SURGICAL MANAGEMENT OF JAW OSTEONECROSIS ASSOCIATED WITH BISPHOSPHONATE USE: THERAPEUTIC APPROACHES AND CHALLENGES

MANEJO CIRÚRGICO DA OSTEONECROSE DOS MAXILARES ASSOCIADA AO USO DE BISFOSFONATOS: ABORDAGENS E DESAFIOS TERAPÊUTICOS

TRATAMIENTO QUIRÚRGICO DE LA OSTEONECROSIS MANDIBULAR ASOCIADA A BIFOSFONATOS: ENFOQUES TERAPÉUTICOS Y DESAFÍOS

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ABSTRACT
Medication-related osteonecrosis of the jaws associated with bisphosphonate use represents a complex clinical condition characterized by impaired bone healing and significant morbidity. Although conservative management has historically been prioritized, surgical approaches have increasingly been incorporated, particularly in refractory cases or advanced stages of the disease. The present study aimed to perform a narrative review of the literature regarding the surgical management of bisphosphonate-associated osteonecrosis of the jaws, emphasizing therapeutic approaches and clinical challenges. A literature search was conducted in PubMed/MEDLINE, SciELO, and internationally indexed scientific databases, including studies published between 2014 and 2024. A total of 20 articles, comprising literature reviews, case series, and case reports, were included. The analysis revealed marked heterogeneity in surgical techniques and a lack of standardized treatment protocols, reflecting the multifactorial nature of the condition. Surgical indication should be individualized, taking into account the extent of necrosis, systemic conditions, and response to conservative therapy. Adequate soft tissue management was identified as a key determinant of successful outcomes, while adjunctive therapies showed promising results despite limited levels of evidence. It is concluded that surgical management represents a relevant therapeutic option for bisphosphonate-associated osteonecrosis of the jaws, requiring careful clinical assessment and a multidisciplinary approach, while further robust clinical studies are needed to establish evidence-based guidelines.

Keywords: Osteonecrosis of the Jaws. Bisphosphonates. Oral and Maxillofacial Surgery. Surgical Management. Adjunctive Therapies.

RESUMO
A osteonecrose dos maxilares associada ao uso de bisfosfonatos representa uma condição clínica complexa, caracterizada por comprometimento do reparo ósseo e elevada morbidade. Apesar do predomínio histórico de abordagens conservadoras, o manejo cirúrgico tem sido progressivamente incorporado como estratégia terapêutica em casos refratários ou em estágios mais avançados da doença. O presente estudo teve como objetivo realizar uma revisão narrativa da literatura acerca do manejo cirúrgico da osteonecrose dos maxilares associada ao uso de bisfosfonatos, enfatizando as diferentes abordagens terapêuticas e os desafios clínicos envolvidos. A busca bibliográfica foi conduzida nas bases de dados PubMed/MEDLINE, SciELO e literatura científica internacional indexada, contemplando artigos publicados entre 2014 e 2024. Foram incluídos 20 estudos, entre revisões de literatura, séries de casos e relatos clínicos. A análise evidenciou ampla heterogeneidade quanto às técnicas cirúrgicas empregadas e ausência de protocolos padronizados, refletindo a natureza multifatorial da doença. Observou-se que a indicação cirúrgica deve ser individualizada, considerando a extensão da necrose, o estado sistêmico do paciente e a resposta ao tratamento conservador. O manejo adequado dos tecidos moles mostrou-se fator determinante para o sucesso terapêutico, enquanto as terapias adjuvantes apresentaram resultados promissores, porém sustentados por evidências limitadas. Conclui-se que o manejo cirúrgico constitui abordagem relevante no tratamento da osteonecrose dos maxilares associada aos bisfosfonatos, devendo ser pautado em avaliação criteriosa e abordagem multidisciplinar, enquanto novos estudos de maior robustez metodológica são necessários para a consolidação de diretrizes clínicas baseadas em evidências.

Palavras-chave: Osteonecrose dos Maxilares. Bisfosfonatos. Cirurgia Bucomaxilofacial. Manejo Cirúrgico. Terapias Adjuvantes.

