

# Analysis of the Degree of Information of Dental Surgeons about Antiresorptive Drugs According to the Time Since Graduation in Dentistry

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## ABSTRACT

**Objective:** To determine the level of scientific information of dental surgeons who carry out their professional activities in Brazil about antiresorptive drugs and indicated pharmacological procedures aiming at the prevention of osteonecrosis of the jaws and the therapy of drug sequelae that may occur, considering the time since graduation in Dentistry. **Material and Methods:** This is a quantitative cross-sectional study in which 339 dentists were consulted using the virtual questionnaire containing topics of personal nature, elements contained in the anamnesis carried out and knowledge about antiresorptive drugs, including indications, adverse effects and treatments applied. Chi-square and Fisher's exact tests were performed to analyze associations of data described by absolute and relative frequencies with professionals' time since graduation. All analyses were performed using the R software, with a 5% significance level. **Results:** Those who revealed to have graduated for more than five years with the highest academic degree were those who demonstrated maximum knowledge of antiresorptive drugs or revealed that, somehow, they had information about them ( $p < 0.05$ ). **Conclusion:** Dental surgeons in Brazil who have more than five years since graduation have more scientific information about antiresorptive drugs and pharmacological procedures, which can positively contribute to the prevention of osteonecrosis of the jaws and treatment of drug sequelae that may occur.

**Keywords:** Diphosphonates; Bone Density Conservation Agents; Oral Medicine.

## Introduction

It is known that the bone tissue is composed of cells – osteoblasts, osteocytes and osteoclasts – and mineralized extracellular matrix [1]. Under conditions of homeostasis, bone tissue cells act in the matrix remodeling process [1]. However, in the presence of some pathologies that promote excessive bone matrix reabsorption, for example, in cases of osteoporosis and bone metastases, bone tissue homeostasis is compromised [1-3]. In order to reduce excessive bone resorption observed in these pathologies, antiresorptive drugs allow for treating or preventing bone metabolism diseases [2,3].

Among antiresorptive drugs, bisphosphonates (BPs) [4] and denosumabs (DMABs) [5] have received greater attention. The commercial names of bisphosphonate drugs include Zoledronic acid, Alendronate sodium, Ibandronate sodium, Pamidronate sodium and Risedronate sodium [6], while commercial names of denosumabs are Prolia and Xgeva [7].

Although these antiresorptive drugs effectively act in the prevention and (or) treatment of diseases related to bone metabolism, their main side effect is osteonecrosis of the jaws, which, in English, receives the acronym ONJ (osteonecrosis of the jaws) [8]. When ONJ is associated with the use of bisphosphonates (BPs), it is called Bisphosphonate-related osteonecrosis of the jaws (BRONJ) [9], and when it is associated with denosumabs, DRONJ, that is, Denosumab-related ONJ [10].

In addition to BPs and denosumabs, other drugs have been associated with the occurrence of ONJ, such as sunitinib, sorafenib and bevacizumab [11,12]. For this reason, the term currently recommended by the American Association of Oral and Maxillofacial Surgeons (AAOMS) is medication-related ONJ (MRONJ) [8].

Some risk factors for the development of MRONJ are tooth extractions, oral surgeries with bone manipulation, poorly-fitting prostheses and previous periodontal disease [13,14]. Furthermore, the high consumption of alcohol and tobacco, the use of glucocorticoids, and preexisting systemic comorbidities may contribute to the development of MRONJ [14].

Prevention is a key issue to reduce the incidence of MRONJ [15,16]. It is essential that the patient seeks dental care to assess their oral conditions, including careful and complete clinical and radiographic examinations to verify the need for adequacy of the oral environment before using antiresorptive drugs [16].

Although there are many treatments for patients with MRONJ, there is still no consensus in the literature about a standard protocol for treating patients with MRONJ [17-20]. However, dentists should always opt for conservative treatments in order to prevent the increase in the exposed area or even worsening of symptoms [21-24].

