

Maxillary osteonecrosis of the jaw. A multidisciplinary approach, communication strategies, and technological tools for prophylaxis

Mihai Vlad Golu, Balint Botond Bogoz, Cecilia Petrovan, Despina Bereczki Temistocle,
Sergiu Guzun, Alina Ormenisan

Faculty of Dental Medicine, "George Emil Palade" University of Medicine, Pharmacy, Science, and Technology of
Targu-Mures, Targu Mures, Romania

ABSTRACT

Background. Maxillary osteonecrosis, particularly medication-related osteonecrosis of the jaw (MRONJ), necessitates prompt identification and a comprehensive approach for effective management. Early diagnosis and proactive dental care are crucial in mitigating the complications associated with this condition.

Aims. This study aims to outline the importance of early detection, multidisciplinary collaboration, patient education, and proactive dental care in the management of maxillary osteonecrosis.

Methods. The study emphasizes the utilization of standardized medical letters to facilitate communication between prescribing physicians and dentists, while ensuring the timely exchange of essential patient information. Additionally, patient education plays a pivotal role, with the distribution of informative leaflets at the initiation of Bone Modifying Agents (BMA) treatment, emphasizing the risks associated with MRONJ and the significance of maintaining oral health and making appropriate lifestyle choices.

Results. Dentists are key stakeholders in the prophylaxis of MRONJ, undertaking primary and secondary prevention measures. Primary prophylaxis encompasses various dental procedures aimed at reducing bacterial load and mucosal irritation. Secondary prophylaxis involves educating patients on maintaining optimal oral health and adopting lifestyle modifications. Furthermore, an Android application assists dentists in assessing MRONJ risk factors and making informed treatment decisions based on factors such as BMA type, dose, duration of administration, and the presence of dental and general risk factors.

Conclusions. In conclusion, a proactive approach to managing Maxillary Osteonecrosis involves early detection, multidisciplinary collaboration, patient education, and proactive dental care. By integrating standardized communication tools, patient education materials, and risk assessment technology, healthcare providers can optimize patient outcomes and minimize the incidence and severity of MRONJ complications.

Keywords: osteonecrosis of the jaw, bisphosphonates, dental care, antiangiogenic treatment, prophylaxis tools

INTRODUCTION

Maxillary osteonecrosis represents a debilitating condition of the maxilla that can significantly impact the quality of life for patients. This pathology is influenced by various external factors and is known by various names, such as Osteoradionecrosis [1]

and MRONJ when related to bisphosphonate or other antiresorptive or antiangiogenic medications. These types of osteonecrosis are characterized by the necrosis of the bone tissues of the maxilla and may result from factors such as radiotherapy in the oro-maxillofacial region, steroid therapy, recreational drug abuse, or the use of bone remodeling

Corresponding authors:

Despina Bereczki Temistocle

E-mail: despina.bereczki-temistocle@umfst.ro

Article History:

Received: 29 February 2024

Accepted: 10 March 2024

medications either for treating bone conditions such as osteoporosis or in the treatment of oncological patients.

Osteonecrosis of the maxilla associated with the administration of bisphosphonate-class drugs, specifically Bisphosphonate-Related Osteonecrosis of the Jaw (BRONJ), which was initially documented in the early 2000s [2,3]. After the recognition of OM occurrences in individuals undergoing treatment with other antiresorptive or antiangiogenic medications, the nomenclature was revised to Medication-Related Osteonecrosis of the Jaw (MRONJ) in 2014 [4]. Furthermore, updates to the staging system were implemented in 2022 [5].

Maxillary osteonecrosis is a complex condition, and its impact on patients can be devastating. Clinical manifestations include intense pain, ulcerations, and even oro-sinus fistulas, leading to significant difficulties in feeding, and speech, and an overall compromised quality of life. In this context, it is essential to carefully understand and investigate the risk factors associated with maxillary osteonecrosis, as well as to identify effective methods of prevention and treatment.

The incidence of MRONJ exhibits variability, spanning a range of 0.2% to 18%. This variance is contingent upon several factors, including the specific type of BMA administered, the underlying pathology for which the BMA is prescribed, the dosage administered, and the duration of the medication regimen [6–10].

Early diagnosis and a multidisciplinary approach are two crucial elements in managing maxillary osteonecrosis. Through early diagnosis, the signs and symptoms can be identified, allowing for prompt and efficient treatment initiation. This could reduce the severity of the disease and prevent subsequent complications.