RESUMEN

La osteonecrosis mandibular asociada a bifosfonatos (ONB) representa una afección clínica compleja caracterizada por un deterioro de la reparación ósea y una alta morbilidad. A pesar del predominio histórico de los enfoques conservadores, el manejo quirúrgico se ha incorporado progresivamente como estrategia terapéutica en casos refractarios o en etapas más avanzadas de la enfermedad. Este estudio tuvo como objetivo realizar una revisión bibliográfica narrativa sobre el manejo quirúrgico de la osteonecrosis mandibular asociada a la ONB, destacando los diferentes enfoques terapéuticos y los desafíos clínicos que implica. La búsqueda bibliográfica se realizó en PubMed/MEDLINE, SciELO y bases de datos internacionales indexadas de literatura científica, incluyendo artículos publicados entre 2014 y 2024. Se incluyeron veinte estudios, incluyendo revisiones bibliográficas, series de casos e informes clínicos. El análisis reveló una amplia heterogeneidad en cuanto a las técnicas quirúrgicas empleadas y la falta de protocolos estandarizados, lo que refleja la naturaleza multifactorial de la enfermedad. Se observó que la indicación quirúrgica debe individualizarse, considerando la extensión de la necrosis, el estado sistémico del paciente y la respuesta al tratamiento conservador. El manejo adecuado de los tejidos blandos demostró ser un factor determinante para el éxito terapéutico, mientras que las terapias adyuvantes mostraron resultados prometedores, aunque con evidencia limitada. Se concluye que el manejo quirúrgico constituye un enfoque relevante en el tratamiento de la osteonecrosis mandibular asociada a bifosfonatos y debe basarse en una evaluación cuidadosa y un enfoque multidisciplinario. Se requieren nuevos estudios con mayor solidez metodológica para la consolidación de guías clínicas basadas en la evidencia.

Palabras clave: Osteonecrosis Mandibular. Bifosfonatos. Cirugía Oral y Maxilofacial. Manejo Quirúrgico. Terapias Adyuvantes.

1 INTRODUCTION

Osteonecrosis of the jaws associated with the use of medications, especially bisphosphonates, is a clinical condition of great relevance in dental and medical practice, due to its functional and aesthetic impact and on the quality of life of patients. Bisphosphonates are widely used in the treatment of osteometabolic and oncological diseases, such as osteoporosis, multiple myeloma, and bone metastases, for their ability to inhibit bone resorption. However, the prolonged use of these drugs has been associated with the development of osteonecrosis of the jaws, a condition characterized by persistent bone exposure, local infection, and difficulty in healing, especially after invasive dental procedures, which reinforces their growing clinical relevance in recent years (ALDHALAAN; BAQAIS; AL-OMAR, 2020; GAUTAM; SAMAGH, 2022).

The pathogenesis of bisphosphonate-related osteonecrosis of the jaws has not yet been fully elucidated, and is considered multifactorial. Among the proposed mechanisms are the suppression of bone remodeling, the inhibition of angiogenesis, direct toxicity to soft tissues, and the presence of bacterial infection associated with oral biofilm. In addition, local factors such as tooth extractions, ill-fitting prostheses, and repetitive trauma play a fundamental role in triggering the disease, especially in the mandible, the most frequently affected region. This etiopathogenic complexity contributes to the difficulty in establishing standardized and effective therapeutic approaches (ROSELLA et al., 2016; ALDHALAAN; BAQAIS; AL-OMAR, 2020).

Historically, the treatment of osteonecrosis of the jaws has prioritized conservative approaches, focusing on infection control, pain relief, and clinical follow-up. However, the unfavorable evolution observed in moderate and advanced cases, often classified as stages II and III, has led to the expansion of surgical indications. Recent evidence shows that surgical management, including procedures such as debridement, sequestrectomy, and bone resection, can promote better healing rates and clinical resolution when correctly indicated and executed, configuring itself as a relevant therapeutic alternative in cases refractory to conservative treatment (DA SILVA et al., 2016; VETTORI et al., 2021).

In addition to conventional surgical techniques, adjuvant approaches have been incorporated with the aim of optimizing therapeutic results. The use of laser, photobiomodulation, platelet-rich fibrin (PRF), and other ancillary therapies has shown promising results in reducing pain, controlling infection, and accelerating tissue repair. However, despite the advances observed in the last decade, there is still no consensus on the ideal surgical protocol, nor on the standardization of associated therapies, which

reinforces the need for individualization of treatment and a critical analysis of the available evidence (VETTORI et al., 2021; EL MOBADDER et al., 2023).

