

Osteorradiationecrosis and Bisphosphonates: A Literature Review

Osteorradiationecrose e Bifosfonatos: Uma Revisão de Literatura

Osteorradiationecrosis y Bifosfonatos: Una Revisión de la Literatura

RESUMO

Introdução: Cerca de 70% dos pacientes diagnosticados com câncer são submetidos à radioterapia como parte da abordagem do tratamento da doença, a qual pode desencadear intercorrências, como a osteorradiationecrose, disfunção multifatorial caracterizada por um quadro de exposição óssea crônica, dor e necrose óssea, que é desencadeada, principalmente, em altas doses de radiação e pode ser associada à algumas medicações comumente utilizadas durante o tratamento de um paciente oncológico, como os bifosfonatos. **Objetivo:** O presente trabalho buscou realizar uma revisão bibliográfica de artigos científicos que descrevem a associação da ORN e dos bifosfonatos e que abordam as condutas clínicas aplicadas no seu tratamento. **Metodologia:** Trata-se de uma revisão onde foram analisados artigos publicados no intervalo de tempo de 2013 a 2025, aplicando filtros selecionados, nas bases de dados Biblioteca Virtual em Saúde e também base de dados Medline (PubMed). Utilizando os descritores Osteorradiationecrose, Osteorradiationecrosis, Bifosfonatos, Biphosphonates, Radioterapia, Radioterapy, Câncer de cabeça e pescoço, Head and Neck Cancer, Tratamento Médico e Medical Treatment. Artigos que não tenham caráter científico, que não se enquadraram na temática do estudo e/ou são duplicados de diferentes bases de busca foram excluídos. **Resultados:** Nas bases de busca foram localizados artigos ao total antes da aplicação dos filtros e resultados após a aplicação dos mesmos, no BVS e no Medline. Em seguida, após a exclusão de artigos fora do escopo da pesquisa, através da leitura dos abstratos, chegou-se a resultados, no BVS e no Medline. Também foram incluídos artigos através de uma busca por citação, totalizando ao final estudos para a análise. A partir dos resultados, foi utilizado o software Excel para remover os artigos duplicados, gerando uma seleção final composta por artigos, os quais foram lidos na íntegra. **Conclusão:** Com a leitura da literatura selecionada foi possível compreender que a etiopatologia da ORN associada a bifosfonatos permanece incerta e sobre acerca das opções de tratamento evidenciou-se que, não existem evidências robustas o suficiente sobre a eficácia do HBO e redução de morbimortalidade. Por isso, se faz necessário estudos prospectivos de logo prazo para melhor compreensão da sua patogenia, para assim explorar e orientar os melhores manejos clínicos para os profissionais de saúde e seus pacientes.3578912

DESCRITORES: Osteorradiationecrose; Bifosfonatos; Câncer de Cabeça e Pescoço.

ABSTRACT

Introduction: Approximately 70% of patients diagnosed with cancer undergo radiotherapy as part of their treatment, which can trigger complications such as osteoradiationecrosis, a multifactorial dysfunction characterized by chronic bone exposure, pain, and bone necrosis, which is mainly triggered by high doses of radiation and may be associated with some medications commonly used during the treatment of cancer patients, such as bisphosphonates. **Objective:** This study sought to conduct a literature review of scientific articles that describe the association between ORN and bisphosphonates and address the clinical approaches used in its treatment. **Methodology:** This is a review in which articles published between 2013 and 2025 were analyzed, applying selected filters, in the Virtual Health Library database and also the Medline (PubMed) database. The following descriptors were used: Osteoradiationecrosis, Biphosphonates, Radiotherapy, Head and Neck Cancer, Medical Treatment. Articles that were not scientific in nature, did not fit the study theme, and/or were duplicates from different search engines were excluded. **Results:** A total of articles were found in the search engines before applying the filters and results after applying them, in the VHL and Medline. Then, after excluding articles outside the scope of the research by reading the abstracts, results were obtained in the VHL and Medline. Articles were also included through a citation search, totaling studies for analysis. Based on the results, Excel software was used to remove duplicate articles, generating a final selection of articles, which were read in their entirety. **Conclusion:** Reading the selected literature, it was possible to understand that the etiopathology of ORN associated with bisphosphonates remains uncertain and, regarding treatment options, it was evident that there is insufficient robust evidence on the efficacy of HBO and reduction of morbidity and mortality. Therefore, long-term prospective studies are necessary to better understand its pathogenesis, in order to explore and guide the best clinical management for healthcare professionals and their patients.3578912

DESCRIPTORS: Osteoradiationecrosis; Bisphosphonates; Head and Neck Cancer.

