATHOLOGY</th>
<th>Routes of application</th>
</tr>
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<tbody>
<tr>
<td>Herniated disc, discoponyltis</td>
<td>MAH: Min C- max C (µg/mL) Vol. Blood/O₂/O₃ Sessions</td>
</tr>
<tr>
<td></td>
<td>RIO₃: Min C- max C (µg/mL) Vol. O₂/O₃ Sessions</td>
</tr>
<tr>
<td></td>
<td>Paravertebral: Min C- max C (µg/mL) Vol. O₂/O₃ Sessions</td>
</tr>
<tr>
<td></td>
<td>Trigger point: Min C- max C (µg/mL) Vol. O₂/O₃ Sessions</td>
</tr>
<tr>
<td></td>
<td>Subcutaneous: Min C- max C (µg/mL) Vol. O₂/O₃ Sessions</td>
</tr>
<tr>
<td></td>
<td>Intradiscal Min C- max C (µg/mL) Vol. O₂/O₃</td>
</tr>
<tr>
<td>Herniated disc, discoponyltis</td>
<td>15-35 1-1.5 mL/kg 6-15</td>
</tr>
<tr>
<td></td>
<td>10-35 3 mL/kg 0-12</td>
</tr>
<tr>
<td></td>
<td>10-20 0.5-10 mL 8-10</td>
</tr>
<tr>
<td></td>
<td>5-20 0.5-5 mL 8-10</td>
</tr>
<tr>
<td></td>
<td>10-20 3-10 mL 8-10</td>
</tr>
<tr>
<td></td>
<td>30 1.5-2 mL/ disk</td>
</tr>
</tbody>
</table>

Main indications in intervertebral disc disease:
✓ High cervical disc disease C1-C5
✓ C6-T2 low cervical disc disease
✓ T3-L3 thoracolumbar disc disease
✓ L4-S2 lumbosacral disc disease

Paravertebral Ozone Therapy in Small Animals © ISCO3. 2023
3.1.1 High cervical disc disease C1-C5

Upper cervical disc disease is a common disorder in small dogs, especially those with chondrodystrophic characteristics, although the disease can occur in any breed. The mean age of onset of clinical signs is 6 years. The predominant clinical sign is severe neck pain that may be acute or chronic. Other clinical signs are: spontaneous howling, wearing the head lowered, lameness or paresis of the thoracic limb, hemiparesis, tetraparesis, the "nerve root sign" is another common finding.

Diagnosis is based on the clinical signs described and the characteristics of the simple radiological study. Decreased intervertebral space or dorsal displacement of mineralized disc material suggest extrusion of the disc. Definitive diagnosis requires advanced imaging tests.

3.1.2 C6-T2 low cervical disc disease

Cervical lesions (C6-T2) are the least common, except in large breed dogs as part of cervical spondylomyelopathy or Wobbler syndrome and also in Pekingese. The early onset of clinical signs is very common in giant breed dogs and from middle age in other breeds. These clinical signs range from mild ataxia (more severe in the pelvic limbs), to severe paresis and limbia, pain to cervical manipulation and lower head. Plain radiographs may not be definitive to specify the lesion, and advanced imaging techniques (CT, myelo-CT and MRI) are necessary to confirm a diagnosis.

3.1.3 T3-L3 thoracolumbar disc disease

Thoracolumbar disc diseases are a common disorder in dogs that mainly affects chondrodystrophic breeds, between 3 and 6 years of age and more than 85% between T11/12 and L2/3 inclusive. In large dogs it affects L1/2 more frequently. The animal may show kyphosis and be reluctant to run and jump. Neurological impairments range from mild ataxia and paraparesis to paraplegia and absence of nociception caudal to injury.

Plain radiographs can indicate if there is a disc disease, but they are only (60-70)% reliable in identifying the exact location. CT and MRI are essential if decompressive surgery is planned.