Furthermore, a particularly important aspect is the multidisciplinary approach to patients at risk of maxillary osteonecrosis. Since osteonecrosis can be induced by a variety of factors, including drug treatments and radiotherapy, close collaboration between prescribing physicians and stomatologists is essential [11]. An individualized treatment tailored to the specific needs of each patient can only be developed through coordinated efforts among the involved specialists and it is assumed that the development and implementation of an appropriate dental management plan for patients at risk of Osteonecrosis can significantly reduce the incidence and severity of this condition. This hypothesis can be supported by reviewing the literature, evaluating existing protocols, and analyzing the outcomes of patients who have undergone these management strategies.

The objective was to evaluate and present dental management strategies for patients at risk of Oste-

onecrosis, including the identification of recommended procedures and protocols for prevention and treatment.

MATERIAL AND METHODS

We conducted an online survey using a questionnaire developed for this purpose, which was sent to several dentists in our center, to find out various opinions from doctors at different levels of experience or familiarity with the studied pathology. The survey aimed to identify awareness of the disease and risk factors, prescribing practices, and current preventive measures used. The questionnaire was developed in multiple-choice format and was distributed in software copies using Google Docs Forms (free). The initial section of the questionnaire gathered their demographic data, and the second included questions on various current practices related to osteonecrosis-producing drugs.

The anonymously generated responses were then compiled and analyzed. A statistical analysis was carried out including elements of descriptive statistics and elements of inferential statistics. To determine the association between qualitative variables, we used the Chi-square test and where appropriate the Fisher exact test. The significance threshold chosen for the p-value was 0.05 and statistical analysis was performed using Microsoft Excel 2020 and IBM SPSS version 20 software.

RESULTS

The investigation comprised responses from 65 dental practitioners within our center, manifesting a heightened response rate among female participants at 63.1% as opposed to 36.9% for their male counterparts. Encompassing a demographic of doctors aged 25 to 52, with an average age of 32 years, the study involved professionals engaged in dental practices across both private and state sectors. Participants exhibited diverse professional backgrounds, reflective of variations in both their formal training and practical maneuvers within the field. The respondents' characteristics are presented in Table 1.

The subsequent section of the questionnaire comprised inquiries pertaining to the pathology of jaw necrosis, adverse reactions associated with BMA, encountered trade names in contemporary clinical practice, and the overarching management approaches employed for patients undergoing antiresorptive or antiangiogenic treatments. Regarding the definition of maxillary osteonecrosis 78.5% preferred the old definition BRONJ. The diagnosis was made based on clinical but also radiological examination especially by young doctors ($p=0.040$) and those physicians who predominantly practice surgical procedures ($p=0.042$). Doctors included in

TABLE 1. Respondent Characteristics

Respondent Characteristics	Number (percent)
Gender	
Masculin	24 (36.9%)
Feminine	41 (63.1%)
Professional status	
Senior physician	4 (6.2%)
Specialist	16 (24.6%)
Resident	29 (44.6%)
General practitioner	16 (24.6%)
Procedures	
Prophylaxis	47 (72,3%)
Odontology	48 (73.8%)
Endodonty	37 (56.9%)
Orthodontics	11 (16.9%)
Surgery	37 (56.9%)
Parodontology	24 (36.9%)

the study reported that they discontinue BMA medication for all dental maneuvers, especially surgical maneuvers. It is also noted that young doctors practice this protocol more often in all dental maneuvers performed ($p=0.008$ for scaling, $p=0.04$ for fillings, $p=0.039$ for endodontic treatments). This is not consistent with the literature and the reasons for this BMA discontinuation management need to be identified and continuing medical education needs to be improved. There is insufficient evidence to support or refute the need to discontinue BMA prior to dental interventions. BMA administration may be deferred at the discretion of the treating physician, in conjunction with a discussion with the patient and dentist.

DISCUSSIONS

The survey analysis incorporated 65 responses from physicians aged 25 to 53, exhibiting an average age of 32, and featuring a predominance of women, constituting 63% of the sample, working across both urban and rural settings. The queried physicians engage in diverse dental procedures encompassing prophylactic, aesthetic, endodontic, and odontological interventions; however, a minority among them undertake surgical operations, for which they enlist the expertise of specialists in dento-alveolar or oro-maxillofacial surgery.

Irrespective of workplace setting – be it public or private – and notwithstanding variations in professional training, discernible disparities in attitudes towards patients undergoing bisphosphonate-associated treatments are not evident.