In view of the methodological heterogeneity of the published studies, the predominance of case reports and clinical series, as well as the absence of universally established surgical guidelines, there is a gap in scientific knowledge regarding the surgical management of osteonecrosis of the jaws associated with the use of bisphosphonates. Thus, the present study aims to carry out a narrative review of the literature, based on studies published in recent years in recognized databases, addressing the main surgical techniques employed, their clinical results and the therapeutic challenges involved, contributing to the updating and foundation of clinical practice.

2 METHODOLOGY

The present study consists of a narrative review of the literature, with a descriptive and qualitative approach, developed with the objective of critically analyzing the current state of scientific knowledge about the surgical management of osteonecrosis of the jaws associated with the use of bisphosphonates, with emphasis on the different therapeutic approaches described and the main clinical challenges reported in the specialized literature.

The bibliographic search strategy was conducted in a structured manner in recognized databases in the health area, including PubMed/MEDLINE, SciELO, and indexed international scientific literature, in the period between January and March 2025. Studies published between 2014 and 2024 were considered, in order to include contemporary evidence relevant to current clinical practice. To identify the studies, controlled and uncontrolled descriptors were used, in Portuguese and English, related to the investigated theme, such as: osteonecrosis of the jaws, bisphosphonates, medication-related osteonecrosis of the jaw, bisphosphonate-related osteonecrosis, surgical management and oral and maxillofacial surgery, combined by means of Boolean operators, mainly the AND operator, with the objective of increasing the sensitivity of the search without compromising its specificity.

Original scientific articles, literature reviews, narrative reviews, case series, and case reports that directly addressed the surgical management of osteonecrosis of the jaws associated with the use of bisphosphonates were included in the analytical corpus. The studies should be available in full, published in indexed scientific journals, carried out in human beings and written in Portuguese or English, regardless of gender or age group of the population studied, as long as they present relevant data on surgical techniques, adjuvant therapies or clinical outcomes.

Duplicate studies, publications that exclusively addressed osteonecrosis of the jaws due to radiotherapy or related to other drugs without direct association with bisphosphonates, as well as articles that did not present clinical or methodological relevance in relation to the proposed objectives were excluded. Additionally, experimental studies in animal models and in vitro research were not considered, as they do not directly reflect human clinical practice.

The study selection process was carried out in sequential stages, starting with the reading of titles and abstracts, followed by the analysis of the full text of potentially eligible publications. At the end of this process, 20 scientific articles met the established criteria and composed the final set of studies analyzed. Data extraction was carried out in a systematic manner, considering variables such as year of publication, study design, type of surgical approach used, use of adjuvant therapies and main reported clinical outcomes.

The synthesis and analysis of the data were conducted in a critical, interpretative and thematic manner, respecting the methodological heterogeneity of the included studies, an inherent characteristic of narrative reviews. The findings were discussed in the light of the available literature, seeking to identify convergences, divergences, and gaps in scientific knowledge. One limitation of the present study is the lack of systematic evaluation of the methodological quality of the publications included, as well as the possibility of selection bias, aspects considered inherent to the adopted design.

3 RESULTS AND DISCUSSION

The analysis of the **20 scientific articles** included in this narrative review demonstrated that the surgical management of osteonecrosis of the jaws associated with the use of bisphosphonates has been widely discussed in the recent literature, but with significant **methodological heterogeneity** regarding the study designs, surgical techniques used, and criteria for evaluating clinical outcomes. There was a predominance of literature reviews, case series, and clinical reports, reflecting the scarcity of prospective and controlled studies on the subject.

The results showed that **surgical approaches** have been progressively indicated, especially in cases classified as moderate and advanced or in those refractory to conservative therapies. Procedures such as **surgical debridement**, **sequestrectomy,** and **bone resection** have been described as effective strategies for infection control, pain reduction, and healing promotion, especially when associated with adequate soft tissue management and control of local risk factors.

However, the studies analyzed diverged regarding the **extent of the surgical intervention**, ranging from more conservative approaches to broader bone resections. Some

authors reported better clinical results with complete removal of necrotic bone until bleeding margins were obtained, while others advocated less invasive procedures, aiming to reduce the risk of necrosis progression. This variability reinforces the lack of consensus on the ideal surgical protocol.

