Brazilian Dental Science

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UNIVERSIDADE ESTADUAL PAULISTA
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Campus de São José dos Campos

ORIGINAL ARTICLE

DOI: https://doi.org/10.4322/bds.2024.e4125

Knowledge of Brazilian dentists about bisphosphonate-associated osteonecrosis of the jaw

Conhecimento de dentistas brasileiros sobre a osteonecrose dos maxilares associada ao uso de bisfosfonatos

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How to cite: Souza TAM, Zucco GR, Almeida JD. Knowledge of Brazilian dentists about bisphosphonate-associated osteonecrosis of the jaw. Braz Dent Sci. 2024; 27(1):e4125. https://doi.org/10.4322/bds.2024.e4125

ABSTRACT

Osteonecrosis of the jaw associated with bisphosphonate use is a matter of utmost importance in clinical practice for the safe treatment of patients using this medication. **Objective:** The aim of this study was to evaluate the level of knowledge of dentists who carry out clinical practice about bisphosphonate-associated jaw osteonecrosis. **Material and Methods:** The methodology used in the present research consisted of a non-probability sampling approach for the selection of participants. To conduct the study, a questionnaire created on the Google Forms platform was sent via Direct on Instagram to the professionals who agreed to participate. The data were sent for analysis, using the frequency for each response, and the professionals were divided into subcategories according to their time of professional practice. **Results:** Participants were familiar with the purpose of the medication (65%) or had heard of it (34%); regarding the professionals' opinion on their knowledge and practice about bisphosphonate-related osteonecrosis a significant percentage (93.24%) responded positively regarding the existence of side effects resulting from the therapeutic use of bisphosphonates and 48.65% self-evaluated their level of knowledge on the subject as insufficient. **Conclusion:** The study reveals that almost all participating dentists have good knowledge about the effects caused by bisphosphonates, but some of them still do not feel specifically confident about the management and knowledge of jaw osteonecrosis.

KEYWORDS

Bisphosphonate-Associated Osteonecrosis; Bisphosphonates; Jaw; Knowledge; Osteonecrosis.

RESUMO

A osteonecrose dos maxilares associada ao uso de bisfosfonatos é um assunto de suma importância na prática clínica para o atendimento seguro dos pacientes que fazem uso terapêutico do medicamento. **Objetivo:** O objetivo deste trabalho foi avaliar o nível de conhecimento de cirurgiões dentistas que realizam atendimento clínico acerca da osteonecrose dos maxilares associada ao uso dos bisfosfonatos. **Material e Métodos:** A metodologia utilizada na presente pesquisa consistiu em uma abordagem de amostragem não probabilística para a seleção dos participantes. Para conduzir o estudo, enviamos um questionário criado na plataforma Google Forms via Direct no Instagram para os profissionais que concordaram em participar. Os dados foram enviados para análise, usando a frequência para cada resposta, sendo que os profissionais foram divididos em subcategorias por tempo de formação. **Resultados:** Os participantes estavam familiarizados com a finalidade do medicamento (65%) ou já haviam ouvido falar deles (34%); em relação à opinião dos profissionais sobre seu conhecimento e prática acerca da osteonecrose relacionada aos bisfosfonatos, observou-se que 48,65% autoavaliaram seu nível de conhecimento sobre o assunto como insuficiente e uma parcela expressiva (93,24%) respondeu positivamente em relação à existência de efeitos colaterais decorrentes ao uso terapêutico dos bisfosfonatos. **Conclusão:** O estudo revela que quase todos os dentistas participantes possuem um bom conhecimento acerca dos efeitos causados pelos bisfosfonatos, mas que parte deles ainda não se sentem seguros especificamente em relação ao manejo e conhecimento da osteonecrose dos maxilares.

PALAVRAS-CHAVE

Osteonecrose Associada aos Bisfosfonatos; Bisfosfonatos; Maxilares; Conhecimento; Osteonecrose.