RESUMEN

Introducción: Alrededor del 70 % de los pacientes diagnosticados con cáncer se someten a radioterapia como parte del tratamiento de la enfermedad, lo que puede desencadenar complicaciones, como la osteorradiationecrosis, una disfunción multifactorial caracterizada por un cuadro de exposición ósea crónica, dolor y necrosis ósea, que se desencadena principalmente por altas dosis de radiación y puede estar asociada a algunos medicamentos que se

utilizan habitualmente durante el tratamiento de un paciente oncológico, como los bifosfonatos. **Objetivo:** El presente trabajo buscó realizar una revisión bibliográfica de artículos científicos que describen la asociación entre la ORN y los bifosfonatos y que abordan las conductas clínicas aplicadas en su tratamiento. **Metodología:** Se trata de una revisión en la que se analizaron artículos publicados en el intervalo de tiempo de 2013 a 2025, aplicando filtros seleccionados, en las bases de datos Biblioteca Virtual en Salud y también en la base de datos Medline (PubMed). Se utilizaron los descriptores Osteorradionecrosis, Osteorradionecrosis, Bifosfonatos, Biphosphonates, Radioterapia, Radioterapy, Cáncer de cabeza y cuello, Head and Neck Cancer, Tratamiento médico y Medical Treatment. Se excluyeron los artículos que no tenían carácter científico, que no se ajustaban a la temática del estudio y/o que eran duplicados de diferentes bases de búsqueda. **Resultados:** En las bases de búsqueda se localizaron artículos en total antes de aplicar los filtros y resultados después de aplicarlos, en la BVS y en Medline. A continuación, tras excluir los artículos que no entraban en el ámbito de la investigación, mediante la lectura de los resúmenes, se obtuvieron resultados, en la BVS y en Medline. También se incluyeron artículos mediante una búsqueda por citas, lo que dio un total final de estudios para el análisis. A partir de los resultados, se utilizó el software Excel para eliminar los artículos duplicados, generando una selección final compuesta por artículos, que se leyeron en su totalidad. **Conclusión:** Tras la lectura de la bibliografía seleccionada, se pudo comprender que la etiopatología de la ORN asociada a los bifosfonatos sigue siendo incierta y, en cuanto a las opciones de tratamiento, se evidenció que no existen pruebas suficientemente sólidas sobre la eficacia de la HBO y la reducción de la morbimortalidad. Por lo tanto, se necesitan estudios prospectivos a largo plazo para comprender mejor su patogenia, con el fin de explorar y orientar los mejores manejos clínicos para los profesionales de la salud y sus pacientes.3578912 **DESCRITORES:** Osteorradionecrosis; Bifosfonatos; Cáncer de cabeza y cuello.

Rafaela de Brito Ribeiro

Medical Student at the Pontifical Catholic University of Minas Gerais
ORCID: <https://orcid.org/0000-0002-3686-2329>

Thiago Oliveira Araújo

Medical Student at the Pontifical Catholic University of Minas Gerais

Danyelle Maria Silva

Medical Student at the Pontifical Catholic University of Minas Gerais
ORCID: <https://orcid.org/0000-0002-4465-4976>

Lucas Ferreira Alves

Professor of Medicine at the Pontifical Catholic University of Minas Gerais
ORCID: <https://orcid.org/0000-0002-8075-0674>

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INTRODUCTION

Radiotherapy plays an important role in the treatment of malignant lesions throughout the body and can be used alone or in combination with chemotherapy and/or surgical removal of the lesion. Currently, according to the WHO, about 70% of patients diagnosed with cancer undergo radiotherapy as part of their treatment approach, with head and neck cancer patients accounting for approximately 50% to 60%, also representing a high rate. 3456⁷