3.1.4 L4-S2 lumbosacral disc disease

There are several abnormalities that can combine to develop lumbosacral disease. These include:

- Stenosis of the vertebral canal
- Hansen II type disc herniation in the L7/S1 intervertebral space
- Subluxation, osteophytosis, or thickening of articular processes
- Epidural fibrosis
- Proliferation of soft tissues, especially in ligament structures
- Instability and misalignment between L7 and S1

Large breed dogs (especially the German Shepherd) and dogs that develop some activity, for which they are subjected to hard training, are more prone to this disorder. Signs of lumbosacral disease have also been documented in small breed dogs.
3.2 Contraindications

- Uncontrolled hemolytic anemia
- Uncompensated diabetes
- Pregnant females, especially in the first third
- Thrombocytopenia less than 50,000 platelets/μL, bleeding and severe coagulation disorders
- Severe cardiovascular instability
- During seizure states
- Animals treated with copper or iron

Therefore, it is very important before starting a cycle of ozone therapy sessions, regardless of the route that is going to be used for its administration and the tests already carried out on the animal related to its spinal pathology, to carry out an evaluation of the health status of the animal that includes a thorough physical examination, measurement of blood pressure, blood and urine tests, ECG and chest x-ray. Sometimes, it is necessary to complement the previous study with other tests such as: abdominal ultrasound, echocardiography, etc.; and thus, be able to better assess, subjectively, the level of oxidative stress (OS) presented by the patient. The higher the OS, the lower the dose of O3-O2 mixture that we are going to administer.

3.3 Mechanism of action

The use of ozone therapy in the treatment of pain generated by herniated disc has been pointed out by more than 30 years of research on the subject. The nucleus pulposus of the herniated disc contains very high values of phospholipase A2 that can initiate the inflammatory cascade and other inflammatory mediators such as prostaglandins, leukotrienes, bradykinin and histamine. When an annular fissure occurs in the disc, which is the first phase of disc degeneration, these substances are released by the nucleus and can cause radiculitis, even if there is no root compression.

3.3.1 Why does ozone work in herniated discs?

Ozone therapy acts by eliminating the inflammation factor because it causes, on the one hand, the oxidation and subsequent elimination of the substances that mediate pain and in particular mediators that, in this particular case, are responsible for amplifying the painful sensation (IL 1, 2, 8, 12, 15, IFN-α). On the other hand, it increases the release of anti-inflammatory cytokines (IL 10 and FTC-β).

It has direct effects on mucopolysaccharides and proteoglycans of the nucleus pulposus, which is called ozonolysis, producing chemical discolysis with water loss and dehydration. Subsequently, there is a degeneration of the matrix, which is replaced by collagen fibers, in approximately 5 weeks, thus reducing the volume of the disc. As ozone is also released along the injection path, it improves oxygenation and corrects local acidosis; inducing an analgesic effect, because the nerve root is very sensitive to hypoxia.
In summary, there is a double mechanism of action of ozone in spinal disc injuries: on the one hand, the dehydration of the disc material that would decrease the mechanical compressive factors on the nerve root and on the other, the interruption of the inflammatory process with analgesic effect of immediate installation.

3.4 Application form

To assess the appropriate protocol in each case, several points will be taken into account:
- Area of the spine to be treated
- Age and OS of the patient
- Character of the animal (aggressive, nervous)
- Availability of the owner

3.5 Dosage

The ozone dose is obtained by multiplying the ozone concentration expressed in μg by its total volume in NmL, with units expressed in μg/NmL. In weakened animals we will use the lowest ozone concentration: 10μg / NmL.

3.6 Materials

Needles are used of various sizes and lengths (0.60 x 25 mm; 0.50 x 16 mm; 0.40 x 12 mm; 0.40 x 25 mm and 0.40 x 40 mm) and Syringes of 3 bodies of 5, 10 and 20 mL. Medical oxygen. Ozone generator well calibrated; shaver; antiseptic solutions; nitrile gloves.

3.7 Method

We prepare the room where the session will be held so that the animal feels as calm and relaxed as possible. We depilate and disinfect the skin area of the column that we are going to treat. We draw with surgical marker the areas to infiltrate. The appropriate volumes are between 2 mL to 10 mL per infiltration point, at a concentration of between 10 μg/mL and 20 μg/mL increasing progressively as the treatment progresses and without forgetting to perform the aspiration maneuver prior to infiltration.

3.7.1 Cervical spine

Due to its anatomy, paravertebral intramuscular infiltration at the cervical level is more complex than in the rest of the spine because, in addition to the anatomical structures involved, we do not have the spinous processes as anatomical references. With the animal in station or sitting, infiltrations of the O2–O3 mixture can be performed in the dorsal area of the neck, on both sides of the midline where the dorsal muscles of the neck converge, from the nape of the neck to the withers. They can also be applied laterally, 1-2 cm above the imaginary line joining the wing of the atlas (C1), the ventral lamina of the Sixth cervical vertebra (C6) and ending in the last third of the cranial border of the scapula.
3.7.2 Thoracolumbar spine

