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Review article

Prophylaxis and therapeutic potential of ozone in buiatrics: Current knowledge

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ABSTRACT

Ozone therapy has been in use since 1896 in the USA. As a highly reactive molecule, ozone may inactivate bacteria, viruses, fungi, yeasts and protozoans, stimulate the oxygen metabolism of tissue, treat diseases, activate the immune system, and exhibit strong analgesic activity. More recently, ozone has been used in veterinary medicine, particularly in buiatrics, but still insufficiently. Medical ozone therapy has shown effectiveness as an alternative to the use of antibiotics, which are restricted to clinical use and have been withdrawn from non-clinical use as in-feed growth promoters in animal production. This review is an overview of current knowledge regarding the preventive and therapeutic effects of ozone in ruminants for the treatment of puerperal diseases and improvement in their fertility. In particular, ozone preparations have been tested in the treatment of reproductive tract lesions, urovagina and pneumomovagina, metritis, endometritis, fetal membrane retention and mastitis, as well as in the functional restoration of endometrium in dairy cows and goats. In addition, the preventive use of the intrauterine application of ozone has been assessed in order to evaluate its effectiveness in improving reproductive efficiency in dairy cows. No adverse effects were observed in cows and goats treated with ozone preparations. Moreover, there is a lot of evidence indicating the advantages of ozone preparation therapy in comparison to the application of antibiotics. However, there are certain limitations on ozone use in veterinary medicine and buiatrics, such as inactivity against intracellular microbes and selective activity against the same bacterial species, as well as the induction of tissue inflammation through inappropriate application of the preparation.

Contents

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1. Introduction

Ozone is a light blue gas of extraordinary odor which can be strongly sensed in the air during electrical discharges into the atmosphere (following thunder and lightning). Christian Friedrich Schönbein was the first to recognize ozone as a chemical substance in 1840, and named it after the Greek word ὄζειν (*ozein*), which means odor (Rubin, 2001). The chemical formula of ozone, O_3, was established by Jacques-Louis Soret (Soret, 1865). He proposed that this molecule, composed of 3 oxygen atoms, is an allotropic modification of oxygen. Ozone is a very strong oxidant, much stronger than O_2, and is unstable in higher concentrations, resulting in its decomposing into oxygen molecules. It is essential for life on Earth due to its ability to absorb wavelengths of harmful UV radiation coming from specters of sunlight (Di Paolo et al., 2004). Nikola Tesla, the brilliant inventor who originated from Croatia, patented the first ozone generator in 1896 in the USA (Tesla, 1896). Four years later, he founded the first firm, the "Tesla Ozone Company", to use ozone for medical purposes (Mandhare et al., 2012). In 1898, Thauerkauf and Luth founded the Institute for Ozone Therapy in Berlin in Germany, where for the first time ozone injections were applied to an animal. In addition, for the first time ozone molecules were synthesized into a solid compound termed haemozon (today known as homozon).

Afterwards, there followed a century of ozone use and improvements in its use for medical purposes. Ozone therapy is classified as an alternative medicine approach. Its therapeutic effect is recognized as a consequence of increased oxygen concentration on or in the body following the application of ozone in various preparation forms and by different routes. Today, ozone is used extensively in industry for sterilization and bleaching, the purification of water and swimming pools, and for the sterilization of operating rooms (Glaze, 1987; Rakness et al., 1993). In addition, its use in medical therapy has been found to be predominantly safe, with extremely rare side effects and negative effects on human health. Recently, the use of ozone has expanded, due to the fact that it is applied for medical purposes, i.e. for the oxygenation of tissue, as well as cosmetic purposes.

There are also numerous diseases which can be successfully treated with bio-oxidative therapy with ozone, such as cardiovascular diseases and circulatory problems (Hernández et al., 1995; Martínez-Sánchez et al., 2012), arthritis (treated with intra-articular therapy, nucleolysis of intravertebral discs, paravertebral infiltration with ozone, periarticular infiltration with ozone) (Iliakis, 1995; Andreula, 2001; Ginanneschi et al., 2006), viral infections (such as hepatitis, Epstein-Barr virus, herpes, etc.), fungal infections, tissue regeneration (wounds and burns), dermatological diseases, and oral cavities and tooth diseases (Loncar et al., 2009; Bhateja, 2012). It is also used in complementary carcinoma therapy (Bocci, 2006; Elvis and Ekta, 2011).

As a highly reactive molecule, ozone exhibits strong bactericidal, fungicidal, antivirus, anti-yeast and anti-protozoa activities. One of the major activities of medical ozone is the specific induction of the synthesis of cell membrane enzymes, such as superoxide dismutase, catalase and glutathione peroxidase, which protect the cell from the damaging effects of O_2 free radicals (Hernández et al., 1995; Mandhare et al., 2012). Sensitivity to ozone is higher in Gram positive bacteria than in Gram negative bacteria. It has been recognized that oxidative processes induced by ozone may damage the capsule of bacteria through the activity of peroxidases and subsequently the cell membrane, and may also block replication of bacterial DNA. The oxidative mechanisms of ozone inhibition of fungal growth and its virucidal activity are performed through the inactivation of viruses following the destruction of lipid molecules in capsids and by blocking their replication. "Naked viruses" can be neutralized by the ability of ozone to produce protein hydroxides and hyperoxides. In addition, ozone may influence the immune system through the stimulation of lymphocytes, monocytes and neutrophils to release cytokines such as interferons α, β, γ, tumor necrosis factor α, interleukins 1, 2, 4, 6, 8 and 10, granulopoietine and transforming growth factor β (Ducusin et al., 2003; Larini and Bocci, 2005; Ohtsuka et al., 2006). These cytokines may re-establish cellular immunity during inflammatory processes (Travagli et al., 2009). Moreover, ozone may stimulate the proliferation of B and T lymphocytes (Korzun et al., 2008).

2. Ozone use in veterinary medicine

There are some products with a special blend of vegetal ozoned oil with a lenitive, emollient, cicatrizing, antibacterial and hygienist action in the form of creams, gasses, syringes, pailletes, foam, boluses and obletes (Travagli et al., 2009). In addition, there are certain products (BIO OZOTECH™) patented according to the regulations of the European Conformity Medical Device (CEMD) and registered by the Italian Health Ministry in accordance with EU Directive 93/42/CEE.

Although the use of ozone in veterinary medicine can be traced back more than 30 years (Altman, 2007), it is still insufficient and related only to certain specific areas, such as the treatment of mastitis, metritis, endometritis, fetal membrane retention, vaginitis, urovagina, enteritis and laminitis, as well as in the local treatment of various lesions and neuromuscular disorders, and in the intravenous application of ozone diluted in saline for flushing equine intestines (Marusi et al., 1999; Alves et al., 2004; Zobel et al., 2012; Đuričić et al., 2014; Zobel et al., 2014a;