In this type of treatment, ionizing electromagnetic or corpuscular radiation is used to induce cell death in tumor cells, ionizing the cells at their moment of greatest proliferative activity, that is, during cell division, a stage called mitosis, stimulating chemical and biological reactions that damage

the DNA and cell division of neoplastic cells.⁵

Radiotherapy treatment is programmed through the analysis of computed tomography, magnetic resonance imaging, and proton emission tomography (PET-CT), which are transferred to a computer that creates a three-dimensional image of the tumor, thus enabling the identification of the anatomical and functional areas of the lesion. In addition, they also enable the radiation to be shaped to the contour of the target area and the use of multiple angular radiation beams, which are uniform in D-RCT but not in IMRT. In this way, high doses of radiation can be administered to the target volume, while seeking to reduce the exposure of tissues adjacent to the lesion and, consequently, minimize secondary damage to the treatment. For example, these modalities

reduced the incidence of osteoradionecrosis from 15% to 5%.⁵⁶¹³

However, despite the positive aspects of radiotherapy, the high doses applied can lead to unwanted side effects in the skeletal, lymphatic, and tissue systems adjacent to the injured area. Patients irradiated in the head and neck regions may present clinical signs indicating xerostomia, hypogeusia, intraoral hemorrhage, mucositis, trismus, chronic dermatitis, developmental abnormalities, and, ultimately, osteoradionecrosis.⁷

Osteoradionecrosis is the most serious complication arising from radiotherapy in the treatment of head and neck cancer. By definition, it is non-vital bone exposure that persists for more than months in the absence of neoplastic disease. The most affected area is the mandible, with a frequency times greater than in the max-

illa.348¹²

Clinically, it is possible to observe a picture of chronically exposed bone, with signs of chronic infection, pain, and bone necrosis, which can lead to complications such as cortical perforation, fistula formation, ulceration of adjacent soft tissues, and pathological fracture. Histopathologically, there is destruction of osteocytes and absence of osteoblasts, as well as new mineralized or osteoid matrix. The walls of regional blood vessels are thickened by fibrous connective tissue, and the tissue that replaces the bone marrow becomes infiltrated by lymphocytes, plasma cells, and macrophages. Finally, radiographically, the affected bone regions show poorly defined radiolucent areas, which can evolve into relatively radiopaque zones as the necrotic bone separates from the residual vital areas. 6⁹

It is a dysfunction with a multifactorial etiology in which the radiation dose is the main trigger for the dysfunction, with doses above 50 Gy. Once radiotherapy has been performed, the patient will be at risk of developing osteoradionecrosis for the rest of their life. However, most cases occur within a range of months to years after the end of radiotherapy. Its development can occur spontaneously or due to trauma. The former accounts for a minority of cases occurring in the first few years after treatment of the neoplasm, while ORN due to trauma accounts for the majority of cases, mainly resulting from local trauma, such as tooth extraction or accidental fracture. 34⁵

Factors such as medication use, proximity of the neoplasm to the bone, presence of remaining teeth, slight predilection for males, advanced age, continuous use of tobacco and/or alcohol, poor hygiene, and unbalanced nutrition are also observed, as an aid to a more accurate diagnosis.⁸

Regarding the use of medications,

cancer patients are susceptible to various complications, which can be prevented by administering certain drug therapies. Bisphosphonates are synthetic analogues of pyrophosphate, consequently forming an oxygen bridge by replacing it with a carbon (P-C-P),, forming two main chains (R1 and R2). The long R chain determines the anti-resorptive potency, since they resemble pyrophosphate in their bond with bone hydroxyapatite. Thus, they act by inhibiting the activity of osteoclasts, the cells responsible for bone resorption. Therefore, they are indicated for the treatment of bone metastases, prevention of fractures in patients with cancer treatment-induced osteoporosis, and to prevent and treat tumor-induced hypercalcemia. However, despite their positive aspects, their association with the development of osteonecrosis of the jaws, which is characterized by the death of bone tissue in the mandible or maxilla, is already prevalent in the scientific literature. 12

