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APPLICABILITY OF THE OZONIOTHERAPY TECHNIQUE IN THE SMALL ANIMAL CLINIC

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Abstract: Ozone gas (O3), discovered in the 19th century, has already been widely used in human medicine and is beginning to gain ground in veterinary medicine. New complementary techniques are gaining space and attention, among them is the use of ozone therapy, which consists of using ozone gas for medicinal purposes, as it has oxidizing power, with bactericidal, fungicidal and virucidal properties. Ozone is capable of enhancing healing action, thus accelerating the resolution of various wounds, it also acts as an analgesic, antiseptic and anti-inflammatory agent. Ozone is formed by three atoms of oxygen, being an unstable, colorless gas with a characteristic odor. It is found in the stratosphere and for medicinal use it is produced artificially by generators. It is not considered a treatment free of contraindications and adverse effects, but when used in a way that respects its concentrations and routes of application individually for each patient, it is safe and non-toxic. However, it is important to emphasize that ozone therapy must not be the main treatment, but together with the conventional treatment, knowing that only a trained and qualified professional must perform it. This review will present the main therapeutic properties of ozone, its benefits and applicability already described in veterinary medicine.
Keywords: Ozone. Ozone therapy. Adjuvant. Clinic.

INTRODUCTION

The search for therapeutic techniques that provide new treatment perspectives to patients guide the veterinarian to deepen the questions related to complementary medicine. In recent decades, ozone therapy has been studied in a deeper and more scientific way, with the aim of proposing new complementary treatment protocols in the most diverse pathologies (BOCCI, 2011; TRALDI, 2019). This way, veterinary medicine has been further explored and improved, increasing the demand for specialists, means of diagnosis and alternative treatments to promote the life expectancy and well-being of animals. The search for integrative treatments has been highlighted in the area of clinical medicine for small and large animals, since the properties that help in the therapeutic conduct can act as an adjuvant and, due to its affordable price and little invasiveness, it can be an alternative feasible for the tutor.

In 1840, the German chemist Christian Friedrich Schönbein observed that when water was subjected to an electrical discharge, a strange smell was also produced, which he called ozon, from the Greek, ozein (odor), this same smell can be felt in days of storms, due to the electrical discharge that catalyzes oxygen in the form of ozone (PENIDO, et al., 2010; SILVA, et al., 2018).

At the time, experiments using ozone were difficult and limited due to the lack of gas-resistant materials (NOGALES et al., 2008; PENIDO, et al., 2010; SILVA, et al., 2018). Today, Christian Friedrich Schönbein is considered the father of ozone therapy (NOGALES, et al., 2008; PENIDO et al., 2010; SILVA, et al., 2018).

From 1959, after the development of plastic materials, there was an advance in ozone therapy, initiated by Joachim Hänsler, a German physicist (PENIDO et al., 2010). He joined the German physician Hans Wolff, to develop the first ozone generator for medical use, which produces ozone in different doses and concentrations, obtaining greater precision of the desired effect (PENIDO, et al., 2010; MOTA, 2020). Its design continues to be the basis of modern equipment (NOGALES et al., 2008; PENIDO, et al., 2010).

Ozone therapy is considered an alternative in the treatment of several pathologies, mainly in the treatment of dermatopathies, through

its healing, bactericidal, fungicidal and virucidal effect. It is a relatively low-cost and easy-to-apply technique with few side effects (PENIDO, et al., 2010; BORGES, et al., 2019; MAGALHÃES, et al., 2021).

It must be noted that this technique is adjuvant, that is, it must be accompanied by conventional treatments, as its use alone as the main treatment is not indicated. The results are promising when the technique is performed correctly and with reliable equipment, making ozone therapy an effective proposal with positive results (PENIDO et al., 2010; MAGALHÃES, et al., 2021).

The objective of the present work is to carry out a review on the applicability of ozone therapy, taking into account its main indications, route of administration, contraindications and as well as treatment aid associated with conventional treatment within veterinary medicine.

REVIEW OF LITERATURE

DEFINITION AND FORMS OF OZONE PRODUCTION

Ozone is a molecule with highly oxidative power, formed from three oxygen atoms (SILVA, et al., 2018; MOTA, 2020). Another aspect related to this gas is that it is one of the most important in the stratosphere, due to its ability to filter ultraviolet rays (NOGALES et al., 2008).

In the natural environment, its formation occurs from two main mechanisms: Through high electrical discharges in storms, the oxygen molecule (O2) breaks down, one of its atoms disperses, thus making a new connection to an oxygen molecule (PENIDO et al., 2010; SILVA, et al., 2018).

