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Knowledge of dental professionals and Dental students on bisphosphonates and bisphosphonate-associated osteonecrosis of the jaws

Conhecimento dos cirurgiões-dentistas e estudantes de Odontologia sobre os bisfosfonatos e a osteonecrose dos maxilares associada aos bisfosfonatos

Conocimiento de los dentistas y estudiantes de Odontología sobre los bisfosfonatos e la osteonecrosis de los maxilares asociada a bisfosfonatos

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Abstract
Introduction and objective: the present study assessed the knowledge of dentists and dental students about bisphosphonates and bisphosphonate-associated osteonecrosis of the jaws (BAONJ). Methodology: a survey was applied to dentists and dental students during dental meetings in the city of Rio de Janeiro/RJ, Brazil. Results were descriptively and comparatively analyzed using the SPSS program. Results: the final sample (n=308) was composed mostly by young adults, females (n=233; 76%) and 52% (n=159) were dental students. Most participants (n=185; 60%) were derived from private dental schools. From the total, 79% (n=243) of the participants told they had some information about bisphosphonates, 68% (n=209) recognized BAONJ as a possible side effect of their use, and 84% (n=259) considered important to ask about bisphosphonates use during anamnesis. Participants with more access to information, derived from public dental schools and graduate dentists demonstrated a higher understanding about the indications for bisphosphonates use, their action mechanism, BAONJ as an adverse effect, risk factors associated with the drugs, oral risk factors and oral care measures important to BAONJ risk reduction. Conclusions: there are several knowledge gaps on bisphosphonates and BAONJ and understanding these difficulties is important for the establishment of strategies of diffusion of the information and changing teaching models in dental schools, dental meetings and extension activities.
Keywords: Bisphosphonates; Bisphosphonate-associated osteonecrosis of the jaw; Knowledge; Teaching; Dentistry.

Resumo
Introdução e objetivo: este estudo avaliou o conhecimento de dentistas e estudantes de Odontologia sobre os bisfosfonatos e osteonecrose dos maxilares associada ao uso de bisfosfonatos (OMAUB). Metodologia: um questionário foi aplicado a dentistas e estudantes de Odontologia durante eventos de Odontologia na cidade do Rio de Janeiro/RJ, Brasil. Os resultados foram analisados de forma descritiva e comparativa utilizando o programa SPSS. Resultados: a amostra final (n=308) foi composta principalmente por adultos jovens, mulheres (n=233; 76%) e 52% (n=159) eram estudantes de Odontologia. A maioria dos participantes (n=185; 60%) eram oriundos de escolas

privadas de Odontologia. Do total, 79% (n=243) dos participantes relataram ter alguma informação sobre os bisfosfonatos, 68% (n=209) reconheceram a OMAUB como um possível efeito colateral do seu uso, e 84% (n=259) consideraram importante perguntar sobre o uso dos bisfosfonatos aos pacientes durante a anamnese. Participantes com mais acesso a informação, oriundos de escolas públicas de Odontologia e dentistas já formados demonstraram um maior entendimento sobre as indicações de uso dos bisfosfonatos, seu mecanismo de ação, a OMAUB como possível efeito adverso, os fatores de risco associados às drogas, os fatores de risco orais e as medidas de cuidado oral importantes para a redução do risco da OMAUB. Conclusões: existem diversas lacunas sobre o conhecimento dos bisfosfonatos e da OMAUB e o conhecimento destas dificuldades é importante para o estabelecimento de estratégias de difusão da informação e para a mudança dos modelos de ensino nas escolas de Odontologia, eventos de Odontologia e atividades de extensão.
Palavras-chave: Bisfosfonatos; Osteonecrose associada aos bisfosfonatos; Conhecimento; Ensino; Odontologia.