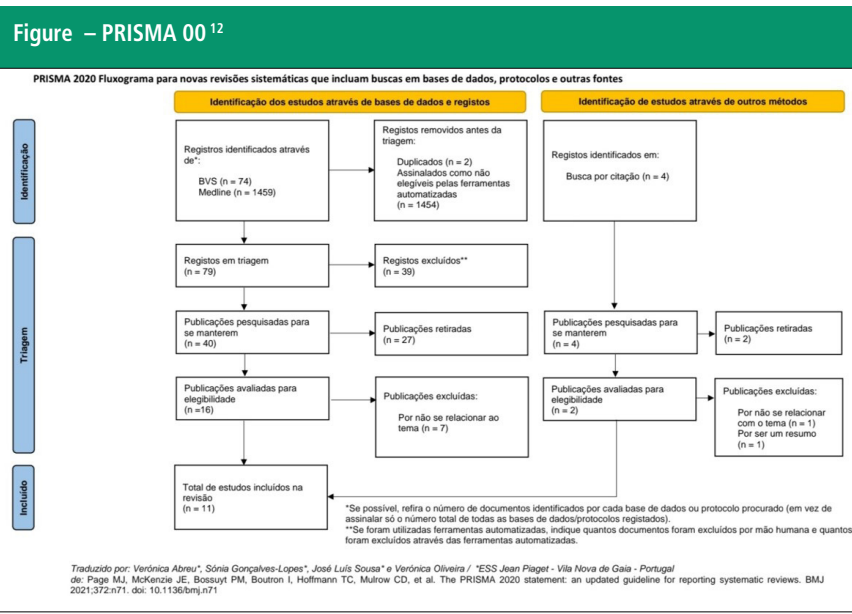
It is also known that radiation therapy or combined chemotherapy and radiotherapy regimens for the treatment of malignancies, especially in the head and neck region, can increase the frequency of osteonecrosis and osteoradionecrosis. Treatment options are limited and may be invasive, such as surgical intervention, or non-invasive, such as the use of hyperbaric oxygen and photobiomodulation. And although there are a considerable number of case reports in the scientific literature, more scientific studies are needed to conduct a comprehensive, detailed, and comparative analysis of these publications in order to establish better standards of association, concepts, and clinical practices for healthcare professionals. Therefore, this study aims to conduct a bibliographic review of scientific articles that describe the association between osteoradionecrosis and bi-

sphosphonates and that address the clinical practices applied in its treatment.⁴¹³

METHODOLOGY

This is an integrative review of the literature conducted between... (Continue) For the present study, articles published between 2013 and 2025 and with the full text available were analyzed. The following databases were used for the research: Virtual Health Library, which includes: Nursing Database (Bdenf), Latin American and Caribbean Health Sciences Literature (Lilacs), and Scientific Electronic Library Online (SciELO); as well as the Medline database, through PubMed - National Library of Medicine National Institutes of Health. The search will be refined using the descriptors Osteoradionecrosis, Bisphosphonates, Radiotherapy, Head and Neck Cancer, Medical Treatment. 35¹²

In the VHL, the following filters were used: full text, systematic review, diagnostic study, observational study, etiology study, English, Portuguese, and osteoradionecrosis. In Medline, the following filters were applied: Free Full Text, Full Text, Meta-analysis, Systematic Review, and Randomized Controlled Trial. Articles that were not scientific in nature, did not fit the study theme, and/or were duplicates were excluded from the final selection.



RESULTS

In the search of the BVS and Medline databases, a total of articles were found before applying the filters and results after applying them, in BVS and in Medline. Then, after excluding articles outside the scope of the research by reading the abstracts, results were obtained, in BVS and in Medline. Articles were also included through a citation search, totaling studies for analysis (figure). Based on the results, Excel software was used to remove duplicate articles, generating a final selection of articles.^{35789¹²}

After the articles were selected and read in full, a table was prepared in alphabetical order containing information such as bibliographic references (article title, authors, year of publication, journal), type of study, objective, and results found, in order to assist in the best analysis of the studies (table).¹

After selecting the articles, a comparative table was created in Excel containing the following information: article title, authors, year of publication, journal, type of study, objective, and results found. From the data col-

lected, it was possible to synthesize and interpret the main findings of the analyzed literature, encompassing its clinical and theoretical implications, as well as trends, contradictions, and gaps, which were discussed below.