Another formation mechanism is through ultraviolet radiation (UV) emitted by the sun, which has the same role as electrical discharges on the O2 present in the stratosphere (DAGOSTIN, 2019) (Figure 1).

Thus, the ozone layer is created, which absorbs most of the UV radiation emitted by the sun (NOGALES et al., 2008).

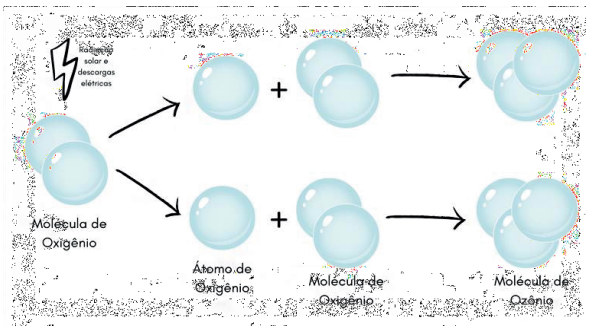

Figure 1: ozone formation

Source: MAGALHÃES, Y.M; et al., (2021)

In addition to the natural forms of O3 production, there are three ways to produce it industrially, through generators, which are: Ultraviolet production system, which produces low concentrations of O3. Electrical discharge system, which produces high concentrations of O3 (BOCCI, 2006; PENIDO et al., 2010) and finally, a cold plasma production system, which is used only for air and water purification (ARAUJO, 2006; NOGALES et al., 2008; PENIDO et al., 2010).

In case of opting for its use, the applicability of ozone formed artificially with the use of a generator (Figure 2), forming the gas with the passage of pure oxygen through an electric discharge of high voltage and frequency (HERNÁNDEZ & GONZÁLEZ, 2001 ; SIMEK & CLUPEK, 2002; MOTA, 2020) and which must be used in a short period of time, as the gas has highly reactive and unstable characteristics, quickly returning to the form of O2 (NOGALES et al., 2008; PENIDO et al, 2010; ABOZ, 2022).

Medical ozone is a mixture of a maximum of 5% ozone and 95% oxygen. The dose used in the field of medicine varies according to the route of administration and the disease; its half-life is approximately 40 minutes at 20°C (HERNÁNDEZ & GONZÁLEZ, 2001;

SANCHEZ, 2008; PENIDO et al., 2010).

It has oxidizing potential and is considered an important disinfectant, its potent bactericidal effect results from the direct attack of microorganisms with the oxidation of the biological material, which can be 3,500 times faster than chlorine (MOTA, 2020).

Figure 2: Ozone generator

Source: personal archive

OZONE THERAPY

Ozone therapy is the application of ozone gas as a therapeutic agent in the treatment of different conditions. After its use, the gas reacts with body tissues producing substances that instigate the entire antioxidant system and enable a great release of oxygen to the cells (WANG, 2018; ESPADA, 2020).

The first clinical applications of ozone therapy were recorded during the First World War (1914-1918) for the treatment of infected wounds, burns and fistulas, making it a tool of great importance for the recovery of wounded soldiers (OLIVEIRA, 2007; VILARINDO, et al., 2013; LIMA, 2020).

In general, ozone therapy is indicated for the treatment of pathologies of inflammatory, infectious and ischemic origin. For example: infected, inflamed, poorly healed wounds and chronic inflammatory processes, such as ulcers, colitis and other intestinal inflammations; circulatory problems; diseases caused by viruses such as hepatitis and herpes; in addition to being used as a complementary therapy in several types of cancer and other diseases (VILARINDO, et al.,2013).

The gas can also serve as an immune activator when administered in specific routes (BOCCI, 2011; VILARINDO, et al., 2013).

Thus, studies demonstrate that the bactericidal effects occur through the interruption of the integrity of phospholipids and lipoproteins of the cytoplasmic membrane and cell wall of bacteria, with gram-negative bacteria being the most sensitive to ozone, through the peroxidation of these membrane components (DAGOSTIN, 2019; KARNOPP, 2021). The virucidal effect of ozone is due to damage the capsid region, since it is made up of phospholipids and glycoproteins (HADDAD, et al., 2009; KARNOPP, 2021). In fungi, ozone has been shown to be effective in controlling the yeast forms of Candida albicans, preventing the formation of germ tubes and biofilms (ZARGARAN et al., 2017; KARNOPP, 2021).