A substantial proportion of dentists, amounting to 87.7%, demonstrate awareness regarding the risk of osteonecrosis of the maxilla in patients undergoing bisphosphonate-associated treatments, with a

predominant attribution to specific bisphosphonates such as alendronate (78.5%) and zoledronate (73.8%).

Contemporary dental practices in Romania employ several forms, some obligatory and others indicative, sanctioned by the Romanian College of Dentists. Notably, the anamnestic questionnaire is frequently administered during initial patient visits, capturing pertinent information concerning the patient's health status, medication history, and identification of any allergies or adverse events in the patient's medical background. Pertinently, within the scope of this investigation, an excerpt from the questionnaire references specific trade names of bisphosphonates like Fosamax, Fosavance, Actonel, Bonviva, Zometa, Aclasta and underscores the pathologies of osteoporosis, as well as the presence or absence of neoplastic diseases. Within the current investigation concerning dentists' knowledge regarding MRONJ, a subset of queries focused on drug molecules linked with MRONJ as a potential side effect. It is pertinent to highlight that most participating dentists successfully recognized the four widely used bisphosphonate names, which are consistent in both the anamnestic questionnaire and our survey. However, it is noteworthy that a limited number of respondents demonstrated recognition of additional bisphosphonate molecules and their corresponding trade names, indicative of a potential gap in awareness among the surveyed dental professionals. The global awareness among dentists regarding Medication-Related Osteonecrosis of the Jaw (MRONJ) remains notably deficient. Challenges persist, particularly in recognizing newly introduced trade names associated with MRONJ, thereby complicating the dental management of patients susceptible to this condition [12-15].

The dentists encompassed in our study exhibit a familiarity rate of 78.5% with the terminology associating maxillary osteonecrosis with BRONJ. It is noteworthy, however, that as of 2014, an alternative nomenclature, MRONJ, was proposed, acknowledging the expanding incidence of osteonecrosis cases linked not only to bisphosphonates but also to other BMAs [4]. As anticipated, practitioners primarily or exclusively engaged in dental surgery demonstrated a notable proficiency in questionnaire completion, relying on clinical examinations for the identification of MRONJ-associated lesions, as indicated by a p-value of 0.04. Conversely, respondents whose practice involved less than 5% surgery exhibited a significantly diminished likelihood of recognizing osteonecrosis as an adverse event linked to BMA, with a p-value of 0.002.

Furthermore, our observations revealed that physicians below the age of 30 tended to diagnose MRONJ primarily through radiological examina-

tions, with a p-value of 0.042. This positive trend is particularly valuable as bone lesions may manifest before the onset of clinical symptoms. Emphasizing the necessity of compiling a comprehensive patient file during the initial dental consultation, including at least a panoramic radiograph, proves critical. Such records can subsequently facilitate comparative analysis with additional radiological investigations, enabling the early detection of any evolving bone changes in these patients.

Concerning the implementation of a dedicated follow-up program, the findings proved to be suboptimal, as only 57% and 43% of practitioners, respectively, extended follow-up services to dentate and edentulous patients. To curtail the incidence of MRONJ, it is imperative to institute a comprehensive clinical and radiological screening protocol for both dentate and edentulous patients, with the results meticulously documented in the patient's record and subjected to comparative analyses in subsequent examinations.

It is imperative for dentists to possess a comprehensive understanding of the management strategies applicable to patients at risk of developing MRONJ. This encompasses a nuanced comprehension of therapeutic modalities and the specific conditions under which they can be judiciously applied. Such knowledge is essential for ensuring optimal patient care and the timely implementation of appropriate interventions aimed at mitigating the risk and potential development of MRONJ.

Multidisciplinary collaboration is imperative in the comprehensive management of patients at risk of developing MRONJ. The prescribing healthcare professional bears the responsibility of informing the patient about this risk and facilitating a timely referral to a dentist for an initial assessment. Subsequently, the dentist assumes a pivotal role by compiling a thorough patient follow-up record and undertaking all requisite dental procedures geared towards minimizing risk factors associated with MRONJ development. Furthermore, it becomes incumbent upon the dentist to educate patients on the critical importance of sustaining optimal oral health practices.

In this context, we advocate for the implementation of a written mode of communication between the prescriber and the dentist. The first segment of this communication would encompass details such as the type of BMA, the administered dosage, the duration of the treatment, and explicit guidance on monitoring these patients. The subsequent section would consist of the dentist's response, tailored to the necessity for dental interventions based on the provided information. This proposed communication framework aims to enhance coordination and information exchange between prescribers and

dentists, ultimately contributing to more effective and collaborative patient care in the context of MRONJ risk management.

