

Experience with the evidence map in oral ozone therapy - importance for integrative and complementary health practices

Mapa de evidências em ozonioterapia bucal: importância para as praticas integrativas e complementares em saúde

Experiencia con el mapa de evidencias en la ozonoterapia oral - importancia para las prácticas de salud integradoras y complementarias

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Abstract

This study aimed to realize the evidence map about ozone therapy, as an approach integrative and / or complementing medical and dental treatment in the form of ozonized water and oxygen / ozone gas mixture and associated with photobiomodulation therapy. The evidence map was based on the 3iE evidence searched in the databases: LILACS, PubMed, EMBASE and Cochrane Library, seeking systematic and narrative reviews, analyzed in an excel characterization spreadsheet. Three independent literature reviewers screened the systematic review search output blinded at the software Rayyan. The full-text publications were screened against the specified inclusion criteria by three independent reviewers; disagreements were resolved through discussion. Forty-two studies were found, 16 of which were systematic reviews and 26 narrative reviews, published between 2006 and 2021, with different levels of confidence. The intervention that most appeared in the literature was oral ozone therapy as a bacterial colony reduction and decontamination agent, with emphasis on topical oxygen-ozone gas mixtures, topical ozonized water. Oral ozone therapy can bring benefits to clinical practice and patients. The evidence map provides an easy

visualization of valuable information for patients, health practitioners and managers, in order to promote evidence-based complementary therapies.

Keywords: Ozone; Dentistry; Health management; Evidence-based dentistry; Integrative medicine.

Resumo

Este estudo teve o objetivo de realizar um mapa de evidências sobre a ozonioterapia, como abordagem integrativa e / ou complementar ao tratamento médico-odontológico na forma de água ozonizada e mistura de oxigênio / gás ozônio e associada à fotobiomodulação. O mapa de evidências baseou-se nas evidências 3iE pesquisadas nas bases de dados: LILACS, PubMed, EMBASE e Biblioteca Cochrane, buscando revisões sistemáticas e narrativas, analisadas em planilha de caracterização excel. Três revisores independentes da literatura examinaram o resultado da pesquisa da revisão sistemática cegos para o software Rayyan. As publicações de texto completo foram selecionadas de acordo com os critérios de inclusão especificados por três revisores independentes; desacordos foram resolvidos por meio de discussão. Foram encontrados 42 estudos, sendo 16 revisões sistemáticas e 26 revisões narrativas, publicadas entre 2006 e 2021, com diferentes níveis de confiança. A intervenção que mais apareceu na literatura foi a terapia de ozônio oral como agente de redução e descontaminação de colônias bacterianas, com ênfase em misturas tópicas de oxigênio-ozônio e água ozonizada tópica. Conclusão: A ozonioterapia oral pode trazer benefícios à prática clínica e aos pacientes. O mapa de evidências fornece uma visualização fácil de informações valiosas para pacientes, profissionais de saúde e gestores, a fim de promover terapias complementares baseadas em evidências.

Palavras-chave: Ozônio; Odontologia; Gestão em saúde; Odontologia baseada em evidências; Medicina integrativa.

Resumen

Este estudio tuvo como objetivo hacer el mapa de evidencias sobre la ozonoterapia, como abordaje integrador y / o complementario al tratamiento médico y odontológico en forma de agua ozonizada y mezcla de oxígeno / ozono gaseoso y asociado a la terapia de fotobiomodulación. El mapa de evidencia se basó en la evidencia 3iE buscada en las bases de datos: LILACS, PubMed, EMBASE y Cochrane Library, buscando revisiones sistemáticas y narrativas, analizadas en una hoja de cálculo de caracterización en Excel. Tres revisores independientes de la literatura examinaron el resultado de la búsqueda de la revisión sistemática cegados en el software Rayyan. Tres revisores independientes examinaron las publicaciones de texto completo en función de los criterios de inclusión especificados; Los desacuerdos fueron resueltos mediante una discusión. Se encontraron 42 estudios, 16 de los cuales fueron revisiones sistemáticas y 26 revisiones narrativas, publicados entre 2006 y 2021, con diferentes niveles de confianza. La intervención que más apareció en la literatura fue la ozonoterapia oral como agente reductor de colonias bacterianas y descontaminación, con énfasis en mezclas tópicas de oxígeno-ozono gaseoso, agua ozonizada tópica. La ozonoterapia oral puede aportar beneficios a la práctica clínica y a los pacientes. El mapa de evidencia proporciona una visualización fácil de información valiosa para pacientes, profesionales de la salud y administradores, con el fin de promover terapias complementarias basadas en evidencia.