In a study carried out by Borges and Lima (2020), the use of ozone therapy together with conventional treatment for canine leishmaniasis was reported, in which an improvement in clinical findings was seen, mainly in the cutaneous tissue, where there was alopecia, exfoliative dermatitis, dry hair and brittle, peeling skin with a positive Larsson sign and ulcerated lesions in various parts of the body. There was also improvement in the gastrointestinal system, which no longer occurred emesis and there was weight gain. Five sessions of ozone therapy were performed and there was a significant improvement in the patient's clinical signs and laboratory results, knowing that ozone therapy contributes to the immune response and wound healing.

MAIN ROUTES OF APPLICATION AND APPLICABILITY DESCRIBED IN CLINICAL CASES

There are several ways of applying ozone in veterinary medicine, always taking into account the patient's state of health and the characteristics of the pathological process. Application routes are divided into systemic and local (LIMA, 2020; MOTA, 2020; KARNOPP, 2021). The systemic ones are classified as: major autohemotherapy (AHTM), minor autohemotherapy (AHTMe), rectal and intramuscular (IM). Local application routes are classified as: local in the form of bagging or cupping, subcutaneous (SC), intra-auricular, intra-vaginal, intra-articular, urethral, optic or conjunctiva (MOTA, 2020; KARNOPP, 2021).

SYSTEMIC ROUTES OF APPLICATION

Major Auto-Hemotherapy (AHTM)

It is a treatment that involves mixing the patient's blood with ozone and its immediate reinfusion by intravenous infusion.

The volume of blood collected can vary between 5 and 150ml, the volume to be extracted is based on the weight of the patient to be treated. Blood is collected by a syringe or transfusion bag containing anticoagulant (ISCO3, 2020; MOTA, 2020). After blood collection, a volume of ozone is collected with a syringe and added slowly into the blood, it is important to homogenize it and then it must be injected into the animal intravenously (MOTA, 2020). This route aims to act in a systemic way, with the intention of stimulating immune responses, activating antioxidant and circulatory action (MOURA, 2020; BRITO, et al., 2021). It is used in cases of hemoparasitosis, such as anaplasmosis, babesiosis, ehrlichiosis, for example, and in cases of canine parvovirus, leptospirosis, canine viral hepatitis and distemper, due to the bactericidal, antiviral, anti-inflammatory and analgesic capacity of ozone. It is contraindicated in animals that have hemolytic anemia (LIMA, 2020; MOTA, 2020).

Minor Auto-Hemotherapy (AHTMe)

Minor autohemotherapy consists of collecting a small amount of blood from the animal, between 2 and 5 ml of blood are removed intravenously using a disposable syringe, pre-filled with the same amount of ozone mixture. Before reapplying intramuscularly, it is important to shake for 30 seconds and inject slowly (ISCO3, 2020; MOTA, 2020; KARNOPP, 2021).

It is mainly indicated for the treatment of dermatological diseases, such as furunculosis, allergies, dermatitis, eczema and as an adjuvant in the treatment of cancer or in chronic debilitating pathologies (NOGALES et al., 2008; ISCO3, 2020; MOTA, 2020), and in cases of recurrent pyoderma, dermatophytosis, demodicosis, among others (VILARINDO, et al., 2013; LIMA, 2020; MOTA, 2020).

Taking into account that ozone is a complementary therapy in cancer treatments, it was observed by Sousa (2009) that, by including in his protocol the adjuvant use of ozone therapy through infusion of saline solution, together with chemotherapy, the treatment of venereal tumor (TVT) had a significant decrease in the number of chemotherapy sessions with vincristine sulfate.

Rectal Insufflation

Rectal ozone insufflation is a systemic route, where the gas is quickly dissolved in the luminal contents of the intestine, being a completely painless and effective procedure since the rectal mucosa has a great absorption power (ISCO3, 2020; MOTA, 2020).

A rectal probe is introduced through the anal sphincter, using a syringe containing ozone and putting a slight pressure on the

anal orifice to prevent the exit of gas, the gas is insufflated, and one must wait 10 minutes to remove the probe (MOTA, 2020). According to Lima (2020) and Mota (2020), this route of application is recommended in a wide range of diseases, such as chronic nephropathy, diseases liver diseases, enteric infectious diseases, immune-mediated diseases, among others. It can also be used postoperatively and even in combination with antibiotics.

Using it with the aim of anti-inflammatory property, Teixeira et al. (2013), Hayashi and Friolani (2018) described that rectal insufflation using ozone gas and the application of ozone injected into acupuncture points, proved to be as effective as the use of meloxicam for analgesia in surgical recovery in canines undergoing ovary- elective hysterectomy (OVH).

