

OZONE THERAPY IN DIABETIC FOOT

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Abstract: Ozone therapy has currently been widely used as an integrative alternative in the treatment of various diseases, due to its antioxidant, healing and bactericidal effects that directly influence biochemical factors of cellular metabolism. **Objective:** To demonstrate the effective and therapeutic use of ozone therapy in the treatment of diabetic feet for healing and decontamination. **Methodology:** This is a critical literature review study, with a descriptive and comparative procedure, using the bibliography on Ozone Therapy in diabetic foot as a data source. The study was carried out through research in databases such as PUBMED, LILACS, SCIELO (Scientific Electronic Library Online) and Google Scholar, in addition to the use of books with complementary. As **Results**, 19 works were selected, being an Association, a Society, a Ministry of Health. The others are articles, books and case reports. This way, proven data on the effectiveness of the use of ozone therapy in patients with diabetic foot are presented. **Conclusion:** Ozone therapy is an effective alternative in the treatment of patients with diabetic foot, however, it requires further studies for this type of pathology. **Keywords:** Ozone; Ozone therapy; Diabetic foot; Diabetes Mellitus.

INTRODUCTION

Ozone (O^3) is a gas composed of three oxygen atoms, a natural gaseous molecule and a powerful oxidant that has important properties, anti-inflammatory, analgesic, antimicrobial, virucidal, bactericidal, fungicidal, immunological regulator, healing, among others. Pre-clinical studies, using ozone therapy with recommended doses, carried out several investigations, and show that O^3 does not have a genotoxic effect, that is, it does not affect the integrity of the cell, and did not present an adverse reaction that would put the patient's health at risk (OLIVEIRA 2011).

One of the pathologies treated with O^3 is diabetes mellitus (DM), a disease of metabolic changes, characterized by hyperglycemia and relative or absolute insulin deficiency or failure in its action, with a tendency to develop long-term complications, being the biggest cause. of diabetic feet. This concept covers changes such as infection, ulceration and/or destruction of soft tissues associated with neurological changes and degrees of peripheral arterial disease in the lower limbs (SBD 2017).

Diabetic foot ulcers are one of the complications of diabetes mellitus that occur due to multifactorial causes such as; The macrovascular levels are where ischemic heart disease, cerebrovascular and peripheral vascular disease occur, and the most common microvascular levels occur, such as neuropathy, retinopathy and ischemia, these are factors that contribute to infections and chronicities of these types of ulcers (CRISPIM, RODRIGUES, ALVES 2019).

Ozone is obtained through a gas composed of three oxygen atoms (O_2) characterized as unstable, and with important properties in curing various diseases, improving tissue oxygenation and accelerating wound healing. The benefits in diabetic feet that present proven studies occur through systemic venous or rectal applications, topical with ozonized waters and oils, plastic bags known as (bags) and hydro ozone therapy.

Therefore, the objective of this work is to carry out and describe the scientific evidence of the effective and therapeutic use of ozone in diabetic feet and its administration routes through literature reviews.

MATERIALS AND METHODS

Kind of study: This is a critical review study of the literature, with a descriptive and comparative procedure, using as a data source the bibliography on Ozone Therapy in diabetic foot.

Databases consulted: The study was carried out through research in databases such as PUBMED, LILACS, SCIELO (Scientific Electronic Library Online) and Google Scholar, in addition to the use of books to complement the search in the collection of the sectoral library of the Faculdade Metropolitana de Manaus (FAMETRO).

Bibliographical sources: 16 articles were used, 02 books and 01 Ordinance from the Ministry of Health. The following keywords were used to search the articles: Ozone; Ozone therapy; Diabetic foot; Diabetes Mellitus.

Inclusion criteria: To fulfill this research, literature and articles were selected in Portuguese, English and Spanish, but published between 2005 and 2020, which offered information on the topic of the work, thus excluding all data published more than 15 years ago. and which did not provide data regarding the topic.

Data collect: It was carried out from February to November 2020 through a survey of literary works already published, highlighting their ideology. The works were published in articles, books and ordinances from the Ministry of Health. The Pubmed, Lilacs and Scielo databases were used to search for terms X, Y and Z.

Data analysis: After the source identification stage, it was necessary to analyze the material to be described in this article, resulting in a selection of authorial ideas, as well as observing and highlighting the necessary material.