Resumen

Introducción y objetivo: el presente estudio evalúa el conocimiento de dentistas y estudiantes de Odontología sobre bisfosfonatos y osteonecrosis de los maxilares asociada a bisfosfonatos (OMAB). Metodología: una encuesta fue aplicada a dentistas y estudiantes de Odontología durante congresos de Odontologia en la ciudad de Rio de Janeiro/RJ, Brasil. El análisis de los resultados fueron descriptivos y comparativos, usando el programa SPSS. Resultados: la muestra final (n=308) fue compuesta principalmente por jóvenes adultos, femenino (n=233; 76%) y 52% (n=159) fueron estudiantes de Odontología. La mayoría de los participantes (n=185; 60%) fueron de escuelas Odontología privadas. Del total de participantes, el 79% (n=243) mencionó tener algo de de información sobre bisfosfonatos, 68% (n=209) reconoció la osteonecrosis como efecto adverso durante su uso y 84% (n=259) consideró importante preguntar sobre bisfosfonatos durante la anamnesis. Los participantes com mayor acceso a la información, de escuelas Odontología públicas y dentistas graduados demostraron um mayor entendimiento sobre las indicaciones para el uso de bisfosfonatos, su mecanismo de acción, la OMAB como efecto adverso, factores de riesgo asociados a los bisfosfonatos, factores de riesgo orales y medidas importantes de cuidado oral para reducer el riesgo de la OMAB. Conclusiones: existen varias lagunas de conocimiento sobre bisfosfonatos e la OMAB y comprender estas dificultades es importante para el estabelecimiento de estrategias de difusión de la información y cambiar los modelos de enseñanza en las escuelas de Odontología, congresos y actividades extra académicas.
Palabras clave: Bisfosfonatos; Osteonecrosis de los maxilares asociada a bisfosfonatos; Conocimiento; Enseñanza; Odontología.

1. Introduction

Bisphosphonates are potent anti-resorptive drugs that have been used in the control and treatment of several bone-affecting conditions associated with bone resorption, including osteoporosis and primary and metastatic malignant diseases (Brown et al., 2005; Yoneda et al., 2017; Young & Grynpas, 2018; Kim et al., 2021; Ruggiero et al., 2022). Although bisphosphonates have shown a beneficial effect in controlling bone resorption, some adverse effects have been already described, especially renal toxicity and bisphosphonate-associated osteonecrosis of the jaws (BAONJ) (Coleman, 2008).

Data from the pathogenesis, prevention and management of BAONJ have been extensively published in the last years, and there was growing evidence that all dental professionals should have information on this drug group and BAONJ as part of their academic background (Saad et al., 2012; Ruggiero et al., 2014; Kim et al., 2021; Ruggiero et al., 2022). However, recent evidences have shown that more than half dental professionals still do not feel comfortable in managing BAONJ and treating patients reporting bisphsphonate use (Alhussain et al., 2015; Tanna et al., 2017).

There is little information derived from Brazilian dental professionals, but it seems that knowledge on bisphosphonates and BAONJ in this group is still deficient (De Lima et al., 2015; Miranda-Silva et al., 2020). Therefore, the objective of the present study was to evaluate the knowledge of dental students and dental professionals regarding bisphosphonates and BAONJ in a Brazilian population.

2. Methodology

The present study was conducted in the city of Rio de Janeiro/RJ, in the southeastern region of Brazil. A questionnaire, based on the model used by De Lima et al. (2015), was specifically designed for the study and applied for dental

students and dental professionals that attended dental meetings in 2018. The questionnaire included personal information (age and gender of the participant), academic and professional information (about the dental school, professional activity and academic background), and information about the bisphosphonates and BAONJ. We focused the survey on bisphosphonates, without including reference to other anti-resorptive drugs associated with osteonecrosis, as the aim was to evaluate the knowledge on the most common drugs associated with this adverse effect, and to reduce the bias that could be introduced when extending the research field, turning data analysis more reliable.

Data derived from the responses were tabulated and descriptively and comparatively analyzed through the use of the software Statistical Program for Social Sciences (SPSS, IBM version 2.0, Chicago, IL, USA). For comparative analysis, the chi-square test was used with a significance level of 5% ($p<0.05$). This study was approved by the local Ethics in Research Committee from the Estácio de Sá University (protocol number 97123818.5.0000.5284).

3. Results

Final sample was composed by 308 participants, including 233 females (75.6%). Mean age of the whole sample was 29.8 years (ranging from 17 to 67 years), and 28.9 for females (ranging from 17 to 67 years), and 32.4 years for males (ranging from 18 to 62 years). Dental students represented 51.6% of the sample (n=159); regarding the professionals, 43 (14%) were general dentists, 74 (24%) were specialists, 28 (9.1%) had a master and/or doctorate degree and 4 (1.3%) did not report their academic degree. Most participants were derived from private dental schools (196, 63.6%), 106 (34.4%) were derived from public dental schools and 6 (1.9%) did not answered this question. Most participants were derived from dental schools located in large metropolitan areas (243, 78.9%), while 53 (17.2%) were derived from institutions located in smaller cities.