Table – Literature review of selected articles¹

Bibliographic Reference	Type of study	Objective	Results
AKASHI, M. et al. Differences between osteoradionecrosis and medication-related osteonecrosis of the jaw. Oral and maxillofacial surgery, v. 22, p. 59-63, 2018.	Retrospective observational study	To compare the clinical data of ORN and MRONJ and identify the key differences between these diseases.	Patients with MRONJ were older (P = 0.0474) and predominantly female (P < 0.0001). They reported more pain than patients with ORN (P = 0.0263) and showed periosteal reaction on CT scans, which was absent in ORN (P = 0.0158). Tooth extraction was a more common etiological factor in MRONJ (P = 0.0352). Minimal debridement was more frequent in MRONJ (P = 0.0093), whereas surgical resection was more commonly used in ORN (P = 0.0002).
ARQUEROS-LEMUS, M. et al. Pentoxifylline and tocopherol for the treatment of osteoradionecrosis of the jaws. A systematic review. Medicina oral, patología oral y cirugía bucal, v. 28, n. 3, p. e293, 2023.	Systematic review	To evaluate the reported efficacy of PENTO in the treatment of ORN.	Eleven studies evaluated the use of pentoxifylline and tocopherol (PENTO) in the treatment of mandibular osteoradionecrosis (ORN). All reported complete mucosal coverage (no exposed bone) in 16.6% to 100% of patients. Clinical improvement or stabilization occurred in 7.6% to 66.6% of cases, while disease progression was observed in 7.6% to 32% of patients in five studies. PENTO demonstrated efficacy in controlling ORN, but the lack of a standardized protocol and the need for more high-quality studies were emphasized.
CAMOLESI, G. C. V. et al. Therapeutic alternatives in the management of osteoradionecrosis of the jaws. Systematic review. Medicina oral, patología oral y cirugía bucal, v. 26, n. 2, p. e195, 2020.	Systematic review	To systematically review the literature comparing the healing of osteoradionecrosis (ORN) among therapeutic alternatives: surgical, pharmacological, and combined.	Surgical treatment was the most common choice (46.3%), followed by pharmacological treatment alone (25.9%) or combined (26.9%). Exclusive surgical treatment appeared to be the most effective option, with 51.2% of healed lesions, odds ratio (OR) for healing of 5.7 (95% CI 1.9–16.9, p = 0.002). Only one case (0.9%) used low-level laser therapy. Early intervention with conservative surgical methods combined with pharmacological therapy improved the prognosis of ORN.