Palabras clave: Ozono; Odontología; Gestión en salud; Odontología basada en la evidencia; Medicina integral.

1. Introduction

Since 2018, Ozone Therapy is one of the 29 complementary therapies included in the Brazilian National Health System. Describe the Ozone Therapy because of the recent extension of the Complementary Therapies Policy, the Brazilian Ministry of Health partner up with Latin American and Caribbean Center on Health Sciences Information BIREME - PAHO - WHO and the Brazilian Academic Consortium of Integrative Health - CABSIn to develop Complementary Therapies Evidence Maps, including this one about ozone therapy (Azevedo & Pelicioni, 2011). The objective of this Evidence Map is to describe different interventions and report related health outcomes.

Scientific evidence is important to support decision making in public management, which is still restricted, partly due to access barriers such as: difficulty in understanding academic language or foreign languages, lack of access or familiarity with academic databases, among others. A map of evidence is a way to organize the production of available knowledge on a given theme, where systematic searches and selections of scientific studies are conducted, which are then synthesized and categorized into themes and outcomes of interest. It demonstrates both the number of studies and the main findings. Through the map of evidence it is also possible to identify gaps in knowledge production (OPAS, 2020).

Specifically in dentistry, the Federal Council of Dentistry (FCD) sought to include the practices in order for the dental surgeon to be able to expand the possibilities of dental care. Thus, according to FCD Resolution 82/2008 the following were

recognized as Qualification in Integrative and Complementary Practices: Acupuncture, Homeopathy, Phytotherapy, Flower Therapy, Hypnosis, and Laser Therapy. And through Resolution 165/2015 FCD, in which it added anthroposophic dentistry and ozone therapy through Resolution 166/2015 (Bueno et al., 2019).

For each practice, a working group of researchers was formed to carry out a systematic search of documents in the main databases, selection of studies according to pre-established criteria, and subsequent characterization of the evidence (BIREME, 2019).

Thus, the aim this study was realize the evidence map about ozone therapy, as an approach integrative and / or complementing medical and dental treatment in the form of ozonized water and oxygen / ozone gas mixture and associated with photobiomodulation therapy.

