Scientific evidence of the effectiveness of ozone therapy use in the face of Brazilian sanitary legislation

As evidências científicas da eficácia do uso da ozonioterapia frente à legislação sanitária brasileira

Evidencia científica de la efectividad del uso de la ozonoterapia frente a la legislación sanitaria brasileña

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How to cite: Ornelas PTSF, Sousa CM, Silva ICR, Fratelli CF. Scientific evidence of the effectiveness of ozone therapy use in the face of Brazilian sanitary legislation. REVISA. 2020; 9(2): 320-6. Doi: https://doi.org/10.36239/revisa.v9.n2.p320a326

REVISA

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Received: 20/12/2019
Accepted: 20/02/2020

RESUMO

Objetivo: Verificar se as evidências científicas existentes, têm alguma concreta relevância e suficiência, para a ozonioterapia ser utilizada como terapia em algumas patologias e observar o andamento da legislação brasileira acerca do tema. **Métodos:** Foi realizado uma revisão literária, em bases de dados, com evidências científicas dos últimos dez anos, que abordam a ozonioterapia e o avanço da legislação brasileira. **Resultados:** Várias evidências científicas demonstraram a eficácia da ozonioterapia, a sua relevância e suficiência em diversas patologias. **Conclusão:** Percebe-se evidências de que a sua liberação por parte dos órgãos sanitários brasileiros frente aos Conselhos Profissionais da área da saúde brasileira, já tarda e esbarra em questões alheias à real eficácia desta terapêutica.
Descritores: Ozônio; Legislação; Eficácia**.**

ABSTRACT

Objective: verify if the existing scientific evidence has any real relevance and sufficiency for ozone to be used as therapy in some pathologies, and to observe the progress of Brazilian legislation on the subject. **Method:** a literary review was performed, in databases, with scientific evidence from the last ten years that address ozone therapy and the advancement of Brazilian legislation. **Results:** Several scientific evidences demonstrated the ozone therapy efficacy, its relevance and its sufficiency in various pathologies. **Conclusion**: Therefore, it is evident that the ozone therapy release by the Brazilian health authorities before the Brazilian Health Professional Councils is delayed and comes up against issues unrelated to the real effectiveness of this therapy.
Descriptors: Ozone; Legislation; Efficacy.

RESUMEN

Objetivo: verificar si la evidencia científica existente tiene gran/particular/real relevancia y suficiencia para que el ozono se use como terapia para algunas patologías y para observar el progreso de la legislación brasileña sobre el tema. **Método:** se realizó una revisión literaria, en bases de datos, con evidencia científica de los últimos diez años que abordan la ozonoterapia y el avance de la legislación brasileña. **Resultados:** Diversas evidencias científicas han demostrado la eficacia de la ozonoterapia, su relevancia y su suficiencia en varias patologías. **Conclusión:** Por consiguiente, es evidente que la liberación de la ozonoterapia por parte de las agencias sanitarias brasileñas ante los Consejos de Salud de Brasil, ya se retrasa y se enfrenta a cuestiones fuera de la eficacia real de esta terapia.
Descriptores: Ozono; Legislación; Eficacia.

Introduction

Ozone therapy is a type of treatment that uses the ozone molecule (O3) as a medical gas. It consists of the mixture of ozone with pure oxygen in concentrations, ranging from 1 to 100μg / mL, produced by a specific device for this purpose.[1]

Medical ozone has been widely studied for over 150 years. Reports of its use are already in the First World War, in which medical resources were few, O3 was used. This was used as an alternative to treat post-traumatic gas wounds and gangrene, due to its antibacterial, anti-inflammatory and hemodynamic and analgesic functions.[2-3]

Ozone is a molecule formed by three oxygen atoms (O2). This molecule is considered unstable, extremely reactive and decomposes into molecular O2 and atomic O2.[4] The mechanism of action of ozone is not yet fully known, however, studies show that it normalizes the amount of oxygen in the body for several days, generating a repair in infectious processes, wound healing and oxidative stress.[5]