LITERATURE REVIEW

OZONE

Ozone is a natural gaseous molecule, composed of three oxygen atoms, unstable and one of the most important in the stratosphere, which was discovered in the 19th century by the German chemist Cristian Friedrich Schönbein (1799-1868). This is formed by the addition of a third atom (of O) to the oxygen molecule (O₂), called O₃. The name ozone has a Greek origin "ozein" (smell), due to its strong odor, the most powerful bio-oxidative in its biological function and protection to humans from ultraviolet rays, absorbing and filtering (SEVERO, MÜLLER, CARVALHO).

The gas is colorless, has a pungent, bitter and explosive odor in liquid and gaseous form. It has a half-life of more or less than 40 minutes at a temperature of 20°C and 140 minutes at 0° C. Ozone occurs less than 20 µg/m³ from the earth's surface in concentrations compatible with life. Even though O₃ is dangerous, researchers believe in its therapeutic effects (ELVIS, EKITA 2011).

With this discovery, Dr. Werner Von Siemens (1816 to 1892) created a device for producing ozone through electrical discharges on O₂ atoms, known as a high frequency generator in 1857. In 1914, O₃ was used during the first war worldwide (1914 to 1918), in soldiers with gangrene, abscesses and fractures, successfully. Then, in 1975, therapeutic use began in Brazil (OLIVEIRA, 2011; FERREIRA et al. 2013).

According to Ana Cristina de Carvalho Barreira, she says that in several countries, ozone, mixed with toxic components and added to the action of the sun and oxygen in the air, becomes toxic to the lung mucosa, eyes, nose and skin, therefore Some people wrongly say that it is a toxic gas, but in the right place and dose it has an effective medicinal action.

When an energetic force, such as electricity or ultraviolet light, is imposed on an O₂ molecule, the two oxygen atoms are temporarily split into single oxygen atoms. But because single oxygen atoms are very unstable, in a matter of nano seconds, they come together again and transform back into O₂ molecules. But a small percentage of them will unite into an oxygen trio and thus is known as ozone. Therefore, ozone, referred to as O₃, is a molecule that consists of three oxygen atoms that share the same number of electrons, which make two oxygen atoms stable. This means that, due to its extra oxygen atom, ozone is a relatively unstable molecule. And it is exactly this instability that makes it so powerful in the human body. Much more powerful than O₂. And that's why, when ozone is introduced into the body, something remarkable happens: it stimulates the mitochondria in your cells ten times better than O₂ to more efficiently use the oxygen they get. (MÜLLER 2020).

Ozone is a modulator of the body's oxidant and antioxidant systems. Oxidative molecules, which include oxygen, play a very important role physiologically, such as; free radicals that cause oxidative stress in cells. Therefore, when controlled, there is an important increase in mediators and therapeutic effects of ozone application (CRISPIM 2011), such as interleukins and interferon.

OZONE THERAPY

Every day, ozone therapy has been more studied and evolved in the treatment of highly complex wounds, fungal, bacterial, viral infections, ischemic injuries and other types of infections, being very effective in all cases, especially in disinfection and healing. of extensive wounds (OLIVEIRA, 2011 et al NEVES; ARAÚJO 2019).

Ozone therapy is a low-cost integrative and complementary practice, with proven and

recognized safety, which uses the application of a mixture of oxygen and ozone gases, through different routes of administration, with therapeutic purposes, already used in several countries such as Italy, Germany, Spain, Portugal, Russia, Cuba, China, among others, for decades (WHO, 2018).

The ozone molecule is a biological molecule, present in nature and produced by the body, and medicinal ozone (always a mixture of ozone and oxygen), in its various mechanisms of action, represents a stimulus that contributes to the improvement of various diseases, as it can help to naturally recover the functional capacity of the human and animal organism. Some health sectors regularly adopt this practice in their care protocols, such as dentistry, neurology and oncology, among others (MS, 2018).

Ozone has the ability to oxidize organic compounds and has toxic effects on the respiratory tract if in high concentration in the environment. Once introduced into the body, ozone has the ability to improve body oxygenation, modulating the inflammatory process, elevating the antioxidant and immune system (MORAIS, TIM, ASSIS, 2020).

Ozone therapy is an alternative treatment that has been available in the SUS since March 2018, for the treatment of injuries and pathologies, as it is an excellent anti-inflammatory, antiseptic, activates oxygenation and peripheral circulation according to (NEVES; ARAÚJO, 2019)

The effects of using therapeutic ozone have been linked since the 20th century, and have useful properties in systemic, intravenous and topical treatments with ozonized water and oil, when used on infected wounds or lesions, dermatoses, eczema and pressure ulcers or no, among other pathologies. The use has no genotoxic or toxicological effect in general, and to date there has never been an adverse or reported reaction, therefore there is no risk

to patient safety (NEVES, BARROS 2019) as long as it is used in the right dose and route.