From the total, 244 participants (79.2%) knew bisphosphonates, mostly by information obtained in the dental school (40.6%). Most (75.6%) recognized at least one indication for bisphosphonates use and about half the participants correctly identified their general action mechanism. Most participants (259; 83.8%) reported that asking to patients about current and past bisphosphonates use during anamnesis is essential, and the two most recognized drugs from this group were alendronate and zolendronate (51.6%). BAONJ was identified as an adverse effect by 209 (67.9%). However, only 33 participants (10.7%) identified the three most important risk factors to BAONJ associated to the bisphosphonates. In addition, 223 participants (72.5%) correctly identified al least one trigger risk dental procedure associated with BAONJ development and 71.4% identified al least one dental care procedure important for its prevention (Table 1).

Table 1. Descriptive analysis of data associated with bisphosphonates and bisphosphonate-associated osteonecrosis of the jaws (BAONJ).

Parameter	N	%
How did you got information on bisphosphonates?		
Dental school	125	40.6
Dental meetings/courses	45	14.6
Internet	33	10.7
More than one source	50	16.2
Non respondants	55	17.9
Indications for bisphosphonates use		
Up to 2 correct indications	183	59.4
3 or 4 correct indications	50	16.2
Do not know any indication	50	16.2
Non respondants	25	8.1
Mechanism of action of bisphosphonates		
Yes	157	51
No	87	28.2
Non respondants	64	20.8
Importance of asking to patients about bisphosphonates		
Yes	258	83.8
No	1	0.3
Do not know	24	7.8
Non respondants	25	8.1
Identifying bisphosphonates		
Alendronate and zolendronate	159	51.6
Others	73	23.7
Non respondants	128	41.6
Identifying BAONJ as an adverse effect		
Yes	209	67.9
No	13	4.2
Do not know any adverse effect	56	18.2
Non respondants	30	9.7
Risk factors associated to bisphosphonates		
One or two risk factors	166	53.9
Three risck factors	33	10.7
Do not know	77	25
Non respondants	32	10.4
Dental procedures associated with BAONJ development		
Up to 3 procedures	148	48.1
From 4 to 6 procedures	75	24.4
Do not know	54	17.5
Non respondants	31	10.1
Dental procedures important for BAONJ prevention		
One or two dental procedures	119	38.6
Three or four dental procedures	101	32.8
Non respondants	88	28.6

Source: Authors (2022).

In general, males and females showed similar knowledge on the subject. Participants that have contact with the subject by more than one source identified more bisphosphonates use indications ($p<0.0001$), their mechanism of action ($p<0.0001$), BAONJ as an adverse effect ($p<0.0001$), BAONJ risk factors related to the bisphosphonates ($p<0.0001$), dental procedures carrying a higher risk for BAONJ ($p<0.0001$) and dental procedures important for BAONJ prevention ($p<0.0001$).

Participants derived from public dental schools identified more bisphosphonate use indications ($p=0.0001$), their mechanism of action ($p=0.002$), BAONJ as an adverse effect ($p=0.001$), BAONJ risk factors related to the bisphosphonates

(p=0.023), dental procedures carrying a higher risk for BAONJ (p<0.0001), and dental procedures important for BAONJ prevention (p<0.0001). Participants working in large metropolitan areas indicated the bisphosphonates mechanism of action more frequently (p=0.021), while participants working in smaller cities identified more often the dental procedures carrying a higher risk for BAONJ (p=0.003); there were no statistically significant differences for the other comparisons.

Professionals identified bisphosphonates use indications (p<0.0001), BAONJ as an adverse effect (p<0.0001), BAONJ risk factors related to the bisphosphonates (p=0.005), dental procedures carrying a higher risk for BAONJ (p<0.0001) and dental procedures important for BAONJ prevention (p<0.0001) more often than dental students.

4. Discussion

All patients should receive a complete and detailed dental evaluation prior to beginning treatment with bisphosphonates, including all necessary interventions to maintain satisfactory oral health conditions, reducing the risk of BAONJ. For this reason, all dentists should have at least a minimum knowledge on these drugs, including information about their medical indications and main adverse effects. Thus, they may identify patients at risk for BAONJ and determine the most appropriate management strategies for patients before, during and after bisphosphonates therapy (Ruggiero et al., 2014; Yoneda et al., 2017; Kim et al., 2021; Ruggiero et al., 2022).