This research aims to determine the level of scientific information of dentists who carry out their professional activities in Brazil, with emphasis on the state of Bahia, about antiresorptive drugs and the indicated pharmacological procedures aiming at the prevention of osteonecrosis of the jaws and the treatment of drug sequelae that may occur, considering the time since graduation in Dentistry.

## Material and Methods

### Ethical Aspects and Study Design

This quantitative cross-sectional study was sent to the Ethics and Research Committee of the Institute of Health Sciences, Federal University of Bahia, being approved under protocol No. 56509422.5.0000.5662.

### Location and Study Population

Dental surgeons working in the state of Bahia, Brazil, were contacted and selected through a virtual invitation sent to Higher Education Institutions located in the state of Bahia that offered *stricto sensu* or *lato sensu* courses for dental surgeons working in this Federation Unit. The Free and Informed Consent Form (FICF) was attached to the survey questionnaire via the Internet so that participants would only respond to the specific tool if they read and/or agree with this document. As the research was developed only in the virtual model, participants could print a copy of the FICF virtually available when they accessed the questionnaires, or they could request a copy of this document via E-mail to the researcher, who made contacts available in the consent form attached to the survey questionnaire. The questionnaire used in this study was a version adapted from the instrument developed by De Lima et al. [25].

This virtual data collection instrument was created through Google Forms and directed to a sample of 1.91%, corresponding to  $n = 339$ , having as a reference all 17,657 dentists working in the state of Bahia.

#### Inclusion and Exclusion Criteria

The inclusion criterion comprised the sample of 1.91% ( $n=339$ ) of dentists who carry out their professional activities in the state of Bahia, with or without being graduated in this federative unit, considering a total of 17,657 professionals, according to the Federal Council of Dentistry, in the year 2022. The exclusion criterion was composed of dentists who did not work in the state of Bahia

#### Variables

The variables related to the sociodemographic and professional profile of the sample ( $n=339$ ) correspond to biological sex, age group, graduation in a public or private institution, type or category of the graduation institution, state of graduation, time since graduation in dentistry, highest academic degree, salary range, specialty, place of work as a dental surgeon and place of activity.

However, regarding variables related to the professional performance of individuals participating in the sample ( $n=339$ ), the following questions were asked: 1) If the patient treated had osteoporosis; 2) If the dentist had performed surgical procedures in clinical practice; 3) If the surgical procedures were minor, with or without bone exposure; 4) In the anamneses of all patients, which medications they were using before performing any procedure; and 5) If the dentist is aware of or has heard about antiresorptive drugs; if the dentist has treated patients who reported using antiresorptive drugs; what is the clinical conduct before performing procedures with patients who use antiresorptive drugs; if the dentist is aware of indications for the use of antiresorptive drugs; if the dentist is aware of the possible adverse effects of antiresorptive drugs; possible adverse effect (s) of antiresorptive drugs; factor (s) increasing the risk of drug-related osteonecrosis of the jaws; incipient sign (s) of osteonecrosis, procedure (s) that the dentist can perform on a patient who uses antiresorptive drugs and what antiresorptive drugs consist of.

#### Statistical Analyses

Descriptive analyses of data were performed with absolute and relative frequencies. To analyze associations with time since graduation, chi-square and Fisher's exact tests were used. All analyses were performed using the R software (R Foundation, Indianapolis, IN, USA) [26] with a 5% significance level.

## Results

With regard to Table 1, among the 339 dentists working in the state of Bahia who participated in the sample, the majority was female (76.4%), aged 31-35 years (25.1%). Furthermore, a large proportion of professionals had a degree in dentistry obtained from a private institution (59.0%), at the University category (49.0%), in the state of Bahia (80.5%).