<p>FORNER, L. E. et al. Hyperbaric oxygen treatment of mandibular osteoradionecrosis: Combined data from the two randomized clinical trials DAHANCA-21 and NWHHT2009-1. <i>Radiotherapy and Oncology</i>, v. 166, p. 137-144, 2022.</p>	<p>Randomized controlled clinical trial</p>	<p>To investigate the effect of hyperbaric oxygen therapy (HBO) in ORN through two multicenter randomized controlled trials.</p>	<p>Seventy percent of ORN patients treated with surgery and hyperbaric oxygen (HBO) healed, compared to 51% with surgery alone, suggesting that HBO did not outperform standard treatment. HBO increased the chance of healing and improved symptoms such as xerostomia and dysphagia. However, due to insufficient recruitment, the risk of type II error increased, making the results not statistically significant ($p > 0.05$).</p>	
<p>MENDONÇA, L. G. M. et al. Osteoradionecrose - uma complicação da radioterapia na região de cabeça e pescoço: revisão de literatura. <i>Brazilian Journal of Development</i>, [S. l.], v. 7, n. 1, p. 7911–7920, 2021.</p>		<p>Literature review</p>	<p>To analyze the clinical characteristics, risk factors, and treatment modalities of ORN.</p>	<p>Twenty articles were selected, and their data were presented in three tables. After analysis, it was concluded that ORN presents different clinical behaviors and treatment modalities, and risk factors may be associated with radiotherapy, tumor characteristics, and patient conditions. ORN treatment is complex, and there is no consensus in the literature regarding the best approach.</p>
<p>MINIELLO, T. G. et al. Influence of bisphosphonates on clinical features of osteoradionecrosis of the maxilla and mandible. <i>Oral Diseases</i>, v. 25, n. 5, p. 1344-1351, 2019.</p>	<p>Retrospective observational study</p>	<p>To compare the characteristics of ORN between patients who use and those who do not use bisphosphonates.</p>	<p>Osteoradionecrosis (ORN) was more common in the mandible, but maxillary involvement was more frequent in patients who used bisphosphonates ($p = 0.014$). Moreover, there was a trend toward earlier ORN development in this group ($p = 0.21$).</p>	
<p>OMOLEHINWA, T. T.; AKINTOYE, S. O. Chemical and radiation associated jaw lesions. <i>Dental clinics of North America</i>, v. 60, n. 1, p. 265, 2016.</p>		<p>Literature review</p>	<p>To present the pathophysiology and diagnostic criteria of ORN and MRONJ.</p>	<p>Radiographic imaging is essential for diagnosing osteonecrotic lesions but has limitations when used alone. Treatment includes antibiotics, analgesics, debridement, and surgery. Both ORN and MRONJ significantly impact quality of life, making this an important area for tissue engineering research. Current studies explore the use of mesenchymal stem cells and pharmacological compounds, such as anti-sclerostin antibodies, for reconstruction and prevention of osteonecrosis.</p>
<p>RAZIEE, H. R. et al. Interventions for preventing osteoradionecrosis of the jaws in adults receiving head and neck radiotherapy. <i>Cochrane Database of Systematic Reviews</i>, n. 11, 2019.</p>	<p>Systematic review with meta-analysis</p>	<p>To evaluate the effects of interventions to prevent osteoradionecrosis (ORN) of the jaws in adult patients with head and neck cancer undergoing curative or adjuvant (non-palliative) radiotherapy.</p>	<p>Four studies (342 adults) evaluated interventions to prevent osteoradionecrosis (ORN): Platelet-rich plasma did not reduce ORN (OR 3.32, 95% CI 0.58–19.09). Fluoride gel and high-fluoride toothpaste showed no difference (no ORN cases). HBO reduced ORN compared to antibiotics after extractions (RR 0.18, 95% CI 0.43–0.76), but no difference was observed between HBO + antibiotics vs. antibiotics alone before implant placement (RR 3.00, 95% CI 0.14–65.16). Evidence remains uncertain due to low quality and small sample sizes.</p>	
<p>SHAW, R. J. et al. HOPON: a randomized controlled trial of hyperbaric oxygen to prevent osteoradionecrosis of the irradiated mandible after dentoalveolar surgery. <i>International Journal of Radiation Oncology Biology Physics</i>, v. 104, n. 3, p. 530-539, 2019.</p>		<p>Randomized controlled clinical trial</p>	<p>To establish the benefit of HBO in the prevention of ORN after high-risk surgical procedures in irradiated mandibles.</p>	<p>A total of 144 patients were randomized, and data from 100 patients were analyzed for the primary outcome. The incidence of ORN at 6 months was 6.4% and 5.7% for the HBO and control groups, respectively (odds ratio 1.13, 95% CI 0.14–8.92; $P = 1$). Patients in the HBO group experienced fewer acute symptoms, but there were no significant differences in late pain or quality of life. The dropout rate was higher in the HBO group. The low incidence of ORN makes the routine recommendation of HBO unnecessary for dental extractions or implant placement in irradiated mandibles.</p>
<p>SILVA, E. C. A. et al. Osteonecrose dos maxilares associada ao uso de bisfosfonatos: Recidiva após radioterapia de cabeça e pescoço. <i>Revista Odontológica do Brasil Central</i>, v. 24, n. 68, 2015.</p>	<p>Clinical case report</p>	<p>To report an unprecedented case describing the recurrence of mandibular osteonecrosis after surgical debridement and PRP infusion in a patient who subsequently underwent head and neck radiotherapy for the treatment of recurrent multiple myeloma (MM).</p>	<p>After the case presentation, the pathophysiology, risk factors, diagnostic criteria, and treatments for ORN were discussed. The use of bisphosphonates is considered an additional risk factor for ORN development. Prevention, including pre-radiotherapy dental evaluation and strict oral care, is emphasized as the best strategy. The scarcity of effective and standardized treatment protocols for ORN is highlighted.</p>	

YIN, Y. et al. Evaluation of hyperbaric oxygen therapy for the osteoradionecrosis of the jaws: Meta-analysis. *Hua xi kou qiang Yixue Zazhi*= West China Journal of Stomatology, v. 39, n. 6, p. 690-697, 2021.

Systematic review with meta-analysis

To systematically investigate the effects of hyperbaric oxygen and other approaches in the treatment of osteoradionecrosis of the jaws (ORN).

A meta-analysis including four randomized clinical trials and seven cohort studies found no significant differences between the group treated with hyperbaric oxygen combined with surgery and antibiotics and the group treated with surgery and antibiotics alone (RR = 1.16, 95% CI 0.86–1.58, $P > 0.05$). Similarly, no significant differences were found between the hyperbaric oxygen group and the groups receiving antibiotics (RR = 0.83, 95% CI 0.63–1.09, $P > 0.05$), antifibrotic drugs (RR = 0.07, 95% CI 0.00–155.86, $P > 0.05$), or other interventions (RR = 0.89, 95% CI 0.67–1.19, $P > 0.05$). Hyperbaric oxygen did not demonstrate superiority in the treatment of mandibular osteoradionecrosis (ORN).