Although the need for dissemination of information about bisphosphonates and BAONJ for the dental community is evident, few studies have been directed to understand the knowledge of dental students and professionals about the subject, in order to identify the most important gaps. Two studies have evaluated this subject in Brazilian populations involving, respectively, dental professionals and dental students in Recife/PE (De Lima et al., 2015) and dentists, physicians and nurses in São Paulo/SP (Miranda-Silva et al., 2020). Both have shown deficiencies in the knowledge about bisphosphonates in the studied populations.

In the present study males and females showed similar knowledge about bisphosphonates and BAONJ, similarly to the results of Escobedo et al. (2017). The present sample was composed mainly by dental students and participants derived from private dental schools, in contrast to the sample studied by De Lima et al. (2015). Some studies have included only dental students (Escobedo et al., 2017; Rosella et al., 2017), while others have included only graduated dental professionals (Alhussain et al., 2015; Vinitzky-Brener et al., 2017; Hristamyan-Cilev et al., 2019; Al-Eid et al., 2020; Al-Maweri et al., 2020; Alqhtani et al., 2020; Arnaud et al., 2021; Ozkan et al., 2021). More recently, Franchi et al. (2020) have showed the results derived from a sample of medical students and Miranda-Silva et al. (2020) compared the results derived from dentists, physicians and nurses. These differences on the profile of the participants are important when analyzing the results of the studies, as they can reveal distinct academic backgrounds and different continuing education resources when comparing different populations.

Almost 80% of the participants answered that they knew the bisphosphonates, similarly to the results of other studies (60% to 80%) (De Lima et al., 2015; Escobedo et al., 2017; Al-Eid et al., 2020; Al-Maweri et al., 2020; Almousa et al., 2021). Information about bisphosphonates was obtained mainly by academic courses (López-Jornet et al., 2010), manuscripts and scientific literature (Alhussain et al., 2015), internet (Escobedo et al., 2017) and dental schools (De Lima et al., 2015; Rosella et al., 2017; Arnaud et al., 2021). More recently, Dahlgreen e Larsson Wexell (2020) reported that most participants obtained information in undergraduate and/or graduate academic courses and scientific meetings, and suggested that the subject should be widely discussed in dental schools. In the present study, most participants obtained information in dental schools (40%), dental meetings (15%) and internet (10%). This specific information derived from each studied population is essential for establishing the most appropriate strategy for dissemination of information on the subject.

Our results showed that from the 4 indications for bisphosphonates use, 60% of the participants identified at least one

and 16% identified three or four, similarly to the results reported by other studies (Alhussain et al., 2015; Vinitzky-Brener et al., 2017; Patil et al., 2020). Most studies have shown that about 40 to 50% of the participants did not know the medical indications for the use of bisphosphonates, and these values seems to be higher when considering dental students (López-Jornet et al., 2010; De Lima et al., 2015; Almousa et al., 2021). We consider that this is an essential point. Dental professionals aware of the medical indications for these drugs may conduct the anamnesis more appropriately, if the patient reports any of these medical comorbidities.

In the present sample, half the participants identified the basic mechanism of action of the bisphosphonates, in comparison with 40% reported by De Lima et al. (2015) and 72% reported by Patil et al. (2020). We have also observed that 84% of the present participants considered important to ask about these drugs during anamnesis, close to the values found by De Lima et al. (2015) (75%), Rosella et al. (2017) (94%), Al-Maweri et al. (2020) (up to 70%), and Arnaud et al. (2021) (84%). De Lima et al. (2015) and Vinitzki-Brener et al. (2017) reported that about 75% and 85% of the participants did not know the bisphosphonates included in the survey and their brand names, respectively. The two most known drugs from this group are alendronate and zolendronic acid. They were recognized as bisphosphonates in 50% of the questionnaries in the present study.