INTRODUCTION

Bisphosphonates are antiresorptive drugs that are part of a class of drugs that have high affinity for bone tissue and bind to hydroxyapatite crystals. The medication has a short half-life in plasma, however, it can remain for up to 10 years inside the tissue, preventing the action of osteoclasts and, consequently, inhibiting bone remodeling [1-4]. This type of medication is often used in the treatment of diseases such as osteoporosis, multiple myeloma, bone metastasis, Paget's disease, heterotopic ossification, fibrous dysplasia, osteogenesis imperfecta and hypercalcemia [1,5]. Depending on the duration of the treatment, route of administration and dosage, they can cause some side effects, such as jaw osteonecrosis [6].

Bisphosphonate-associated jaw osteonecrosis is characterized by exposed bone for more than eight weeks in individuals treated with bisphosphonates and with no history of radiotherapy, in addition, it is considered a complex and multifactorial process because it presents some risk factors that contribute to its development, such as the administration of intravenous bisphosphonates, tooth extraction, jaw injuries and poorly positioned partial dentures [1,7]. In addition to bisphosphonates, alendronate, zoledronate, and other drugs such as denosumab and antiangiogenics are related to osteonecrosis of the jaw [8]. For preventing, diagnosing, and treating this disease in the most appropriate manner, it is essential that dentists possess knowledge about this pathology [9].

The maxillary bones are affected due to their location, intimate contact with the oral cavity and their corresponding microbiota [7,10]. This condition can be categorized into four stages: (0) no evidence of necrotic bone, but with the presence of undefined symptoms; (1) bone stripping with no signs of infection; (2) pain and swelling, suggesting bacterial infection; (3) infection beyond the alveolar level; (4) bone exposure with the addition of other symptoms [7,11].

In dentistry, preventive measures are recommended before, after and during initiation of bisphosphonate therapy. Thus, the professional must carry out a complete and careful anamnesis, leading the appointment based on the medical history and use of pharmacological medication of each patient and paying attention to the groups of risk for the development of osteonecrosis [12-14].

Bearing in mind the factors that lead to the unfolding of jaw osteonecrosis, it is understood that this is a topic that should have the attention of dentists, therefore it is necessary to know what is the level of knowledge of professionals around the subject. This research aimed to evaluate the level of knowledge of dentists with clinical practice on the theme bisphosphonate-associated osteonecrosis of the jaw.

MATERIALS & METHODS

This is a descriptive observational study of a qualitative nature, with data collection through questionnaires applied to volunteers. The methodology used in the present research consisted of a non-probability sampling approach to select the participants. The questionnaire was carried out with general dentists and specialist, and distributed through the Instagram social network during the COVID-19 pandemic due to the impossibility of face-to-face interviews.

After receiving approval with protocol number 5.006.594 from the Human Research Ethics Committee (CAAE 48569821.0.0000.0077), the questionnaire, previously prepared and adapted from Hristamyan-Cilev et al. [1] and Masson et al. [15], on knowledge about osteonecrosis induced by bisphosphonates, was sent to dentists via Direct on Instagram. All participants that agreed to answer the questionnaire, first signed the Consent Form. This form outlined the research objective, the benefits of professional participation, and assured the confidentiality and secrecy of responses. Participants completed the questionnaire using the digital platform "Google Forms" which was individually dispatched through Direct on Instagram.

It is crucial to emphasize that the research was conducted during the COVID-19 pandemic, a challenging period to secure the participation of a significant number of individuals. The adopted strategy aimed to encompass maximum diversity within the target population, taking into account the availability and willingness to respond to the questionnaire. Therefore, participant selection was conducted for convenience, based on the analysis of the bio/profile of professionals in the field of Dentistry.

The questionnaire consisted of 30 questions (27 objective questions and 3 discursive questions) divided into three blocks. The first block addressed topics of a personal and professional nature

(gender, age, length of experience, area of specialization, main place of work). The second block consisted of questions related to clinical practice and knowledge about bisphosphonates; the third block formed by the 3 discursive questions addressed the self-assessment of dentists about their own knowledge and professional colleagues knowledge.

A pre-test with 10 questions was used before sending the 30-question questionnaire to the professionals to ensure cohesion and compliance to validate the answers. The pre-test used was reviewed by a Linguistics Professsor from the Federal University of Rio Grande do Sul (UFRGS), Brazil, Maria José Bocorny Finatto.

The data obtained from the objective questions were analyzed in SPSS® (version 20), MiniTab® (version 16) and Microsoft Excel 2010, and a quantitative exploratory study was carried out. For the discursive questions, discourse analysis was carried out.