**Table 1. Descriptive analysis of variables related to the sociodemographic profile.**

Variables	Category	N	%
Sex	Female	259	76.4
	Male	80	23.6
Age Group	20-25 years	37	10.9
	26-30 years	80	23.6
	31-35 years	85	25.1
	36-40 years	55	16.2
	41-45 years	47	13.9
	46-51 years	26	7.7
	55-60 years	8	2.4
	Over 60 years	1	0.3
Graduation	Private Institution	200	59.0
	Public Institution	139	41.0
Higher Education Institution	University Center	27	8.0
	Isolated Higher Education Institution	146	43.1
	University	166	49.0
State of Graduation	Amazonas	1	0.3
	Bahia	273	80.5
	Ceará	3	0.9
	Espírito Santo	3	0.9
	Maranhão	1	0.3
	Mato Grosso	1	0.3
	Minas Gerais	9	2.7
	Pará	1	0.3
	Paraíba	1	0.3
	Paraná	10	2.9
	Pernambuco	4	1.2
	Piauí	1	0.3
	Rio de Janeiro	6	1.8
	Rio Grande do Sul	3	0.9
Santa Catarina	2	0.6	
São Paulo	14	4.1	
Sergipe	4	1.2	
Tocantins	2	0.6	

According to Table 2, a large number of respondents had up to 10 years since graduation (59.6%), the highest academic title was specialist (47.5%), with wages ranging from R\$ 5.000,00 to R\$ 20.000,00 (54.3%). In addition, most professionals did not have a specialty (23.3%) and worked in private office (85.8%), with the state capital being the place of exercise of their activity (48.4%).

**Table 2. Descriptive analysis of variables related to the professional profile.**

Variables	Category	N	%
Time Since Graduation	Up to 5 years	109	32.2
	From 6 to 10 years	93	27.4

	From 11 to 20 years	93	27.4
	From 21 to 30 years	37	10.9
	Over 30 years	7	2.1
Highest Academic Degree	Graduation	82	24.2
	Specialist	161	47.5
	Master	61	18.0
	PhD	33	9.7
	Post-doctorate studies	2	0.6
Wage Range	Up to R\$ 5.000,00	108	31.9
	R\$ 5.000,00 to R\$ 20.000,00	184	54.3
	R\$ 15.000,00 to R\$ 30.000,00	38	11.2
	Over R\$ 30.000,00	9	2.7
<sup>1</sup> Specialty	Geriatric dentistry	1	0.3
	Oral and Maxillofacial Pathology	1	0.3
	Oral and Maxillofacial Prosthesis	1	0.3
	Forensic Dentistry	3	0.9
	Occupational Dentistry	4	1.2
	Dental Radiology and Imaging	5	1.5
	Temporomandibular disorders and orofacial pain	7	2.1
	Functional Jaw Orthopedics	8	2.4
	Dentistry for Patients with Special Needs	10	2.9
	Pediatric dentistry	16	4.7
	Oral and Maxillofacial Surgery and Traumatology	19	5.6
	Dentistry	23	6.8
	Stomatology	23	6.8
	Endodontics	27	8.0
	Collective health	30	8.8
	Periodontics	40	11.8
	Dental prosthesis	43	12.7
	Implant dentistry	55	16.2
	Orthodontics	55	16.2
	None	79	23.3
<sup>1</sup> Location Working as Dental Surgeon	Public college/ university	22	6.5
	Hospital dentistry	30	8.8
	Private university/college	72	21.2
	Basic Health Unit (BHU)/Unified Health System	85	25.1
	Private office	291	85.8
Place of Activity Exercise	Inner state	135	39.8
	State capital	164	48.4
	State capital and Inner state	40	11.8

<sup>1</sup>The total percentage adds up to more than 100% because it was possible to mark more than one alternative.