Another relevant aspect identified in the results was the increasing use of **adjuvant therapies associated with surgery**, such as laser, photobiomodulation, and platelet concentrates, especially platelet-rich fibrin (PRF). In general, studies that employed these strategies reported additional benefits, including improved tissue repair, reduced pain symptoms, and better infection control. However, these findings are predominantly based on low-level evidence, which limits the generalizability of the results.

3.1 PATHOPHYSIOLOGICAL ASPECTS OF OSTEONECROSIS OF THE JAWS AND SURGICAL IMPLICATIONS

The contemporary interpretation of osteonecrosis of the jaws associated with the use of bisphosphonates is based on the understanding that the prolonged suppression of bone remodeling, associated with the inhibition of angiogenesis, significantly compromises the repairing capacity of maxillomandibular bone tissues. Rosella et al. (2016) emphasize the direct interference of bisphosphonates in bone turnover as a central factor for the development of necrosis, while AlDhalaan, Baqais, and Al-Omar (2020) expand this perspective by incorporating soft tissue toxicity and the role of oral biofilm in maintaining the inflammatory-infectious process. Although they start from different approaches, these authors converge in recognizing that the persistence of biologically non-viable bone is a key element for the progression of the disease.

From this perspective, surgical management should not be understood only as a late therapeutic alternative, but as a rational strategy aimed at removing a tissue incapable of biological reintegration. Thus, the surgical decision is directly related to the inability of the necrotic bone to respond to conservative therapies, establishing a conceptual link between pathophysiology and surgical indication.

3.2 EVOLUTION OF THERAPEUTIC STRATEGIES IN THE TREATMENT OF OSTEONECROSIS OF THE JAWS

The literature shows a clear evolution in the therapeutic understanding of osteonecrosis of the jaws over the last decades. Initially, conservative treatment was widely advocated as a priority approach, especially with the aim of minimizing surgical morbidities in patients who are often systemically compromised. However, Da Silva et al. (2016) question

the effectiveness of this approach in more advanced stages, demonstrating that necrotic bone maintenance is associated with persistence of infection and symptomatic recurrence.

In partial contrast, Rosella et al. (2016) recognize that conservative approaches still play a relevant role in the early stages of the disease, especially when associated with strict control of local factors. This apparent divergence does not represent a conceptual contradiction, but rather the consolidation of a more refined understanding, in which the therapeutic choice should be guided by the clinical stage and the individual biological response. In this context, surgery progressively emerges as an indicated approach when conservative therapy proves to be insufficient, reflecting a paradigmatic change based on the critical analysis of clinical outcomes.

3.3 SURGICAL APPROACHES AND EXTENSION OF THE INTERVENTION: COMPARATIVE ANALYSIS OF THE LITERATURE

The definition of the ideal extent of surgical intervention is one of the most controversial points in the literature analyzed. Da Silva et al. (2016) report favorable clinical outcomes with different levels of intervention, ranging from limited debridement to more extensive resections, without establishing unequivocal superiority of a specific technique. In contrast, Romanos et al. (2022) argue that more aggressive approaches, with complete removal of necrotic bone until viable margins are obtained, are associated with better healing rates and clinical resolution.

This divergence should not be interpreted as an inconsistency of scientific evidence, but as a reflection of the multifactorial nature of osteonecrosis of the jaws. The response to surgical treatment depends on the interaction between the extent of necrosis, individual biological response, drug history, and the patient's systemic conditions. Thus, the absence of a universal surgical protocol reinforces the understanding that the management of the disease should be adaptive and individualized, and not based on rigid therapeutic models.

3.4 SOFT TISSUE MANAGEMENT AND IMPACT ON SURGICAL OUTCOMES

Unlike the controversy observed regarding the extent of bone intervention, the literature shows greater convergence regarding the role of soft tissues in the success of surgical treatment. Vettori et al. (2021) highlight that primary closure without tension is a determining factor for adequate healing, while Medeiros et al. (2019) reinforce that failures in this closure are directly associated with recurrence of bone exposure.

These findings indicate that surgical success is not exclusively conditioned to the removal of necrotic bone, but to the reconstruction of a tissue environment favorable to

healing. Thus, regardless of the bone technique employed, careful management of soft tissues plays a central role in the predictability of clinical outcomes, becoming an essential component of surgical planning.