To characterize the distribution of the relative frequency (percentages) of each of the questions, the Equality of Two Proportions test was used to compare the percentages (indices) between them and we emphasize that the indices were always calculated for a total of 74 respondents. The level of significance was of 0.05 (5%).

RESULTS

Seventy-four professionals answered the questionnaire. Considering the profile of the professionals, it was found that most of the participants were women (81.08%) and mean age was 31.6 ± 1.9 years. The majority (55.41%) have up to 5 years of graduation and professional experience, and only 26% of them said they had encountered patients who had complications due to the use of bisphosphonates.

Regarding knowledge about the indication of bisphosphonates, the participants were familiar with the purpose of the medication (65%) or had already heard about it (34%); correctly identified the indication for osteoporosis (93%), bone metastasis (49%) and Paget's disease (15%) (Table I).

In Table II, it is possible to verify that most professionals (95%) identified the dental implant surgery as one of the risk procedures for jaw osteonecrosis in patients who use bisphosphonates. As for the route of administration, 31% answered that the intravenous administration had the highest risk for jaw osteonecrosis.

Table III reports the clinical conduct of professionals in cases of osteonecrosis, where the majority of participants (93.24%) believe it is necessary to perform a dental examination before starting treatment with bisphosphonates. In case of doubt, whether or not the patient has complications due to the medication, 74.32% would refer the case to the general surgeon or oral and maxillofacial dentist.

About the opinion of professionals on their knowledge and practice regarding osteonecrosis related to bisphosphonates, it was observed that 48.65% self-assessed their level of knowledge on the subject as insufficient, however, 48.65% claimed to have acquired knowledge about the complications during graduation from dental school (Graph 1), and also, a significant percentage, 93.24% responded positively in relation to the existence of side effects resulting from the therapeutic use of bisphosphonates.

Table I - Dentists knowledge about the indication of bisphosphonates

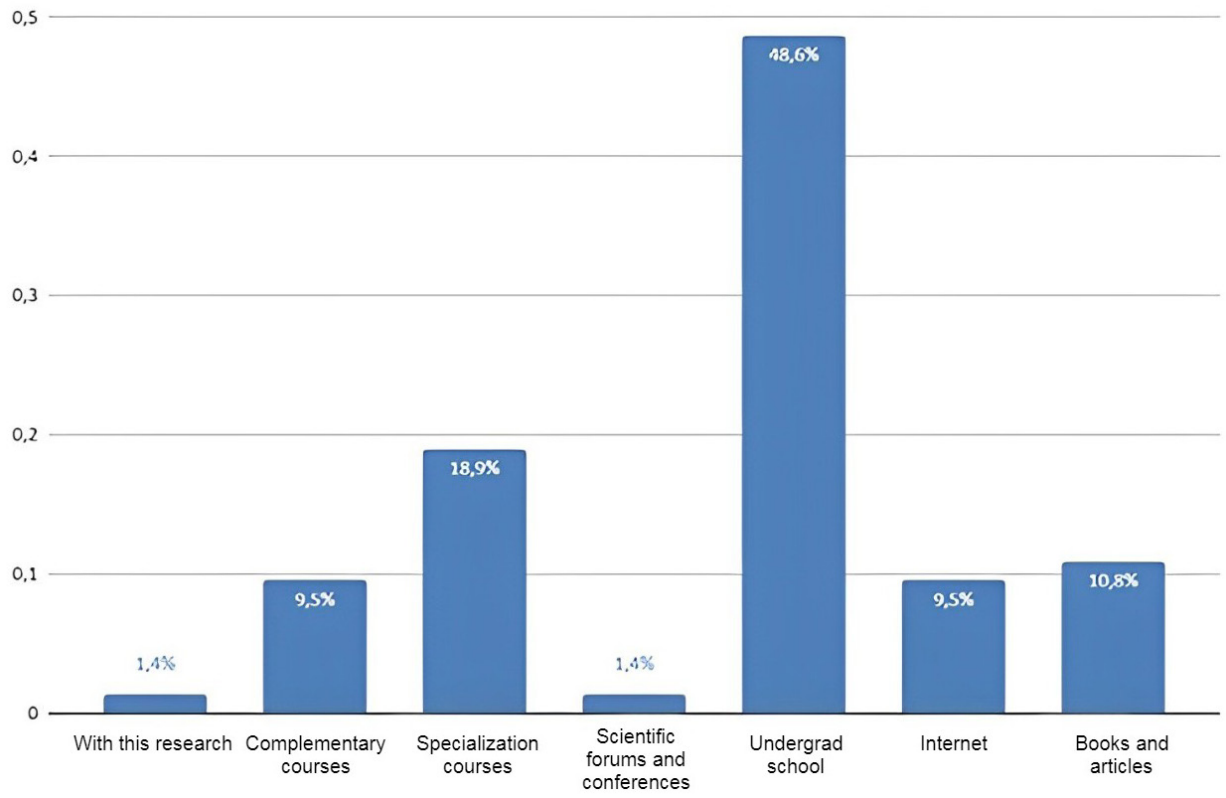
Bisphosphonates Indications	Total n (%)	P-value
Osteoporosis	69 (93.2)	Ref.
Bone Metastasis	36 (48.6)	<0.001
Rheumatoid Arthritis	7 (9.5)	<0.001
Diabetes	-	-
Paget's Disease	11 (14.9)	<0.001
Hypertension	-	-