Regarding variables related to the professional performance (Table 3), 76.4% perform surgical procedures, 58.4% perform surgical procedures with bone exposure, 62.8% ask the patient if he/she has osteoporosis and 94.7% of professionals ask in the anamneses of all patients which medications they are using, before performing any procedure. At the same time, 70.8% know or have heard about antiresorptive drugs, 46.6% have already treated patients who reported the use of antiresorptive drugs, 34.5% responded that they treat patients who use medication, but always choose conservative treatments in order to avoid bone exposure, while 12.4% forward the decision to the physician and 4.7% suspend the oral anti-resorptive drug treatment for three months before and three months after the invasive dental procedure. Furthermore, 65.2% claimed to know the possible adverse effects of antiresorptive drugs, indicating osteonecrosis of the jaws as the possible adverse effect of antiresorptive drugs (68.1%).

Still in relation to variables related to the professional performance of individuals participating in the sample (Table 3), (75.5%) inferred that oral surgeries with bone manipulation increase the risk of drug-related osteonecrosis of the jaws after tooth extraction (61.4%), while 76.1% consider the presence of exposed bone or fistula for at least eight weeks, in a patient with a previous or current history of the use of antiresorptive drugs, and who did not undergo radiotherapy in the cervicofacial region, as an incipient sign of osteonecrosis. In addition, 60.8% stated that the professional can perform all procedures on a patient who uses anti-resorptive medications, provided that great care is taken to avoid bone exposure and 60.8% indicated nitrogenous and non-nitrogenous bisphosphonates, denosumab and sunitinib, sorafenib and bevacizumab as antiresorptive medications.

**Table 3. Descriptive analysis of variables related to the professional performance of dentists.**

Variables	Category	N	%
Performs surgical procedures	No	80	23.6
	Yes	259	76.4
Performs minor surgical procedures with or without bone exposure	Performs surgical procedures with bone exposure	198	58.4
	Performs surgical procedures without bone exposure	61	18.0
	Does not perform surgical procedures	80	23.6
Asks if the patient has osteoporosis	No	126	37.2
	Yes	213	62.8
Asks in the anamneses of all patients which medications they are using before performing any procedure	No	18	5.3
	Yes	321	94.7
Knows or has heard about antiresorptive drugs	No	99	29.2
	Yes	240	70.8
Has already treated patients who reported the use of antiresorptive drugs	No	181	53.4
	Yes	158	46.6
What is the clinical conduct before performing procedures with patients who use antiresorptive drugs	Modifies the dosage of antiresorptive drugs	2	0.6
	Discontinues oral antiresorptive drugs 3 months before and 3 months after the invasive dental procedure	16	4.7
	Forwards the decision to the doctor	42	12.4
	Always opt for conservative treatments in order to avoid bone exposure	117	34.5
	Never treated a patient who reported the use of antiresorptive drugs	162	47.8
Knows the indications for antiresorptive drugs	No	128	37.8
	Yes	211	62.2
Knows the possible adverse effects of antiresorptive drugs	No	118	34.8

	Yes	221	65.2	
Possible adverse effect of antiresorptive drugs	Osteonecrosis of the jaws	231	68.1	
	Does not know the possible adverse effects of antiresorptive drugs	108	31.9	
	Use of corticosteroids	67	19.8	
<sup>1</sup> Factors that increase the risk of drug-related osteonecrosis of the jaw	Inadequate hygiene	95	28.0	
	High consumption of alcohol and tobacco	98	28.9	
	Poorly-fitted prostheses	126	37.2	
	Prior periodontal disease	127	37.5	
	Systemic comorbidities	130	38.3	
	Tooth extraction	208	61.4	
	Oral surgeries with bone manipulation	256	75.5	
	Does not know	60	17.7	
	Incipient signs of osteonecrosis	Presence of exposed bone or fistula for at least 8 weeks in patient with previous or current history of the use of antiresorptive drugs, who did not undergo radiotherapy in the cervical-facial region	258	76.1
		Others	10	2.9
Does not know		71	20.9	
Procedures that the dentist can perform on a patient who uses antiresorptive drugs	Primary tooth extraction	2	0.6	
	Anesthesia	26	7.7	
	Can perform all procedures, as long as great care is taken to avoid bone exposure	206	60.8	
	Does not know	105	31.0	
What do antiresorptive drugs consist of	Denosumab only	1	0.3	
	Bisphosphonates only	31	9.1	
	Nitrogen and Non-nitrogen bisphosphonates and sunitinib, sorafenib and bevacizumab	206	60.8	
	Does not know	101	29.8	

<sup>1</sup>The total percentage adds up to more than 100% because it was possible to mark more than one alternative.