DISCUSSION

The pathophysiology of osteoradionecrosis is explained by a triad consisting of hypovascularization of the affected region, hypoxia, and hypocellularity. These factors, associated with poor oral hygiene, high doses of radiation, and the use of bisphosphonates, favor the onset of the condition. Regarding the treatment of the condition, there are limited options available, ranging from conservative approaches, such as the use of antibiotics and mouthwashes, to more aggressive surgical interventions, including debridement and bone reconstruction.¹⁵

Bisphosphonates are drugs widely used in the treatment of conditions such as osteoporosis and bone metastases, due to their ability to inhibit bone resorption by osteoclasts by stimulating apoptosis and osteoblastic activity in the formation of new bone tissue. The association between bisphosphonates and ORN remains unclear, however, there are reports that show that their use contributes to the early development of ORN, especially in patients who have undergone high-dose radiation therapy (>0Gy).

Patients receiving bisphosphonates, especially intravenously, and undergo radiotherapy in the head and neck region, have an increased risk of developing bone necrosis. This is due to the fact that these patients are constantly exposed to radiation, compromising vascularization, one of the three points of the triad, and decreas-

ing bone regeneration capacity, thus leaving viable tissue more susceptible to necrosis.⁶¹⁵

Therapeutic options for the treatment of ORN include surgical resection of the lesion, treatment with antibiotics, or treatment with antifibrotic drugs. Therapy is individualized and can be used alone or in combination with existing treatments. The possibility of treatment with platelet-rich plasma has also been suggested, but there has been no significant improvement in the treatment of patients undergoing such treatment.¹⁷

A recent therapeutic alternative is treatment with PENTO, which achieved complete control of the disease in a significant number of patients in all studies analyzed (n=). However, there is no standardized protocol or pharmacological doses for the administration of this therapy. It is necessary to evaluate the possibility of combining this treatment with antibiotics, in addition to studies with larger, high-quality samples to develop a successful algorithm for the management of ORN.¹⁸

A new therapeutic option to be used in conjunction with traditional treatment is currently being discussed. The use of hyperbaric oxygen is being discussed, although its effectiveness remains controversial and there are no studies robust enough to indicate or contraindicate its use. The study with the largest N conducted to date was of 00 patients, which showed that the incidence of ORN at months was ,% and ,% for the HBO and con-

trol groups, respectively (odds ratio, ; confidence interval, %, 0,-,; $P =$). However, patients in the HBO-treated group had fewer acute symptoms, but there were no significant differences in late pain or quality of life. The dropout rate was higher in the HBO group.³⁴⁵⁶⁷⁸⁹¹²

Another study conducted in 2000 analyzed four randomized clinical trials and seven cohort studies and also found no significant differences between the group treated with hyperbaric oxygen combined with surgery and antibiotics and the group that received only surgery and antibiotics. Hyperbaric oxygen did not demonstrate superiority in the treatment of osteoradionecrosis of the jaws.¹²

A third study, conducted by FORNER, divided patients into randomized groups, one receiving HBO before and after necrotic bone removal surgery, while the other underwent surgery alone. Although the HBO-treated group had a higher healing rate (0% vs. %), the difference was not statistically significant due to insufficient recruitment (n=0). In addition, improvements in xerostomia, salivary flow, and dysphagia were observed in patients who received HBO before and after surgery.⁵⁷¹²

FINAL CONSIDERATIONS

In summary, the interrelationship between osteoradionecrosis and the use of bisphosphonates highlights the importance of a multidisciplinary approach in the management of patients

undergoing these treatments, especially those undergoing high levels of radiation. Furthermore, the best treatment options currently remain traditional alternatives, including surgical resection of the lesion, treatment

with antibiotics, or treatment with antifibrotic drugs, either alone or in combination. Despite the prospect of new treatments such as PENTA and hyperbaric oxygen, long-term prospective studies are needed to better

understand the pathogenesis of ORN in order to explore and guide the best clinical management for healthcare professionals and their patients.

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