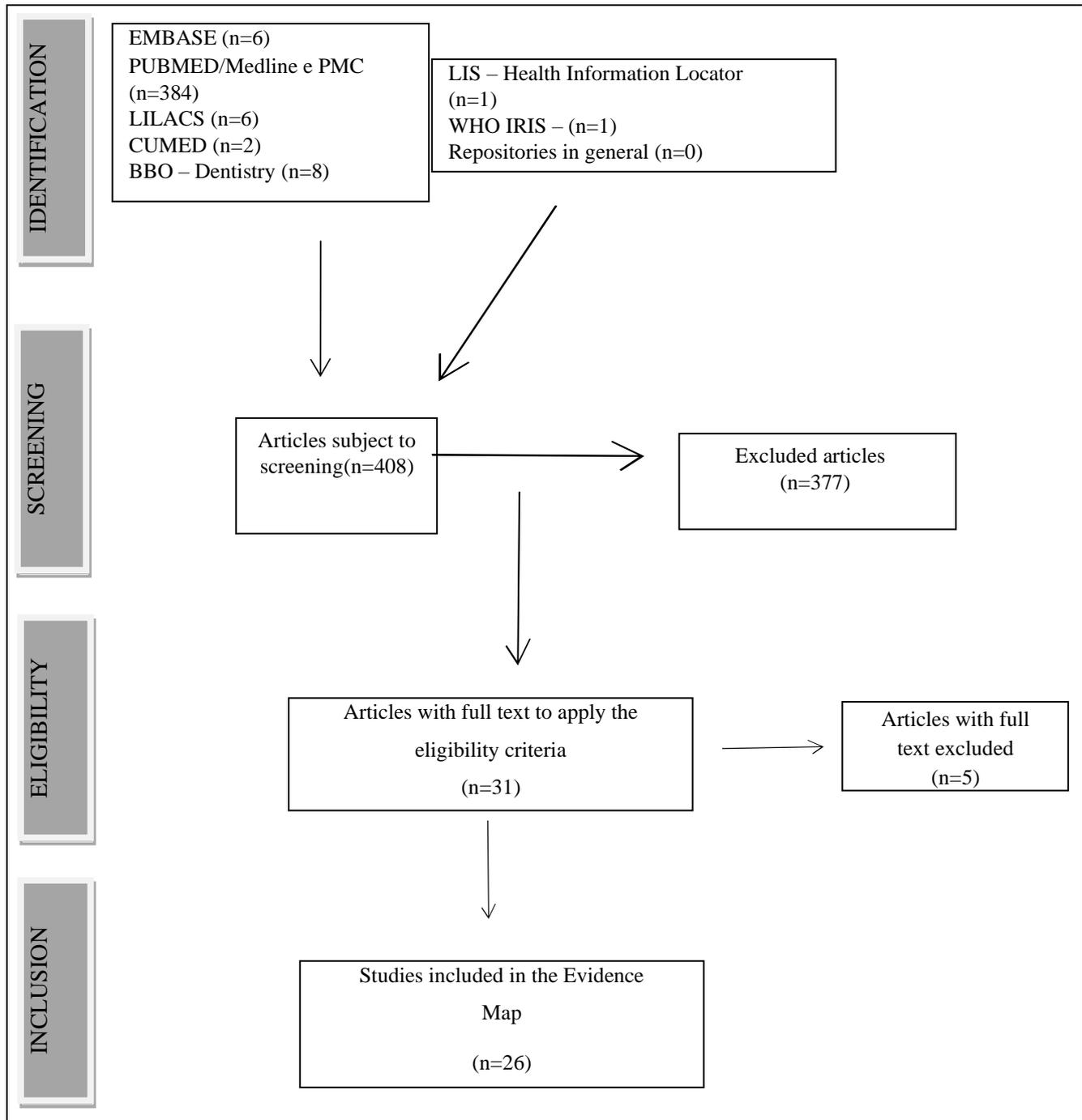
2. Methodology

This Evidence Map is based on systematic reviews and summarizes interventions and health outcomes related to ozone therapy. Systematic reviews provide reliable process that summaries the best available evidence.

The research was in the major databases LILACS, PubMed, EMBASE, CUMED, BBO, Cochrane Library (shared in PUBMED and EMBASE) and gray literature from October 2019 to September 2021. Studies of published and unpublished completed and ongoing systematic reviews were selected at first, were selected and evaluated within the parameters of AMSTAR 2 (Shea et al., 2017) (*Measurement Tool to Assess Systematic Reviews*). Due to the low number of systematic reviews, a search for narrative reviews was then performed, using the same search and databases that were used for the systematic reviews, but for the confidence level item that would be evaluated within the parameters of AMSTAR 2 (Shea et al., 2017), as there is not enough data, it was considered low level for all.

We report the method and results according to PRISMA guidelines (Moher et al., 2009) (Figure 1) and adapted from the International Initiative for Impact Evaluation (3iE) Evidence Gap Methodology (Snilstveit et al., 2016). This evidence map was supported by a technical expert panel of librarians, practitioners, policy makers, and researcher content experts.

Figure 1 - Flow diagram of the information flow through the different phases of the systematic review.



Source: The PRISMA. Moher et al. (2009).

2.1 Data sources

The initial steps are performed by identifying the scope of the study. At the same time, the inclusion criteria and the search terms that guided the search of documents in the databases are defined, applying additional relevant inclusion criteria throughout the process, helping to delimit the scope. The search terms are searched in the DeCS-MeSH Health Science Descriptors specific to ozone therapy and the terms used to search strategy is in the table 1.

The screening of systematic review studies was performed in the largest number of national and international databases, such as: PUBMED/PMC, PUBMED/Medline, LILACS, MOSAICO, EMBASE, SCOPUS, Google Scholar, Web of

Science and thesis bank. The gray literature search in thesis banks, google academic and general repositories is necessary to exclude the risk of publication bias, which favors the publication of studies with positive results or rejects studies that presented unfavorable results.

Table 1 - Terms used to search strategy.