With regard to Table 4, the longest time since graduation showed a statistically significant association with the fact that the professional knows or had, in some way, information about antiresorptive drugs ( $p < 0.05$ ). Among professionals with more than five years since graduation, 74.8% knew or had, in some way, information about antiresorptive drugs, while among those with up to five years since graduation, this percentage was from 62.4%. At the same time, a significant association was observed between the longest time since graduation and clinical conduct before performing procedures with patients using antiresorptive drugs ( $p < 0.05$ ). Among professionals with less time since graduation, there was a higher percentage of those who have never treated patients who reported using antiresorptive drugs (61.5%) when compared to professionals with more time since graduation (41.3%). In addition, a longer training period was associated with knowing indications for antiresorptive drugs ( $p < 0.05$ ) and their possible adverse effects ( $p < 0.05$ ).

**Table 4. Analysis of associations with time since graduation.**

Questions	Answer	Time Since Graduation		p-value
		Up to 5 years N (%)	More than 5 years N (%)	
Knows or has heard about antiresorptive drugs	No	41 (37.6)	58 (25.2)	<sup>1</sup> 0.0190
	Yes	68 (62.4)	172 (74.8)	
What is the clinical conduct before performing procedures with patients who use antiresorptive drugs	Modifies the dosage of antiresorptive drugs	0 (0.0)	2 (0.9)	<sup>1</sup> 0.0005
	Discontinues oral antiresorptive drugs 3 months before and 3 months after the invasive dental procedure	4 (3.7)	12 (5.2)	
	Forwards the decision to the doctor	3 (2.8)	39 (17.0)	
	Always opts for conservative treatments in order to avoid bone exposure	35 (32.1)	82 (35.7)	
Knows the indications for antiresorptive drugs	Never treated a patient who reported the use of antiresorptive drugs	67 (61.5)	95 (41.3)	<sup>1</sup> 0.0093
	No	52 (47.7)	76 (33.0)	
Knows the possible adverse effects of antiresorptive drugs	Yes	57 (52.3)	154 (67.0)	<sup>1</sup> 0.0141
	No	48 (44.0)	70 (30.4)	
Possible adverse effect of antiresorptive drugs	Osteonecrosis of the jaws	67 (61.5)	164 (71.3)	<sup>1</sup> 0.0694
	Does not know the possible adverse effects of antiresorptive drugs	42 (38.5)	66 (28.7)	
Incipient signs of osteonecrosis	Presence of exposed bone or fistula for at least 8 weeks in patient with previous or current history of the use of antiresorptive drugs who did not undergo radiotherapy in the cervical-facial region	82 (75.2)	176 (76.5)	<sup>1</sup> 0.1506
	Others	6 (5.5)	4 (1.7)	
	Does not know	21 (19.3)	50 (21.7)	
Procedures that the dentist can perform on a patient who uses antiresorptive drugs	Primary tooth extraction	1 (0.9)	1 (0.4)	<sup>2</sup> 0.4022
	Anesthesia	9 (8.3)	17 (7.4)	
Procedures that the dentist can perform on a patient who uses antiresorptive drugs	Can perform all procedures, as long as care is taken to avoid bone exposure	60 (55.0)	146 (63.5)	<sup>1</sup> 0.0862
	Does not know	39 (35.8)	66 (28.7)	
	Denosumab only	1 (0.9)	0 (0.0)	
What do antiresorptive drugs consist of	Bisphosphonates only	10 (9.2)	21 (9.1)	<sup>2</sup> 0.0862
	Nitrogen and Non-nitrogen bisphosphonates and sunitinib, sorafenib and bevacizumab	58 (53.2)	148 (64.3)	
	Does not know	40 (36.7)	61 (26.5)	

<sup>1</sup>Chi-square test; <sup>2</sup>Fisher Exact Test.