To bolster patient support, we have formulated an informative leaflet encompassing essential details pertinent to MRONJ. This informational resource delineates key insights into the pathology, elucidates associated risk factors, and provides practical tips aimed at potentially delaying the onset of MRONJ. This leaflet serves as a valuable educational tool, equipping patients with knowledge essential for proactive engagement in their oral health and MRONJ risk mitigation.

To streamline the workflow for dentists, we have developed an Android application that calculates the risk of MRONJ based on various parameters. These parameters include the type of BMA, dosage, treatment duration, prescribed pathology, patient age, and the presence of additional risk factors. The application categorizes patients into low, medium, or high-risk groups based on these criteria. Subsequently, the app provides guidance on permissible dental treatments and their conditions according to the assigned risk category.

The initial section of the application focuses on information pertaining to the prescribed drug (antiresorptive, immunomodulators, angiogenesis inhibitors), the method of administration (oral or intravenous), treatment duration (less or more than 5 years), and the primary indication for which the BMA treatment was recommended (oncological or non-oncological). Subsequent sections inquire about the existence of risk factors such as periodontal disease, compromised teeth necessitating extraction, poorly fitted prosthetic work, and radiological indicators. Additionally, the application prompts questions related to comorbidity factors such as smoking, diabetes, chemotherapy, age, and any history of MRONJ. The comprehensive assessment provided by the application facilitates a more nuanced risk stratification and guides practitioners in determining appropriate dental treatments based on individual patient profiles. Beyond immediate utility, the Android app emerges as a dynamic learning hub for Continuing Medical Education in dental practice. Integrating seamlessly into daily workflows, it encourages dentists to stay current with evidence-based practices and advancements in MRONJ risk management. As an integral part of ongoing education, the app serves as a practical resource, reinforcing best practices, nurturing a culture of continuous learning, and elevating the quality of care for patients at MRONJ risk.

Doctors participating in the study reported a consistent practice of discontinuing BMA medication for various dental procedures, particularly surgical interventions. Notably, it was observed that

younger doctors adhered to this protocol more frequently across all dental maneuvers, as evidenced by statistically significant findings ($p=0.008$ for scaling, $p=0.04$ for fillings, $p=0.039$ for endodontic treatments). This departure from established literature warrants an exploration of the underlying reasons for such BMA discontinuation practices, and there is a recognized need for enhanced continuing medical education to address these discrepancies.

It is crucial to acknowledge that the prevailing evidence does not decisively support or refute the necessity of discontinuing BMAs prior to dental interventions. The decision to defer BMA administration should be made judiciously by the treating physician, involving a thorough discussion with both the patient and the dentist. This underscores the importance of ongoing medical education to align clinical practices with the current evidence-based recommendations to optimize patient care.