Data base	Search strategy
BVS	((((mh:"ozonio/tu" OR mh:"ozonio/ad" OR ozonioterapia OR ozonoterapia OR "ozone therapy" OR ozonotherapy OR "ozonio terapia" OR "Ozonated water" OR "Ozonated oleo" OR ("Ozone water" OR "ozone gas" OR "Aqueous ozone") (terapia* OR tratament* OR therapy)) OR "Gaseous ozone" OR "Medical ozone" OR (ozon* (hidrozonot* OR balneoterap*)) OR (TI:(ozone OR ozonio OR ozono OR ozonat* OR ozoniz*) AND TI:(therapy OR terapia OR terape*) OR (tratamento OR treatment))) AND (periodont* OR odontol* OR dentistr* OR "root canal" OR caries OR dental OR oral OR bucal OR MH:C07.793* OR gingival OR estomatolog* OR endodon* OR "Infection oral" OR "Oral surgery" OR Perimplant OR "Peri-implant" OR "Oral chronic lesion" OR "Jaw osteonecrosis" OR "Temporomandibular joint" OR "Oral microbiota")) ("systematic review" OR "revisión sistemática" OR "revisão sistemática" OR ti:review or ti:revisao or ti:revision)) (da:2020* OR da:2021*)
Pubmed	(ozone/tu[MH] OR ozone/ad[MH] OR "ozone therapy" OR "ozone bath therapy" OR ((Balneotherapy OR bath*) ozone*) AND (periodont* OR odontol* OR dentistr* OR "root canal" OR caries OR dental OR oral OR gingival OR estomatolog*)) Filters applied: Review, Systematic Review, from 2020/1/1 - 2021/9/9.
Embase	('ozone therapy' OR 'ozone bath therapy' OR ((balneotherapy OR bath*) AND ozone*) OR 'ozonated water' OR 'ozonated oil' OR (('ozone water' OR 'ozone gas' OR 'aqueous ozone therapy') AND therapy) OR 'gaseous ozone' OR 'medical ozone') AND (periodont* OR odontol* OR dentistr* OR 'root canal' OR caries OR dental OR oral OR gingival OR estomatolog* OR endodon* OR 'infection oral' OR 'oral surgery' OR perimplant OR 'peri-implant' OR 'oral chronic lesion' OR 'jaw osteonecrosis' OR 'temporomandibular joint' OR 'oral microbiota') AND [embase]/lim NOT ([embase]/lim AND [medline]/lim) AND ('meta analysis' OR 'systematic review')

Source: Authors.

Based on the results of these searches, the studies that will compose the prototypes are selected considering filters of year in which the study was conducted, relevance to the subject of ozone therapy, and availability of full text online. The proposed categorization of the studies varied according to the focus of the researchers

2.2 Inclusion criteria

Systematic reviews about ozone therapy interventions and adequate description of health outcomes were eligible for inclusion. We defined systematic reviews as reviews that self-identified as systematic reviews, however, due to the low number of systematic reviews found, narrative reviews were included in the scope of this research, even though this would have impaired the confidence level analysis performed using the AMSTAR 2 questionnaire (Shea et al., 2017). All participants of all ages regardless of health status were eligible for inclusion in the review. We excluded systematic reviews that did not focused in ozone therapy health outcomes. We included interventions of ozone therapy applied to the oral or oral cavity, of any duration and follow-up.

2.3 Procedure

Three independent literature reviewers screened the systematic review search output blinded at the software Rayyan (Ouzzani et al., 2016). Citations deemed potentially relevant by at least one reviewer and unclear citations were obtained as full text. The full-text publications were screened against the specified inclusion criteria by three independent reviewers; disagreements were resolved through discussion. This process is displayed at the PRISMA Flow Diagram (Moher et al., 2009) (Figure 1).

We applied AMSTAR 2 (Shea et al., 2017) (Figure 2) to analyze the quality (high, moderate, low) of the included systematic reviews. From each included systematic review, we extracted the intervention ozone therapy and the main health outcomes that were summarized across included studies. We retrieved data about population, treatment effect (positive, potential positive, mixed findings, negative estimates for health outcomes and systematic review characteristics.

2.4 Data synthesis

We developed a characterization matrix at Excel to synthesize the findings. This matrix included: Full Text Citation; Interventions; Outcomes Group; Outcomes; Effect; Population; Database ID; Focus Country; Publication Country; Publication Year; Type of Review; Review Design; Study Design; Confidence Level. Systematic reviews outcomes were drafted by one reviewer and discussed in the review team, also the matrix was discussed in two workshops organized by BIREME. We organized the Evidence Map considering outcomes, effects and level of confidence of the included systematic reviews.