## Discussion

Paredes et al. [27] conducted a cross-sectional study using a questionnaire for dentists and dentistry students during dentistry events in Rio de Janeiro, Brazil. Their sample (n=308) was mainly composed of young adults, women (n=233) and 52% were dentistry students. The authors concluded that participants from public dentistry schools and graduated dentists demonstrated a greater understanding about indications for the use of bisphosphonates, their mechanism of action, drug-related osteonecrosis of the jaws and possible adverse effects of these drugs and oral care measures important to reduce the risk of osteonecrosis of the jaws related to these drugs.

In our studies, the majority of dentists were female (76.4%), which result differs from that of Paredes et al. [27], who found that most of those who knew or had, in some way, information about these drugs were professionals with Master/PhD/Post-doctorate degree (85.4%), followed by specialist workers (69.6%) and those who only had dentistry degree (56.1%). This result helps to raise even more awareness about the importance of disseminating in a more discriminating manner subjects related to the use and indications of antiresorptive drugs, especially in undergraduate Dentistry courses and also in private institutions, considering the side effects of these drugs on maxillary osteonecrosis.

Marlière et al. [28] carried out a cross-sectional study using a questionnaire applied to a sample of 101 dentists, whose aim was to assess the knowledge and clinical conduct of these professionals regarding antiresorptive drugs and osteonecrosis of the jaws. When asked whether they asked in the anamnesis of all patients which medications they were using before performing any procedure, 83% of dentists reported that it was important to know during anamnesis whether the patient was under the use of antiresorptive drugs. The results corroborate those found in this study, demonstrating that most professionals ask in the anamneses of all patients which medications they are using, before performing any procedure (94.7%). Although it is unanimous on the part of dentists in the present study and those of Marlière et al. [28] that it is extremely important to know during anamnesis which medications are under use by patient, and it will not be useful to know that the patient uses one of the Zometa group, for example, if the dentist is not aware that this is an antiresorptive drug and that, as such, it can cause maxillary osteonecrosis for those who use this medication.

Marlière et al. [28] also asked their participants if they knew about the possible adverse effects of antiresorptive drugs. Thus, 53% indicated that they knew that osteonecrosis of the jaws was a side effect of antiresorptive drugs. This result is in agreement with that of this work, in which it is possible to observe that most professionals knew the possible adverse effects of antiresorptive drugs, and these professionals elected osteonecrosis of the jaws as the possible adverse effect of these drugs (68.1%). Perhaps, dentists in the aforementioned studies were unaware that the possible adverse effects of antiresorptive drugs were maxillary osteonecrosis, if they were asked about the possible side effect of antiresorptive drugs, taking into account the commercial names of these drugs.

Another question in the questionnaire developed by Marlière et al. [28] was whether dentists performed surgical procedures on individuals using antiresorptive drugs. Thus, half of the participants reported that they did not perform any invasive dental treatment in patients under these drugs (50%). Although this question was also used in this study, it was not taken into account whether surgical procedures were performed on individuals using antiresorptive drugs, but rather on their clinical practice. Thus, most dentists interviewed reported performing surgical procedures in their clinical practice (76.4%), while more than half of the sample reported performing surgical procedures with bone exposure (58.8%) in their dental routine. If dentists interviewed in studies by Marlière et al. [28] had more knowledge about antiresorptive drugs, the number of professionals who

would perform surgical procedures on patients using antiresorptive drugs would be greater, provided that care is taken to avoid bone exposure. On the other hand, the interviewees of the present study in fact need to know if patients submitted to surgical procedures with bone exposure are or have been under the use of antiresorptive drugs, so that they cannot cause maxillary osteonecrosis in these individuals.