Some descriptions of use in canine infectious diseases, such as parvovirus and distemper, deserve mention. Traldi (2019) described the use of ozone therapy in a complementary way in the treatment, rectally in canine parvovirus and through acupuncture points in the subcutaneous tissue of dogs with distemper. The response was resolving power of half the mean hospital stay in patients with parvovirus and reduction in myoclonal and neurological signs in patients with distemper.

Intramuscular injection

With a syringe, ozone is collected with a volume between 1 and 1.5 ml. The application of ozone must be carried out in the area of the paraspinal muscles, in the femoral biceps.

This technique is widely used for the treatment of skeletal muscle diseases such as arthrosis, arthritis, etc. (LIMA, 2020; MOTA, 2020). Knowing that ozone has great analgesic and anti-inflammatory power (BOCCI, 2006; LIMA, 2020).

LOCAL APPLICATION ROUTES

Bagging and cupping

In the bagging method, it consists of a topical application with the aid of a bag, bag or cap, which will be introduced into the affected limb of the animal. Before being inserted into the affected member, this member must be previously washed with ozonated water and the skin moist to facilitate the action of the ozone. In a plastic bag, bag or cap, which must be sealed with the aid of a sticking plaster or masking tape at the upper end with to prevent gas from escaping (LIMA, 2020; MOTA, 2020). After being sealed, a gas inlet hose is placed inside this bag, plastic bag or cap. The bagging is inflated with gas, using a hose connected to the ozone generator for 10 minutes, with satisfactory results after a few sessions (OLIVEIRA, 2007; LIMA, 2020; MOTA, 2020).

In the cupping method, it is performed with a glass suction cup that must be placed exactly on the injured area, in this method, it is used in cases of local skin infections, ulcers, bedsores, exposed fractures before undergoing surgery and even as a treatment. post-surgery, thus accelerating healing (VILARINDO, et al., 2013; LIMA, 2020; MOTA, 2020). It is generally used when the injury is in areas where it is not possible to use bagging, such as injuries in the abdominal region and cranial region (BOCCI, 2006; MOTA, 2020).

Subcutaneous Injection

In this method, the gas from the generator is collected using a syringe and applied close to the injured area. This application is widely used for the treatment of degenerative arthritic processes for pain relief and can be used in cases of dermatitis caused by mites (LIMA; 2020; MOTA, 2020). This route of application can also be combined with the systemic route, through minor autohemotherapy, in order to modulate the animal's immune response

(LIMA, 2020).

There are reports of the healing progress of dog bite injuries in a feline patient. In this case, 7 applications of ozone therapy were recommended, by subcutaneous technique and ozonated sunflower oil applied directly on the wound. As a result, wound healing was achieved in 25 days (DAGOSTIN, 2019).

Auricular Insufflation

Due to the drying properties of ozone, it is recommended to moisten the ear canal and tympanic membrane before applying ozone. In this procedure, you can use a special syringe or earphone, or perform it with a modified stethoscope with silicone tubes, connected with a "Y". So that ozone can be absorbed into the ear canal and tympanic membrane, it must be applied slowly. The main indications for this procedure are in cases of otitis, dermatitis in the ear canal, sinusitis and circulatory problems of the head and neck (ISCO3, 2020).

Fritzen et al., (2018) describe the use of ozone therapy as an aid in the treatment of canine external otitis, which is carried out by means of infusion of gas directly into the patient's ear and, combined with this, with the application of ozonized oil leading to improvement of the frame. In this specific case, sunflower oil was used.

OZONATED OIL

Ozonated oil can be an important means of using ozone. It is formed through the continuous bubbling of the gas mixture and its appropriate proportionate fractions with vegetable oil, such as sunflower, olive, coconut, sesame or other sources of unsaturated fatty acids at room temperature until it solidifies (KARNOPP, 2021). When the ozonized oil comes into contact with the tissue, ozone is released, favoring the healing process. It could be stored in a glass container to avoid its degradation and/or contamination, protected from light and under refrigeration with a shelf life of up to one year (MARCHESINI & RIBEIRO, 2020; KARNOPP, 2021).

Ozonated oil is a very efficient method for treating injuries, ulcers, bedsores, open wounds and post-operative injuries located on the animals' limbs, requiring the creation of a closed system to limit the area of action of the gas (VILARINDO, et al., 2013; SILVA, et al., 2014; KARNOPP, 2021). Thus, the entire member is coated with an ozone-resistant material to restrict the gas concentration only to the interior of this material (VILARINDO, et al., 2013; KARNOPP, 2021).