The results are presented on an online, interactive platform that allows the identification of existing evidence, as well as visualizing gaps. The circles located at the intersections between the interventions and the results represent the identified studies. The size of the circle represents the volume of studies. The color of the circles represents the level of confidence (high, moderate, low) according to a methodological qualification of the studies included in the map. Review studies are evaluated using the AMSTAR2 tool (Shea et al., 2017). When the map includes reviews and primary studies, the confidence level classification is predefined according to the types of study (Ouzzani et al., 2016; Shea et al., 2017). Map of evidence on the clinical application of oral ozone therapy is available: <https://public.tableau.com/profile/bireme#!/vizhome/ozonioterapia-bucal-pt/evidence-map>.

3. Results

We identified 26 citations of which 10 systematic reviews (Albedah et al., 2013; Azarpazhoo & Limeback, 2008; Brazzelli et al., 2006; Deepthi & Bilichodmath, 2020; German et al., 2013; Moraschini et al., 2020; Santos et al., 2020; Sharda et al., 2021; Silva et al., 2020; Sridharan & Sivaramkrishnan, 2021) and 16 narrative reviews (Almaz & Sönmez, 2015; Chirumbolo et al., 2021; Domb, 2019; Gupta & Mansi, 2012; Haghghat & Oshaghi, 2020; Lacerda et al., 2021; Lio et al., 2020; Mohammadi et al., 2013; Nogales et al., 2008; Re et al., 2020; S, 2019; Seidler et al., 2008; Suh et al., 2019; Swanson et al., 2021; Tiwari et al., 2017; Trevor Burke, 2012; Tricarico et al., 2020); met the criteria for inclusion in the Map. Most of the reviews were published in the 2008, 2012 and 2014.

For Ozone therapy buccal the topical ozonated water and topical oxygen-ozone gas mixture were the most researched interventions, and the most common outcome was reduction of bacterial colonies, followed by reduction of dental (hard tissues) and oral (soft tissues) and dental carie. The reviews covered a wide variety of results, effects and populations and reviews spanned a wide diversity of outcomes, effects and populations. From the 31 references, 26 reviews were included, of which ten systematic reviews (39%), and sixteen narrative reviews (61%); that met the inclusion criteria.

As specific results of our experience in the preparation of the evidence map in oral ozone therapy, for each added review it was extracted as treatment: topical ozonized water, topical ozonized oil, topical oxygen-ozone gas mixture, parenteral

oxygen-ozone gas mixture, ozone gas / photodynamic therapy. The main outcomes for oral health and ozone therapy were: reduction of bacterial colonies, reduction of plaque, dental caries, enamel demineralization, endodontic diseases; and other outcomes with fewer revisions were found for: viral load, pain relief, post-surgical healing, halitosis, caries prevention, temporomandibular joint disorder, bone implant integration, dental reimplantation, mandibular osteonecrosis and dentin hypersensitivity.

Regarding the effects of treatment for primary health outcomes, most systematic reviews were assessed as positive (14.8%), inconclusive / mixed (11.1%), with no effect (7.4%). The vast majority of studies evaluated were narrative reviews, where the vast majority (66.7%) were not evaluated as to the effect obtained, left as without effect.

3.1 Confidence level

Systematic reviews were analyzed based on AMSTAR 2, resulting in the following confidence levels: 2,8% High, 22,2% Moderate and 75% Low in all narrative reviews. Of these reviews regarding the study design, the majority, 83.3%, are of effectiveness followed by safety and effectiveness (13.9%), cost effectiveness (1.9%) and safety and effectiveness (0.9%).

3.2 Countries

The systematic reviews included analyzed data from the following countries: Egypt, United Kingdom and Germany. However, in narrative reviews, most studies do not cite this information, as they approach the topic based on several published studies, without considering a specific type.

3.3 Lack of research

The most researched intervention groups for oral ozone therapy, mainly in systematic reviews, were: topical ozonized water in (41.7%), topical oxygen-ozone gas mixture (38%), topical ozonized oil (16.7%) followed by mixture of parenteral oxygen-ozone gas and ozone gas / photodynamic therapy each with 1.9% of the surveys (Table 2).

When analyzed by groups of outcomes, the group of chronic diseases has the largest number of primary outcomes, 37.5%, the group in which they are inserted: endodontic infections, gingivitis, periodontitis, alveolitis, stomatitis, mandibular osteonecrosis, halitosis, disorders of temporomandibular joint, dentin hypersensitivity, tooth extraction. In this group, the four different types of interventions are used: topical ozonized water, topical oxygen-ozone gas mixture, topical ozonized oil and parenteral oxygen-ozone gas mixture.