Vinitzky-Brener et al. [29] carried out a cross-sectional study using a questionnaire applied to 410 Mexican dentists with the aim to evaluate their knowledge about osteonecrosis of the jaws related to bisphosphonates. When asked about their clinical conduct before performing procedures with patients using antiresorptive drugs, 32.2% of them reported that they would perform tooth extractions, 90 of them would previously administer antibiotics and 50 would not. On the other hand, 22.4% of professionals would not perform tooth extractions, while 40.5% of respondents would refer the patient to specialized care. Furthermore, 4.9% of dentists did not respond or did not know how to proceed with care for patients under the use of these drugs. All these data were statistically significant ( $p=0.01$ ).

Data obtained by Vinitzky-Brener et al. [29] differed from those of this work, since 47.8% of respondents had never treated patients who used antiresorptive drugs. On the other hand, 34.5% responded that they always opted for conservative treatments in order to avoid bone exposure, while 12.4% forwarded the decision to the doctor and 4.7% discontinued the oral antiresorptive drug for 3 months before and 3 months after the invasive dental procedure. Perhaps, dentists in the present study had treated patients who used antiresorptive medications, but they declared not to have treated these patients, as they might not have known the commercial names of these drugs. In addition, dentists need to know the systemic condition of patients through the medical report; however, the dental surgeon should know the adequate therapeutic approach to prevent the appearance of maxillary osteonecrosis. If dentists in the present study were aware of all procedures that can be performed on individuals using antiresorptive drugs, provided that care is taken to avoid bone exposure, they would not suspend oral antiresorptive drug treatment while performing any invasive dental procedure.

Dahlgren and Wexell [30] carried out a cross-sectional study using a questionnaire applied to a total of 656 Swedish dentists with the aim of evaluating the level of knowledge of these professionals regarding the behavior and management of patients treated with bisphosphonates and denosumab. Thus, complicated tooth extraction (74.4%) and surgical extraction (73.6%) were the procedures that left participants insecure about performing them in patients using antiresorptive drugs, maybe because the literature shows that tooth extractions and oral surgeries with bone manipulation are among the risks for developing osteonecrosis of the jaws.

In this work, a large part of the interviewees is in line with the information that dental extractions and oral surgeries with bone manipulation are among the risks for developing osteonecrosis of the jaws, since most of them inferred that oral surgeries with bone manipulation increase the risk of drug-related osteonecrosis of the jaws (75.5%) after tooth extraction (61.4%). In addition, most professionals in this study also reported that the dentist can perform all procedures on a patient under the use of antiresorptive drugs as long as great care is taken to avoid bone exposure (60.8%).

Ruggiero et al. [31] claimed in their studies that osteonecrosis of the jaws related to the use of drugs could be defined as a necrosis of the bone tissue characterized by the presence of exposed non-scarring and necrotic bone in the oral and maxillofacial region persisting for more than 8 weeks, with no history of radiotherapy in the cervical-facial region. This definition is in line with the interpretation of the majority of interviewees who indicated the presence of exposed bone or fistula for at least 8 weeks as incipient signs of osteonecrosis in patients with previous or current history of the use of antiresorptive drugs, who did not undergo

radiotherapy in the cervical-facial region (76.1%). In this study, in addition to the answer option chosen by most dentists, there were “others” and “doesn't know” as answer options for the incipient signs of osteonecrosis. Perhaps due to the fact of not having other alternatives that could influence participants of the present study to be confused, the answers of most dentists was consistent with the findings in the literature, especially Ruggiero et al. [31].