3.5 ADJUVANT THERAPIES IN THE SURGICAL MANAGEMENT OF OSTEONECROSIS OF THE JAWS

The use of adjuvant therapies has been widely explored as an attempt to overcome the limitations imposed by the pathophysiology of osteonecrosis of the jaws. Vettori et al. (2021) report improved healing with the use of platelet-rich fibrin (PRF) associated with surgery, while El Mobadder et al. (2023) describe significant pain reduction and functional improvement with photobiomodulation. These results suggest a potential benefit of these strategies in supporting tissue repair.

However, Gautam and Samagh (2022) warn that most of the available evidence derives from case reports and clinical series, which limits the generalization of findings. This contrast between promising clinical results and methodological fragility reinforces the need for cautious interpretation of the data, as well as prospective studies that allow for a systematic evaluation of the real contribution of these therapies as a complement to surgical management.

3.6 INFLUENCE OF SYSTEMIC AND PHARMACOLOGICAL FACTORS ON SURGICAL TREATMENT

The literature analyzed converges in recognizing that systemic factors exert a determining influence on the outcomes of surgical treatment of osteonecrosis of the jaws. AlDhalaan, Baqais, and Al-Omar (2020) highlight that the time and route of administration of bisphosphonates significantly increase the risk of developing the disease, while Fusco et al. (2022) point out that cancer patients have greater clinical and biological complexity, directly impacting the response to treatment.

Despite addressing different clinical contexts, these authors agree that therapeutic decision-making should be multidisciplinary and individualized, especially with regard to the continuity or suspension of drug therapy. In this sense, surgical planning goes beyond the limits of isolated dental practice, requiring integration between different areas of health to optimize clinical results.

3.7 LIMITATIONS OF SCIENTIFIC EVIDENCE AND IMPLICATIONS FOR CLINICAL PRACTICE

Despite the advances observed in the surgical management of osteonecrosis of the jaws, the literature still has significant limitations. Da Silva et al. (2016) and Gautam and Samagh (2022) agree in pointing to the scarcity of prospective studies and controlled clinical trials as the main obstacle to the establishment of high-level evidence-based therapeutic guidelines.

More than a methodological limitation, this gap reflects the biological and clinical complexity of the disease, which makes it difficult to standardize therapeutic interventions. Thus, clinical practice remains based on low to moderate level evidence, requiring critical judgment, clinical experience and constant scientific updating from the professional.

4 CONCLUSION

A critical analysis of the literature shows that the surgical management of osteonecrosis of the jaws associated with the use of bisphosphonates represents a relevant but complex therapeutic strategy, whose indication and management should be based on an in-depth understanding of the pathophysiology of the disease and on the individualized evaluation of each patient. The persistence of biologically non-viable bone, associated with the suppression of bone remodeling and angiogenic deficiency, limits the efficacy of exclusively conservative approaches in more advanced stages, justifying the careful expansion of surgical indications.

The studies analyzed demonstrate that there is no consensus regarding the ideal extent of surgical intervention, reflecting the multifactorial nature of osteonecrosis of the jaws and the clinical heterogeneity of the affected patients. In this context, the success of the treatment is not conditioned by the adoption of a specific surgical technique, but by the ability to adapt the approach to the biological characteristics of the bone tissue, the extent of necrosis and the systemic conditions of the individual. The absence of universal protocols reinforces the need for flexible surgical planning, based on critical analysis of the available evidence.

Consistently, the literature converges in recognizing adequate soft tissue management as a central element for the predictability of surgical outcomes. Tension-free primary closure and control of the local environment are determinant for healing and prevention of recurrence, regardless of the bone technique employed. In addition, the use of adjuvant therapies, such as photobiomodulation and platelet concentrates, has potential clinical benefit, although there is still a lack of robust evidence to allow their incorporation as standardized protocols.

Systemic and pharmacological factors exert a decisive influence on the planning and results of surgical treatment, especially in patients undergoing prolonged or intravenous bisphosphonate therapies and in individuals with oncological comorbidities. Thus, the multidisciplinary approach becomes indispensable for therapeutic decision-making, particularly with regard to the continuity or suspension of drug therapy.

Finally, although advances in the surgical management of osteonecrosis of the jaws are evident, the literature is still characterized by the predominance of observational studies and the scarcity of controlled clinical trials. This limitation prevents the consolidation of high-level evidence-based guidelines and reinforces the need for methodologically robust future research. Until such evidence is available, the management of the disease should be supported by careful clinical judgment, multidisciplinary integration, and constant scientific updating, aiming at optimizing therapeutic outcomes and improving the quality of life of patients.

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