The total value of responses to items exceeds the number of respondents. as the question allowed more than one answer. Ref. (reference): most prevalent answers.

Table II - Dentists knowledge about risk factors for jaw osteonecrosis

Risk factors for jaw osteonecrosis	Total n (%)	P-value
Dental implant surgery	70 (94.6)	Ref.
Tooth extraction	63 (85.61)	0.057
Orthodontic treatment	24 (32.4)	<0.001
Partial dentures	10 (13.5)	<0.001
Endodontic treatment	10 (13.5)	<0.001
Tartar removal	6 (8.1)	<0.001
Other surgical manipulations	54 (73)	<0.001
Intravenous administration	23 (31.1)	0.387
Oral administration	5 (6.8)	<0.001
All forms of administration present the same risk	18 (24.3)	0.076

Ref. (reference): most prevalent answers.



Graph 1 - How/where did you learn about the possible complications of treatment with bisphosphonates?

Table III - Conduct of professionals facing osteonecrosis of the jaws

Clinical Conduct	Total n (%)	P-value
Is a dental examination necessary before starting treatment with bisphosphonates?		
Yes	69 (93.2)	Ref.
No	1 (1.4)	<0.001
I'm not sure	4 (5.4)	<0.001
Routine exams		
Clinical examination	4 (5.4)	<0.001
Clinical examination + imaging exams + biopsy	19 (25.7)	<0.001
Clinical examination and biopsy	1 (1.4)	<0.001
Clinical examination and imaging exams	50 (67.6)	Ref.
Would you do the mentioned exams?		
Yes	56 (75.7)	Ref.
No	5 (6.8)	<0.001
I'm not sure	13 (17.6)	<0.001
Would refer the case to which professional?		
General surgeon or oral and maxillofacial dentist.	55 (74.3)	Ref.
Oncologist	5 (6.8)	<0.001
Orthopedist	3 (4.1)	<0.001
Periodontist	4 (5.4)	<0.001

Ref. (reference): most prevalent answers.

DISCUSSION

The aim of this study was to assess dentists' knowledge concerning bisphosphonate-associated jaw osteonecrosis, a condition reported by Marx [16] and Migliorati [17]. Intravenous bisphosphonates, as highlighted by Ruggiero et al. [11], are antiresorptive drugs prescribed for cancer-related conditions such as malignant hypercalcemia, bone metastasis in solid tumors (e.g., breast, prostate, lung cancer), and for the management of lytic lesions such as multiple myeloma. Orally ingested bisphosphonates are indicated for osteopenia and osteoporosis [11,16-18].

In our study, a significant majority of dentists (93.24%) demonstrated awareness of side effects resulting from bisphosphonate use. However, when asked to self-evaluate their knowledge and management of jaw osteonecrosis, 48.65% felt they lacked sufficient expertise. This echoes findings from studies by Hristamyan-Cilev et al. [1], Alhussain et al. [19], El Osta et al. [20], and others, emphasizing a need for targeted education [21,22].