With the animal in station or seated, both floating ribs are palpated and in the horizontal line that joins them, the midpoint indicates the spinous process of T13. After hair removal and asepsis of the area, it is a useful practice to draw on the skin of the animal and establish neighborly relations. When drawing, a mark is placed 0.5-3 cm from the corresponding spinous process and with a needle, of length that the medical veterinarian considers suitable according to the dimensions of the animal, slowly infiltrate between 0.5 mL and 10 mL, with a concentration of between 10 μg/mL and 20 μg/mL; thus, the mixture of oxygen and ozone will be infiltrated below the thoracolumbar fascia, placing the level of application 2 vertebrae above and 2 vertebrae below the injury (hernia, protrusion or painful point) and on both sides of the spine, with a frequency of 1-2 times a week until clinical improvement and then every 15 days until completing cycles of 9-12 sessions.

3.7.3 Lumbosacral spine

With the patient in season, both iliac crests are palpated, and in the horizontal line that joins them, the midpoint coincides with the spinous process of the L7 vertebra. The therapeutic application in this area of the spine, patient preparation, dose, volume of gas and frequency of application, coincides with that described in the thoracolumbar spine. It is convenient, to enhance clinical improvement, to complement paravertebral infiltrations of medical ozone with systemic ozone therapy sessions: rectal insufflations, MAH or MiAH.

Table 2. Dose range for paravertebral infiltration according to the Declaration of Madrid, veterinary branch.

<table>
<thead>
<tr>
<th>Method</th>
<th>OR3</th>
<th>Dose</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paravertebral</td>
<td>C. (μg/NmL)</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>V. (mL/kg)</td>
<td>0.5-10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dosage (μg /kg)</td>
<td>10-200</td>
<td>7.5-150</td>
</tr>
</tbody>
</table>

Legend: C, concentration; V, volume. * The concentrations and volumes of ozone described in the table for intramuscular use should be infiltrated slowly to minimize pain and avoid a possible vasovagal reaction.

4. Side effects and precautions

➢ It can be very painful for the animal if it is applied very quickly, we find resistance when injecting it or we use high concentrations, which can cause a vasovagal reaction.
➢ There is a risk of embolism when applied directly into the bloodstream. Therefore, aspiration is necessary before the introduction of the gas.
➢ Ozone has bactericidal properties, but as in any injection procedure it is necessary to comply with the necessary asepsis measures to avoid possible iatrogenic infections.
➢ Personnel working with ozone are exposed to risks from acute or chronic inhalation of ozone.

Therefore, it is essential to periodically review security measures such as:

• Well calibrated and good quality equipment
• Well-ventilated environment with exhaust fan
• Absence of leaks in hoses and connections

The side effects, above all, derive from the sometimes-difficult handling of the animal. In these cases, and in order to maintain the welfare of the animal, it is necessary to have sedation.

4.1 Sedation protocol for aggressive animals

4.1.1 Dogs

Medetomidine hydrochloride, 1mg/mL; volume: 0.01 mL/kg b.w. plus Methadone hydrochloride, 10 mg/mL; volume: 0.05 mL/kg of b.w. Both drugs are mixed in the same syringe, to be administered intramuscularly or intravenously.

4.1.2 Cats

Medetomidine hydrochloride, 1mg/mL; volume: 0.05 mL/kg b.w. plus Methadone hydrochloride, 10 mg/mL; volume: 0.05 mL/kg of b.w. Both drugs are mixed in the same syringe, to be administered subcutaneously, intramuscularly or intravenously.

5. Warning, Contingencies, Corrective Actions

Warning: in case of aggressive animals, it becomes necessary to sedate the animal. For other side effects, follow the instructions in ISCO3/CLI/00/01 "First Aid in ozone therapy (Inhalatory 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".

6. References

6.1 SOP References

ISCO3/QAU/00/03. Madrid Declaration on Ozone Therapy 2020-2024 Eng
ISCO3/DEV/00/01 Guidelines and Recommendations for Medical Professionals Planning to Acquire a Medical Ozone Generator.
ISCO3/CLI/00/01. Fist Aids in ozone therapy (Inhalatory exposition and accidental over dose)
ISCO3/MET/00/01 Major Autohemotherapy (MAH)
ISCO3/MET/00/02. Rectal insufflation
ISCO3/REC/00/03 The ISCO3 Safety Information and Adverse Event Reporting Program Form.
ISCO3/CLI/00/07. Ozone in Non-Rheumatic Locomotor System Pathologies
6.2 References


7. Change History

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8. Document Records

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