BAONJ was identified as an adverse effect of bisphosphonates use by 68% of the participants from the present study, in contrast to 41% (De Lima et al., 2015) and 83% (Patil et al., 2020) reported by other authors. López-Jornet et al. (2010) reported that 50% of the dental students and 68% of the dentists had contemporary information about BAONJ. Some factors associated with these drugs, such as type, administration route and time period of use, influence the risk for BAONJ (Dodson, 2015; Ruggiero et al., 2014; Ruggiero et al., 2022). In the present sample, only 10% of the participants identified these 3 factors. De Lima et al. (2015) and Patil et al. (2020) reported that about 40% of the participants showed any knowledge on the risk factors associated to the bisphosphonates, in contrast to 71% found by Rosella et al. (2017) and less than 50% reported by Al-Maweri et al. (2020).

The most important dental procedures associated to the risk of BAONJ are dental extractions, other dental surgeries, trauma by ill-fitting prosthetic removable appliances, periodontal disease and dental implants (Fliefel et al., 2015; Ruggiero et al., 2022). Identification of these dental procedures by the professionals that are going to deal with bisphosphonates users is essential to proper treatment planning. In a study from Turkey, 40% of oncologists reported that an appointment with a dental professional was essential for their patients before starting bisphosphonates use (Senturk et al., 2016). Acharya et al. (2022) have reinforced that physicians prescribing bisphosphonates should advise patients on the importance of dental visits and their essential role in patient morbidity. Miranda-Silva et al. (2020) reinforced that professionals directly dealing with oncologic patients have more knowledge about bisphosphonates. In the present study, 72% of the participants recognized at least 3 dental procedures associated with a higher risk for BAONJ, a higher value in comparison with the results from other studies (De Lima et al., 2015; Vinitzki-Brener et al., 2017; Al-Eid et al., 2020). As there are a two-year interval among the present and these two previous studies, it can be suggested that spreading of information and discussion on this subject in the dental community is, at least partially, already taken place.

It is also essential that dentists responsible for the treatment of bisphosphonates users should be able of teaching them the daily dental care orientations necessary for reducing the risk for BAONJ. De Lima et al. (2015) reported that 52% of the participants identified these dental care strategies to reduce BAONJ development risk and 71% of the present participants identified at least one adequate dental care strategy.

Our results showed that professionals that had more contact with information about bisphosphonates showed, in general, higher knowledge about the subject. Professionals graduated less than five years (De Lima et al., 2015) and 10 years (Arnaud et al., 2021; Ozkan et al., 2021) before, showed more information on bisphosphonates and BAONJ, reinforcing that

this is a relatively new subject that should be intensively divulgated and updated. Dental students from the last years showed more knowledge on the subject than students from the initial years and dentists graduated 20 or more years before, probably because they had more contact with the subject during their academic activities (Escobedo et al., 2017; Rosella et al., 2017; Escobedo et al., 2018). In the present study we have also identified that dental students and professionals derived from public schools showed, in general, more knowledge on the subject. Highlighting these differences is important for planning new academic strategies for offering more complete and updated information about the subject for all dental students.

In general, the results from the present study showed that dental students presented less information about bisphosphonates and BAONJ than dentists, similarly to another study (López-Jornet et al., 2010). Oral and maxillofacial surgery specialists demonstrated more knowledge about the subject in other studies (Alhussain et al., 2015; Hristamyan-Cilev et al., 2019), but we were not able to compare the results from professionals derived from different specialties due to the limited number of participants. Vinitzki-Brener et al. (2017) showed that general dentists demonstrated less knowledge about bisphosphonates and BAONJ, in accordance with some results from the present survey. Al-Maweri et al. (2020), Miranda-Silva et al. (2020), and Bruckmoser et al. (2021) have also shown that specialists and more trained and specialized professionals showed better knowledge when compared to general dentists about the subject. Taken together, these results reinforce the need for continous education about bisphosphonates and BAONJ for both dental students and dentists (Al-Eid et al., 2020; Alqhtani et al., 2020; Almousa et al., 2021; Ozkan et al., 2021).

5. Conclusion

The results from the present study showed that there are several knowledge lacunae about bisphosphonates and BAONJ in the studied population. Despite the study limitations, the results provide useful information on the knowledge of dental students and professionals about the subject in a Brazilian large metropolitan area. It is expected that these results would stimulate the diffusion of this topic in dental schools, dental meetings and other academic activities, and direct well-planned teaching strategies about BAONJ prevention, diagnosis and management, to consolidate the knowledge about bisphosphonates and BAONJ to the dental community. Future studies focusing on teaching strategies on this topic are encouraged.

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