The group of metabolic and physiological indicators where we have the reduction of bacterial colony, as the most researched primary outcome, in 22.2% of reviews, for three different interventions: topical ozonized water, topical oxygen-ozone gas mixture, ozonized oil and using two different therapies that is ozone gas together with photodynamic therapy. Then, in the same group, we have the second most researched outcome, which is plaque in 12% of reviews, with the interventions of topical ozonized water, topical oxygen-ozone gas mixture.

Table 2 - Outcome and Intervention Groups for Oral Ozone Therapy.

Outcome Groups for Oral Ozone Therapy	Intervention
Metabolic and physiological indicators (34,2%) - reduction of bacterial colony (22.2%) - reduction of bacterial plaque (12%)	- topical ozonized water - topical oxygen-ozone gas mixture - ozonated oil - ozone gas and photodynamic therapy
Acute diseases (33,3%) - endodontic infections (10.2%), - periodontitis (7.4%), - gingivitis (6.5%), - alveolitis (1.9%), - dentin hypersensitivity (1.9%), - temporomandibular joint disorders (1.9%), - stomatitis (0.9%), - mandibular osteonecrosis (0.9%), - halitosis (0.9%), - dental infection (0.9%), - tooth extraction (0.9%).	- topical ozonized water - topical oxygen-ozone gas mixture - topical ozonated oil - parenteral topical oxygen-ozone gas mixture
Cicatrization (15,8%) - enamel demineralization (6.5%) - implant osseointegration (3.7%) - bone density (2.8%) - post-surgical healing (1.9%) - dental reimplantation (0.9%)	- topical ozonized water - topical oxygen-ozone gas mixture - ozonated oil
Pain and Chronic Diseases (13,9%) - caries (10,2%) - herpes simplex (1,9%) - - viral load (0.9%) - lichen planus (0.9%)	- topical ozonized water - topical oxygen-ozone gas mixture
Vitality, Well-Being and Quality of Life (0,9%) - Caries Prevention (0,9%)	- Topical Ozonized Water

Source: Authors.

The primary healing outcome group had 15.7% of primary revisions where enamel demineralization was present in 6.5% of primary studies. In this group are included: dental reimplantation, implant osteointegration, bone density, post-surgical healing.

The groups with main outcomes pain and chronic illness, each had 13% of primary studies endorsed. The chronic disease group with the specific outcome of dental caries, was the third most studied outcome, 10.2% of primary reviews, where the topical oxygen-ozone gas mixture was used followed by topical ozonized water, cold sores and lichen planus.

Vitality, well-being and quality of life was also an outcome group, where the prevention of caries with the intervention of ozonated water appears in 0.9% of reviews with an inconclusive / mixed effect, which demonstrates the need for better-designed and focused studies.

4. Discussion

The Evidence Map is not able to answer more refined questions, such as the most appropriate method of application to Ozone Therapy, difference between health services, adequate training of professionals, patient access and the effects of self-application. Future research, including qualitative research and case studies, is necessary to answer these questions, which are extremely important for the development of Ozone Therapy and their inclusion and access to SUS.

This evidence map for ozone therapy is based on 26 published reviews and provides a broad overview of available evidence of these intervention, related outcomes and effects. It shows the volume of available research and highlights areas where the interventions showed positive effects.

The group of physical and metabolic effects were the most present in the reviews in general, with the effects of topical ozonized water and the oxygen-ozone gas mixture were positive for reducing bacterial colony, reducing dental biofilm and decreasing viral load (Domb, 2019; German et al., 2013; Gupta & Mansi, 2012; Santos et al., 2020; Sharda et al., 2021). For these same types of interventions and outcomes when applied for root canal disinfection it did not have the same effects on the result, which were inconclusive and even negative, as well as ozone gas and photodynamic therapy for the outcome of bacterial reduction (Seidler et al., 2008; Silva et al., 2020).

For healing, this Map presented positive effects regarding necrotic area, reduction of biofilm, improvement of alveolar bone crest, bone density, chronic wound closure, cutaneous / subcutaneous infection, dental reimplantation, enamel demineralization and implant osteointegration using (Suh et al., 2019).