Conflict of interest: none declared

Financial support: none declared

REFERENCES

- Chronopoulos A, Zarra T, Ehrenfeld M, Otto S. Osteoradionecrosis of the jaws: definition, epidemiology, staging and clinical and radiological findings. A concise review. *Int Dent J*. 2018 Feb;68(1):22-30. doi: 10.1111/idj.12318
- Marx RE. Pamidronate (Aredia) and zoledronate (Zometa) induced avascular necrosis of the jaws: a growing epidemic. *J Oral Maxillofac Surg*. 2003 Sep;61(9):1115-7.
- Marx RE, Sawatari Y, Fortin M, Broumand V. Bisphosphonate-induced exposed bone (osteonecrosis/osteopetrosis) of the jaws: risk factors, recognition, prevention, and treatment. *J Oral Maxillofac Surg*. 2005 Nov;63(11):1567-75. doi: 10.1016/j.joms.2005.07.010
- Ruggiero SL, Dodson TB, Fantasia J, Goodday R, Aghaloo T, Mehrotra B, et al. American Association of Oral and Maxillofacial Surgeons Position Paper on Medication-Related Osteonecrosis of the Jaw – 2014 Update. *J Oral Maxillofac Surg*. 2014 Oct 1;72(10):1938-56. doi: 10.1016/j.joms.2014.04.031
- Ruggiero SL, Dodson TB, Aghaloo T, Carlson ER, Ward BB, Kademani D. American Association of Oral and Maxillofacial Surgeons' Position Paper on Medication-Related Osteonecrosis of the Jaws-2022 Update. *J Oral Maxillofac Surg*. 2022 May;80(5):920-43. doi: 10.1016/j.joms.2022.02.008
- Choi WS, Lee JI, Yoon HJ, Min CK, Lee SH. Medication-related osteonecrosis of the jaw: a preliminary retrospective study of 130 patients with multiple myeloma. *Maxillofac Plast Reconstr Surg*. 2017 Jan 5;39(1):1. doi: 10.1186/s40902-016-0099-4
- Yarom N, Shapiro CL, Peterson DE, Van Poznak CH, Bohlke K, Ruggiero SL, et al. Medication-Related Osteonecrosis of the Jaw: MASCC/ASCO Clinical Practice Guideline. *J Clin Oncol*. 2019 Sep 1;37(25):2270-90. doi: 10.1200/JCO.19.01186
- Aljohani S, Fiefel R, Ihbe J, Kühnisch J, Ehrenfeld M, Otto S. What is the effect of anti-resorptive drugs (ARDs) on the development of medication-related osteonecrosis of the jaw (MRONJ) in osteoporosis patients: A systematic review. *J Craniomaxillofac Surg*. 2017 Sep;45(9):1493-502. doi: 10.1016/j.jcms.2017.05.028
- Mirelli C, Marino S, Bovio A, Pederelli S, Dall'Agnola C, Gianni AB, et al. Medication-Related Osteonecrosis of the Jaw in Dental Practice: A Retrospective Analysis of Data from the Milan Cohort. *Dent J (Basel)*. 2022 May 19;10(5):89. doi: 10.3390/dj10050089
- Mhaskar R, Kumar A, Miladinovic B, Djulbegovic B. Bisphosphonates in multiple myeloma: an updated network meta-analysis. *Cochrane Database Syst Rev*. 2017 Dec 18;12(12):CD003188. doi: 10.1002/14651858.CD003188.pub4
- Golu MV, Pascanu I, Toganel C, Petrovan C, Cosarca A, Bereczki Temistocle DL, et al. What Do Prescribers of Bone Modifying Agents Know about Medication-Related Osteonecrosis of the Jaw? Is Current Prevention Enough? *Applied Sciences*. 2022 Jan;12(18):9224. <https://doi.org/10.3390/app12189224>
- Al-Maweri SA, Alshammari MN, Alharbi AR, Bahein AA, Alhaji MN, Al-Shamiri HM, et al. Knowledge and Opinions of Saudi Dentists Regarding Dental Treatment of Patients Undergoing Bisphosphonates. *Eur J Dent*. 2020 Feb;14(1):144-51. doi: 10.1055/s-0040-1701542
- de Lima PB, Brasil VLM, de Castro JFL, de Moraes Ramos-Perez FM, Alves FA, dos Anjos Pontual ML, et al. Knowledge and attitudes of Brazilian dental students and dentists regarding bisphosphonate-related osteonecrosis of the jaw. *Support Care Cancer*. 2015 Dec;23(12):3421-6. doi: 10.1007/s00520-015-2689-6
- Bruckmoser E, Palaoro M, Latzko L, Schnabl D, Neururer SB, Laimer J. Choosing the Right Partner for Medication Related Osteonecrosis of the Jaw: What Central European Dentists Know. *Int J Environ Res Public Health*. 2021 Apr 22;18(9):4466. doi: 10.3390/ijerph18094466
- Patil V, Acharya S, Vineetha R, Nikhil K. Awareness About Medication-Related Osteonecrosis of the Jaw Among Dental Professionals: A Multicentre Study. *Oral Health Prev Dent*. 2020;18(1):505-9. doi: 10.3290/j.ohpd.a43361

CONCLUSIONS

A consistent level of awareness is observed, emphasizing the efficacy of current educational practices. However, the study highlights potential gaps in knowledge concerning alternative bisphosphonate molecules and their trade names, suggesting areas for targeted education.

Dental practices are advised to revise and modernize their historical documentation forms to effectively identify individuals at heightened risk for specific health concerns.

The study exposes suboptimal adherence to dedicated follow-up programs, revealing a gap in post-treatment monitoring, especially for edentulous patients.

The development of an Android application to calculate MRONJ risk marks a groundbreaking stride. More than a risk assessment tool, the Android app acts as a catalyst for informed decision-making among healthcare professionals.

Acknowledgments: for this article all the authors have equal contributions.