Studies show that the efficiency of red blood cells increases and increases with ozone, improving the supply of oxygen to tissues. The high reactivity of ozone causes it to have rapid biochemical reactions as soon as it comes into contact with blood and Bocci et al. 2011 show that, 200 ml of human blood with 200 ml of oxygen and ozone, in five minutes, the ozone is eliminated and the oxygen saturates the hemoglobin.

And yet, at therapeutic doses, it activates intracellular molecular pathways, for example the pathways responsible for the inflammatory response (via NF- κ B and Nrf2), which consequently reduces the release of pro-inflammatory cytokines (TNF α , IFN γ , IL1 β , IL6, IL8), and also in pro-inflammatory genes (cyclooxygenase-2 [COX-2] and inducible nitric oxide synthase pathways (MORAIS, 2020).

In this context, ozone therapy reestablishes signaling pathways lost in pathological conditions, maintaining cellular balance, mitochondrial function and the regulation of transcription factors and modulation of the immune system MENENDEZ - CEPERO, 2018).

DIABETIC FOOT

Diabetic foot ulcers are one of the complications caused by diabetes mellitus, caused by multifactorial causes, such as the development of peripheral neuropathies; altered foot pressure, peripheral diseases and less resistance to bypassing infections (CRISPIM et al 2019).

The Diabetic Foot, the main cause of amputation of the lower limb (risk 15 to 40 times greater), is more than just a complication of diabetes, its clinical situation is considered complex, affecting the feet and ankles of diabetic individuals, its risk factors main risks,

and peripheral neuropathy, deformities and limitation of joint mobility; thus, it can bring together varied clinical characteristics, such as changes in foot sensitivity, the presence of complex wounds, deformities, gait changes, infections and amputations, among others (BATISTA, 2010).

Epidemiological data demonstrate that diabetic foot is responsible for the main cause of hospitalization for people with diabetes. The World Health Organization cites that public health has a serious problem in relation to diabetes. The forecast for the year 2030 is that more than 550 million people will have diabetes. Of these, at least 25% will have some type of significant impairment to their feet. Currently, it is estimated that, worldwide, two amputations occur per minute at the expense of diabetic foot, with 85% of these being preceded by ulcers (SBD, 2016).

The current trend, due to the more efficient approach and results, has been pointing to the need to include all patients with diabetes in centers integrated by multidisciplinary professionals trained in specialized management of the diabetic foot (SBD, 2019)

Among the wounds that are difficult to heal, diabetic ulcers, pressure ulcers and surgical dehiscence deserve to be highlighted. Management must be individualized and carried out by professionals trained for such a scenario. Different and innovative proposals to support healing have been reported, however, one must be aware of the real clinical relevance and scientific evidence of each method (SBD, 2019).



Figure 1: Diabetic foot
Source: Google (2009)

Foot ulcers and lower limb amputations are very serious and costly complications for the patient and society, and are often associated with high morbidity and mortality and high recurrence rates. Complicated wounds require an interdisciplinary approach, carried out by a trained team familiar with the diabetic foot approach (BATISTA, 2010).

In summary, a true “Prevention and Treatment Program for Diabetic Foot and Complex Wounds” is not restricted to changing dressings, properly cutting nails and suggesting the use of footwear, nor is it covered by isolated therapeutic options and so-called miraculous. It must be an extremely comprehensive and complex program, requiring an effectively trained, integrated team that is literally committed to the health and quality of life of the individual and society (SBD, 2019).

The effectiveness of ozone therapy after unsuccessful conventional treatment is a reality in chronic ischemic and infectious diseases, and in various orthopedic and dental conditions, and there were no adverse effects but reports of well-being (CRISPIM et al 2019).

DIABETES MELLITUS

Diabetes mellitus is a chronic metabolic disease in which the body does not produce insulin or is unable to properly use the insulin it produces. This is a hormone that controls the amount of glucose in the blood. The body needs this hormone to use glucose, which we obtain through food, as a source of energy. A person who has diabetes has a body that does not manufacture insulin and cannot use glucose properly. It is an endocrine disorder, that is, a defect in the secretion and/or action of insulin produced by the pancreas, manifested by the inadequate use of glucose by the tissues, which causes hyperglycemia. The pancreas is made up of two organs, the endocrine and the exocrine, the endocrine being responsible for the production of the hormone insulin, among others, and any change in this organ results in damage to the body (VIANA, RODRIGUEZ, 2010).