The use of ozone gas topically proved to be effective with the use of ozonized oil and water in the treatment of fungal lesions in turtles (MARCHESINI & RIBEIRO, 2020). Silva Júnior (2018) described faster healing of contaminated wounds in a dog with the practice of ozone therapy.

CONTRAINDICATIONS AND SIDE EFFECTS

To avoid risks to the patient and the professional, precise preparation techniques and adequate concentrations are extremely important, as contraindications and side effects must not be underestimated (BRITO, et al., 2021).

Using the proper technique can lead to few side effects. However, when ozone is used in high concentrations and with exposure of the gas for a long time, it may cause adverse effects such as: irritation of the mucous membrane and eyes, disturbances in vision, loss of memory, fever, fatigue, fibrosis, bronchitis, in addition to in variations in the respiratory tract such as dyspnea (FREITAS, 2011; BRITO, et al., 2021).

The administration of ozone gas cannot be used by inhalation, as gas inhalation can be harmful to the pulmonary system, as ozone is capable of promoting oxidative stress, which

can cause progressive toxicity, starting with coughing and tearing, and depending on the concentration it can lead to death (MOTA, 2020; KARNOPP, 2021).

In addition to the toxicity caused to the respiratory system, other systems can be harmed and other effects can be observed, such as irritation, rhinitis, migraines, nausea and vomiting, however, these effects are not frequent, with occurrence of less than 0.0007% (NOGALES et al., 2008; HAYASHI & FRIOLANI, 2018). The eyes are very sensitive to O3, as it has a minimal amount of antioxidants and neutralizers, so they must never come into contact with the gas (BOCCI, 2006).

In case of eventual intoxication, the patient must be kept in dorsal decubitus, inhaling O2 and taking vitamin E, ascorbic acid and N-acetylcysteine (NOGALES et al., 2008; PENIDO, et al., 2010; LIMA, 2020; KARNOPP, 2021).

It is not indicated in patients with endocrine diseases such as hyperthyroidism, since ozone has properties to stimulate the production of thyroid hormones. Ozone therapy must not be applied in elderly patients, with hypoglycemia and for animals with deficiency of the enzyme Glucose-6-Phosphate-Dihydrogenase, a clinical condition known as favism (hereditary anomaly that affects the blood), as there is a risk of hemolysis (HERNÁNDEZ & GONZÁLEZ, 2001; MOTA, 2020; KARNOPP, 2021). For the same reason, it must not be used in cases of severe anemia and active bleeding (PENIDO et al., 2010; BRITO, et al., 2021). According to NOGALES et al., 2008, it is also contraindicated in cases of pregnancy and severe myasthenia.

REGULATION IN BRAZIL AND IN THE WORLD

Currently, ozone therapy is recognized in Bulgaria, Cuba, Czech Republic, France, Germany, Israel, Italy, Mexico, Romania and Russia, however, despite this recognition, its use remains restricted in medicine. veterinarian (ARAUJO, 2006; PENIDO, et al., 2010). Cuba has 39 clinical centers for ozone therapy, while in Russia the practice is used and available in all public hospitals. Nowadays, there are also national ozone therapy societies, the main countries of which are: Australia, Switzerland, Japan, France, United States, and these are affiliated with the International Ozone Association (PENIDO, et al., 2010). In Brazil, the Brazilian Association of Ozone Therapy (ABOZ) was founded in 2006, with the mission of legalizing the practice, computerizing and training professionals, based on experiences carried out in Brazil and abroad (PENIDO et al., 2010; LIMA, 2020).

Recently, the use of ozone therapy has been regulated and recognized by the Federal Council of Veterinary Medicine (CFMV), acting as a practical application in clinical medicine in the treatment of animals by veterinarians (BRITO, et al., 2021).

FINAL CONSIDERATIONS

It is concluded that ozone therapy has attracted the attention of researchers from several countries because it presents itself as a cost-effective alternative with excellent results against a variety of pathologies and different species. Even knowing that ozone is an unstable molecule, it has great power against a wide variety of microorganisms and deserves attention. There are many references on ozone therapy used in medicine, but in veterinary medicine, it is still an expanding field that needs to be explored, so more studies are needed that elucidate it more clearly. However, it is important to point out that ozone gas must be produced with care using reliable equipment and must be used immediately after its synthesis so that it does not produce poor quality ozone, knowing that

this could harm the patient or not have the desired result and only trained and qualified professionals must use it.

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