A survey carried out by Hristamyan-Cilev et al. [1] with 323 dentists in Plovdiv, Bulgaria, showed that approximately 70% of the participants knew for which uses bisphosphonates

are directed, however only 14.86% were aware that partial dentures are one of the risk factors for the occurrence of jaw osteonecrosis in patients who make use of the drug [1]. A research by Al-Eid et al. [21] in Saudi Arabia, pointed out that 60.8% of the interviewed dentists were aware of bisphosphonate-associated jaw osteonecrosis, and 39.2% said they did not know what this condition was. Another study conducted with a sample of 100 dentistry students from private institutions in the state of São Paulo, Brazil, showed that their knowledge about bisphosphonates and bisphosphonate-related osteonecrosis of the jaw were variable, where 60% of the students recognized osteonecrosis of the jaws as a side effect of bisphosphonates and 56% identified at least one risk factor associated with the drug, but on the other hand, 66% of the students did not recognize any bisphosphonate and 79% did not recognize their trademark names [22].

Understanding the frequency of patients using bisphosphonates (35.14% of participants annually), we underscore the importance of all dentists being aware of the drug's effects, as patients are often unfamiliar with their medications [23]. Risk factors highlighted by the American Association of Oral Maxillofacial Surgeon, including dentoalveolar surgeries (extractions, implants, periodontal procedures) and anatomical factors (more common in the mandible than in the maxilla, due to greater bone mineral density), further emphasize the need for a thorough anamnesis and proactive measures before initiating bisphosphonate therapy [5,6,15,24,25].

The diagnosis of bisphosphonate-associated jaw osteonecrosis is reliant on a comprehensive clinical history, complemented by imaging exams like CT scans and MRIs [21]. Our study revealed a positive inclination among participants toward routine exams and clinical dental examinations for patients on or starting bisphosphonate treatment.

Recognizing the imperative to disseminate our findings, especially among dentists and health professionals nationwide, we draw attention to a significant gap in dental education, as highlighted by Maeda et al. [22]. Urging investment in continuous education, we propose integrating bisphosphonate-focused classes into academic curricula to better prepare future professionals from the outset.

Our findings underscore the need for a strategic enhancement of educational curricula within institutions to ensure a more comprehensive understanding among dentists. By incorporating topics pertinent to our study, we aim not only to bolster dentists' knowledge but also to enhance safety protocols associated with procedures related to bisphosphonates. This focused educational approach will empower dental professionals to navigate challenges confidently, ultimately contributing to the overall improvement of patient care in the evolving landscape of oral healthcare.

Continuous education is paramount in cultivating a dental community that is well-informed about bisphosphonate-associated conditions and equipped with the confidence to manage such cases effectively. These ongoing efforts will bridge existing knowledge gaps, leading to a safer and more proficient dental practice. This, in turn, will benefit both practitioners and patients alike, ensuring a higher standard of care within the dental community.

CONCLUSION

In conclusion, our study highlights a commendable level of awareness among participating dentists regarding the effects of bisphosphonates. However, a notable percentage expresses reservations about their confidence in managing and understanding jaw osteonecrosis. This underscores the importance of addressing specific aspects of bisphosphonate-associated conditions in dental education.

Acknowledgements

Prof. Dr. Maria José Bocorny Finatto (Federal University of Rio Grande do Sul, UFRGS) for reviewing the pre-test.

Author's Contributions

TAMS: Formal Analysis, Investigation, Resources, Data Curation, Writing – Review & Editing, Visualization. GRZ: Formal Analysis, Investigation, Resources, Data Curation, Writing – Review & Editing, Visualization. JDA: Conceptualization, Methodology, Formal Analysis, Writing – Original Draft Preparation, Writing – Review & Editing, Visualization, Supervision.

Conflict of Interest

The authors have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

Funding

PIBIC Unesp for the scientific initiation scholarship (process 4004 - Notice 4/2022) and São Paulo Research Foundation (FAPESP) grants #2020/10362-0 (Almeida JD) and #2021/06500-1 (Zucco GR).

Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of: Human Research Ethics Committee. The approval code for this study is: (CAAE 48569821.0.0000.0077).

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Date submitted: 2023 Nov 01
Accept submission: 2024 Mar 13