If this condition persists for long periods, there may be damage to organs, blood vessels and nerves (SBD, 2019).

ROUTES OF ADMINISTRATION

Ozone can be administered by different routes and administration techniques, depending on the disease in which it is used, in the treatment of diabetic foot ulcers, the main ones are:

- Intravenous (auto hemotherapy and ozonized serum)
- Rectal Insufflation
- Topical (ozonized oil)
- Ozonated water
- Hydro-ozone therapy
- Bags with ozone

AUTO HEMOTHERAPY

50 to 250 ml of venous blood is removed, homogenized with ozone outside the body and transfused again or injected intramuscularly (BRASIL, 2013).



Figure 2: Major ozonized autohemotherapy.

Source: (Google, 2019)

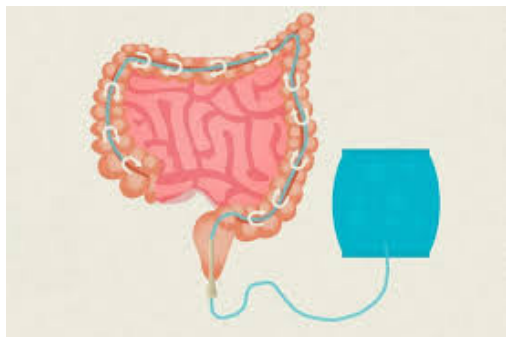


Figure 3: Ozonized minor autohemotherapy.

Source: (Google, 2020)

RECTAL INSUFFLATION

The gas is introduced using a probe and syringe.



Source: (Google, 2020)

TOPICAL

Consists of local application with ozonized oils, promoting an antiseptic reaction, activating local circulation, accelerating cellular oxygen metabolism, stimulating the enzymatic antioxidant defense system and stimulating granulation and epithelialization (BARREIRA,2019)



Figure 4: Ozonized sunflower oil

Source: (Google 2020)

OZONIZED WATER

In this process, an ozone concentration of 20 to 100µg/ml is used in double-distilled water bubbled in small bubbles, on average for 5 to 20 minutes, to reach a final solution concentration of 5 to 25µg/ml (CRISPIM et al 2019).

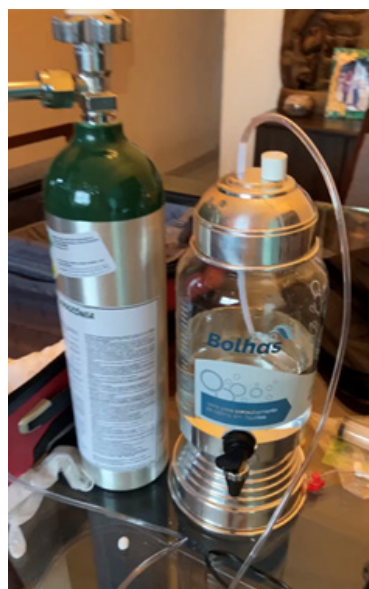


Figure 5: Ozonated water

Source: (The authors 2019)

HYDRO OZONE THERAPY

Consists of removing secretion and organic matter, promoting hydration, improving peripheral circulation, facilitating the removal of fibrin and ischemic tissue (CARDOSO, et al 2019). Performs a gentle peeling, removes pain and foul odor from exposed diabetic foot wounds, relieves local pain, reduces extravascular edema, hygiene, in addition to diffusion oxygen therapy (BARREIRA, 2019).



Figure 6: Hydro-ozone therapy with Ozonomatic® equipment (emulsion with 1% ozonized sunflower oil + ozonized water)

Source: (CARDOSO, et, al 2009).

BAGS WITH OZONE

A transcutaneous immersion is carried out, where gaseous ozone is applied by insufflation after the area is bagged by a plastic bag, also using a low-pressure boot, built for this purpose (Rokitansky boot) or by ozone suction cup (NUNES, 2019).



Figure 7: Bag with ozone

Source: (Google 2020)

CONCLUSION

Ozone therapy is a treatment with proven effectiveness in various chronic diseases, wound healing ranging from small to highly complex, ischemic, allergic and other processes. It is a conventional therapy that favors the healing of diabetic foot ulcers, as it has several antiseptic properties, induced local oxygenation and accelerates tissue repair.

Therefore, treatment using Ozone has been attracting researchers from all over the world, as it has a low cost and benefits with proven results.

In all studies, reports are unanimous and point to this therapy as very promising.

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