Some studies have shown a general improvement in metabolism with the use of this treatment. This is due to the increased supply of oxygen, as well as the induction of the activation of the immune system. In addition, there is also a probable stimulation of the neuroendocrine system, neuroprotective systems and regularization of cellular antioxidant enzymes.[6]

Ozone therapy is currently regulated by health surveillance agencies in countries such as Germany, China, Russia, Cuba, Portugal, Greece, Spain and Turkey. This therapy has a high degree of scientific evidence and generates a decrease in public spending on surgical procedures and attenuation of treatments for various pathologies, such as the side effects of radiotherapy. For this reason, the Federal Senate Bill no. 227/2017 proposes the regularization of ozone therapy in the Brazilian health system.[7]

Thus, the objective of this study is to verify whether the existing scientific evidence is highly relevant and sufficient for ozone therapy to be used as therapy in some pathologies and to observe the progress of Brazilian legislation on the subject.

Method

This study is presented in a bibliographic review, which was carried out from November 2018 to January 2020. The data included in this work were articles from the years 2010 to 2020, in addition to Brazilian legislation, which bring as relevant the studied subject.

The databases and sources covered were CAPES, Evidence-Based Health Portal, Pubmed, Scielo, BVS, ANVISA and the Ministry of Health website. For its realization, some descriptors were used: ozone therapy, dentistry, ozone, nursing, medical ozone, Brazilian legislation and Health Professional Councils.

In the first moment, more than 300 articles were found that report the use of ozone as therapy in several anomalies. Therefore, as an inclusion criterion, articles that were published in the last 10 years were chosen, which referred to the effectiveness of ozone in several pathologies and that were freely accessible.

As an exclusion criterion, articles that repeated diseases earlier addressed were removed. At the end, 23 articles composed the final sample.

Results and Discussion

O3 Therapy – Ozone

Ozone has been applied in several areas for many decades. It has utility in the food industry in the processes of surface sanitization, in the treatment of reuse water, and in the various branches of the health area.[8-9]

Smith et al[10] produced a very broad literary review considering the therapeutic value of ozone in diseases in the cardiovascular system, gastrointestinal tract, genitourinary system, nervous system, head and neck, musculoskeletal, subcutaneous tissue and peripheral vascular disease reported between the years of 1980 to 2017. From this study, they concluded that ozone therapy can beneficially alter the natural history of various diseases and organic disorders.

Ozone has a high reactive oxidation action due to the hydroxy radicals released when it undergoes a decomposition, and in its action mechanism, it reacts with unsaturated fatty acids and proteins from the bacterial cell membranes. Thus, its metabolic functioning is altered through the modification of enzymes, respiratory activity and protein denaturation.[11]

Medicinal or therapeutic ozone activates the Nrf2 system (erythroid nuclear factor 2), which is part of the body's protection against many diseases, such as carcinogens and nephropathologies. Generating the inhibition of cytokine-mediated inflammation and leukotriene B4 reductase, added to these are the improvement of fatty acid and red cell metabolism and its antibacterial and antiviral effect.[12]

Although many show its benefits, there are still controversies and questions about the beneficial use of ozone therapy. The medical society has created treatment protocols based on research and experience of 30 years, standardizing ozone applications, concentrations, doses and indications.[13]

Benefits of ozone therapy studies

Lumbociatalgia, or low back pain, was addressed in a systematic review by the Cochrane Center of Brazil in 2013 . This was seen as one of the pathologies whose effectiveness of ozone therapy is evidenced in long-term applications.