The combined interventions of ozone gas and photodynamic therapy had a positive effect on mandibular osteonecrosis. as well as topical ozonized water in cases of gingivitis, dentin hypersensitivity, halitosis, periodontal diseases, prosthetic stomatitis (Deepthi & Bilichodmath, 2020; Lio et al., 2020; Suh et al., 2019; Tiwari et al., 2017; Tricarico et al., 2020).

For dental caries, considered a chronic disease, ozone therapy showed positive potential effects when the oxygen-ozone gas mixture was used (Brazzelli et al., 2006). The treatment and prevention of caries with the use of the oxygen-ozone gas mixture was observed to have a positive potential regarding the control of anxiety and phobia towards dental treatment (Brazzelli et al., 2006; Suh et al., 2019), and with potentially positive effects on improving the quality of life with regard to the prevention and reduction of caries (Brazzelli et al., 2006; Suh et al., 2019; Tiwari et al., 2017). However, we must interpret it with caution, as there are few randomized clinical trials that support its use for caries prevention (Santos et al., 2020).

Although evidence gap maps can only provide a broad overview of research, the findings presented more positive effects than negative, including reviews of high, moderate and low confidence level. The duration and frequency of ozone therapy has not been analyzed and need more research.

Pain was divided into three types: toothache, acute pain and postoperative pain, where the use of ozonized water as irrigation for toothache (Gupta & Mansi, 2012) in the post-operative action that both ozonized water can be used for irrigation of soft tissues and parenteral gas mixture with intra-sinusal application (Seidler et al., 2008; Tiwari et al., 2017). The topical oxygen ozone gas mixture for intra-channel application, and in the outcome, toothache had a positive and high impact

according to Azarpazhooh (Azarpazhooh & Limeback, 2008). The application of topical ozonized oil obtained two positive outcomes, one for acute pain and the other for postoperative pain (Gupta & Mansi, 2012).

Furthermore, the effects classified as mixed evidence warrants further research and can help to guide different institution's funding calls.

The creation and publication of evidence maps consists of graphically representing the best evidence found, analyzed and categorized, in addition to linking with the bibliographic records and full texts (when available) of the studies in order to facilitate access to information for all those interested.

Even though Evidence Maps have several limitations, like the fact that we used only published reviews to provide an overview over the research on ozone therapy and more evidence, including qualitative studies, were not included. We did not calculate effect sizes in a meta-analysis, neither provide risk of bias assessments, but we tried to overcome these limitations by evaluating the quality of the included systematic reviews by applying AMSTAR 2. In addition, the grouping of outcomes was review-content driven, even though individual primary research studies would have more contributions to add in the analysis, these was not the focus of the Map. Also, we were unable to avoid overlap between included studies across reviews but did not repeat results from update reviews. Furthermore, we relied on the review author's skills in conducting systematic reviews and narrative reviews, evaluation of primary studies quality, choice of outcomes, analysis of effects and susceptibility to publication and outcome reporting bias.

This Evidence Map will also not be able to answer more refined questions, such as the most adequate method of Ozone therapy application, difference between health services, adequate training for practitioners, access of patients and self-application effects. Future research, including qualitative research and case studies, are necessary to answer these questions, extremely important to the development of ozone therapy.

Outcomes and effects information of ozone therapy presented in these Map will further advance our evidence-based knowledge of Complementary Therapies, such as proposed by the Complementary Therapies Policy in Brazil and promoted by the WHO 2014-2024 and BIREME.

A limitation of the evidence map result is that it does not show us the contraindications of the techniques. Thus, it requires that the professional, when interpreting it, can seek more information about the forms of application.

5. Conclusion

Evidence gaps remain for all types of interventions and outcomes in oral ozone therapy. This therapy is promising in the integration of treatments in dentistry, however additional well-designed studies are necessary and essential with adequate sample size, carefully standardized measures and analysis, including the social dimension of management and quality of life in order to assess its efficiency, effectiveness and safety to justify clinical use. All areas of interventions and outcomes deserve to have increments of future research.

Despite the outlined limitations, this evidence map provides an easy visualization of valuable information for patients, health practitioners and managers, in order to promote evidence-based complementary therapies.

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Ethics approval and consent to participate

Not applicable.

Availability of data and materials

All included systematic reviews are in the public domain; see the “Reference” section for full citation details. Study flow was tracked in citation management software and data were extracted in online systematic review programs – Mendeley, Rayyan and Excel; all files can be obtained from the authors. The Evidence Map is available at the Virtual Health Library - <http://mtci.bvsalud.org/en/evidence-map/>

Competing interests

Not applicable.

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