In addition, they found that ozone therapy applied for back pain, in correct doses, is not harmful, causing a hormone effect and tolerable acute oxidative stress, capable of recovering the body's homeostasis.[14]

As a bactericide, ozone was also tested on eight strains of bacteria, which were exposed to a unique application of low-dose ozone nebulization and had their growth totally inhibited, being pathogenic and multidrug-resistant.[15]

In the study by Borges et al16, the antimicrobial potential of ozone in *Candida albicans* and *Staphilococcus aureus* was confirmed. We noted that the association of ozone with chlorhexidine potentiated the growth inhibition of bacteria and yeasts. In another study, it was evidenced that, in the bacteria present in the oral cavity, ozone therapy promotes a neutralizing power and

inhibits pathological growth, being superior to several conventional techniques within dentistry.[17]

Still in the field of dentistry, it was observed that ozone acts on cariogenic and acidogenic bacteria, benefiting the treatments of caries disease, since it decarboxylates pyruvic acid, produced by cariogenic bacteria, in acetic acid.[18]

Hayashi et al[19] bring the use of ozone nanobubbles in water (ONBW), for oral washing in rats, with mucositis induced by chemotherapy for cancer. In this study, an antibacterial effect was demonstrated, in which there was a decrease in the bacterial count. In addition, the encouragement of ozone nanobubbles in curing stomatitis was observed, and its advantage was realized in not risking the potential emergence of drug-resistant bacteria.

In addition, ozone research has found satisfactory results in repairing damaged cartilages, inhibiting the inflammatory medium that damages the cartilaginous matrix.[20] In a pilot study, O3-AHT- (auto-hemo ozonotherapy), performed in patients with hyperuricemia and gout, brought results that show that its use, as a complementary treatment, has great therapeutic potential.[21]

In joint diseases, Daif et al[22] demonstrated the benefit of using intra-articular ozonized water. In this study, randomized with 60 patients, with bilateral internal derangement of the temporomandibular joint and disc displacement, it was found that the ozone gas injection in the joint space resulted in total recovery.

Regularization

The Federal Senate Bill (PL 227/2017) authorizes the prescription of ozone therapy as a complementary medical treatment.[7] In a note published by the Regional Council of Medicine of São Paulo, together with other councils, the concern of this is demonstrated trough the Bill approval. They mention that there is no evidence considered consistent and that, for this, the therapy must be carried out experimentally, observing the research protocols defined by the Research Ethics Committee / National Council of Research Ethics.[23]

In March 2018, the Brazilian Ministry of Health, through Ordinance 702, included new practices in the National Policy of Integrative and Complementary Practices - PNPIC, one of which is ozone therapy. This ordinance defines it as low cost, safe, proven, recognized and with therapeutic potential to recover the organism functioning, both of humans and animals. It contemplates the different professionals categories in the Brazilian health area.[24]

Although its applicability is wide and covers several categories of health professionals, today in the Brazilian health area, only the Federal Council of Dentistry and the Federal Council of Physiotherapy have their use regulated.[25-26]

In nursing, professionals were restricted to the use of ozonized water in the treatment of wounds, through a favorable opinion from the Federal Nursing Council (Opinion 308/2015). At the Biomedicine Professional Council, there is no defined authorization, however, there is also nothing contrary to the professionals performance in this area with ozone therapy. Recently, the Federal Pharmacy Council published a note stating the regulation of the pharmaceutical professional with ozone therapy.[27-28]

Abroad, the therapeutic advance of ozone is a reality. The Federal Service of Control in the Area of Public Health and Social Development of Russia, in

2007, regularized ozone therapy. After this event, other countries sought regularization, such as Spain and Emília-Romana in 2007, Cuba and Madrid in 2009 and, between 1996 and 2003, progress was made in Italy in favor of ozone therapy.[29]

Conclusion

In view of all the scientific evidence researched and knowing that there are still many other scientific data that support the ozone therapy effectiveness, it is clear the relevance and sufficiency of this therapy for the pathologies addressed.

The literature still lacks the full legislative support addressing the therapeutic use of ozone. The National Health Surveillance Agency (ANVISA) corroborates the absence of a pronouncement regarding ozone therapy, which delays its legal use and leaves something to be desired, since the Ministry of Health has already included ozone therapy in the National Policy of integrative practices and complementary. It is evident, therefore, that its release before the Professional Councils of the Brazilian health area, is already delayed and comes up against issues different of the real effectiveness of this therapy.

Acknowledgement

This work was carried out with the support of the Coordination for the Improvement of Higher Education Personnel - Brazil (CAPES) - Financing Code 001. FAP-DF.

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