Tanna et al. [32] carried out a cross-sectional study using a questionnaire applied to 129 dentists, whose aim was to verify the knowledge of these professionals regarding osteonecrosis of the jaws related to antiresorptive drugs and its causes. When asked about the existence of other drugs in addition to bisphosphonates that could lead to the development of osteonecrosis of the jaw, only 3 (2%) were aware that denosumab could lead to the development of osteonecrosis of the jaw, while the majority (55%) was not aware of any drugs other than bisphosphonates that could lead to the development of osteonecrosis of the jaws.

Although the majority of interviewees in the study by Tanna et al. [32] are unaware of drugs other than bisphosphonates that could lead to the development of osteonecrosis of the jaws, a large part of professionals interviewed in this study indicated the alternative corresponding to Nitrogen and Non-nitrogen bisphosphonates, Denosumab and sunitinib, sorafenib and bevacizumab as antiresorptive drugs (60.8%). It is known that, in the present study, dentists who have or had, in some way, information about antiresorptive medications were professionals with master's, doctoral and post-doctoral degrees (85.4%), followed by specialists (69.6%) and those who had only dentistry degree (56.1%); perhaps, the presence of more participants with a higher academic degree could more safely indicate antiresorptive medications.

Alqhtani et al. [33] showed a weak correlation between knowledge about drug-related osteonecrosis of the jaws and time of experience in dentistry. This finding contrasted with that of this study, which demonstrated that the time since the graduation of interviewees showed a statistically significant association with the fact that the professional knew or had heard about antiresorptive drugs. Perhaps, the time since graduation in Alqhtani et al. [33] had a weak correlation between knowledge about drug-related osteonecrosis of the jaws and years of experience because these studies did not include sample with – professionals holding higher academic degrees, such as master, PhD, post-doctoral and specialist, instead of Dentistry degree only, a fact that, according to the present research, can influence the greater knowledge about antiresorptive drugs.

A study in Spain showed that the knowledge of the side effects of antiresorptive drugs decreases with increasing years of professional practice [34]. This analysis differs from results obtained in this work, which identified that 56.0% and 69.6% of professionals with up to 5 years and with more than 5 years since graduation, respectively, are aware of the possible adverse effects of antiresorptive drugs ( $p < 0.05$ ), as well as 52.3 % and 67.0% of professionals with up to 5 years and more than 5 years since graduation, respectively ( $p < 0.05$ ). All works mentioned above alert dentists, in general, to train themselves in relation to subjects they are unaware of, especially about antiresorptive drugs and appropriate conduct. At the same time, these works can also alert for the need to highlight issues related to the use of antiresorptive drugs in undergraduate dentistry courses, as professionals with skills are needed to avoid and (or) interrupt the serious sequelae that may occur in the jaws of individuals using these drugs.

## Conclusion

Dental surgeons in Brazil, with more than five years since graduation, have more scientific information about anti-resorptive drugs and pharmacological procedures, which can positively contribute to the prevention of osteonecrosis of the jaws and treatment of drug sequelae that may occur.

## Authors' Contributions

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All authors declare that they contributed to critical review of intellectual content and approval of the final version to be published.		

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## Conflict of Interest

The authors declare no conflicts of interest.

## Data Availability

The data used to support the findings of this study can be made available upon request to the corresponding author.

## References

- [1] Kim JM, Lin C, Stavre Z, Greenblatt MB, Shim JH. Osteoblast-osteoclast communication and bone homeostasis. *Cells* 2020; 9(9):2073. <https://doi.org/10.3390/cells9092073>
- [2] Kuźnik A, Październiak-Holewa A, Jewula P, Kuźnik N. Bisphosphonates—much more than only drugs for bone diseases. *Eur J Pharmacol* 2020; 866:172773. <https://doi.org/10.1016/j.ejphar.2019.172773>
- [3] Xing L, Ebetino FH, Boeckman RK Junior, Srinivasan V, Tao J, Sawyer TK, et al. Targeting anti-cancer agents to bone using bisphosphonates. *Bone* 2020; 138:115492. <https://doi.org/10.1016/j.bone.2020.115492>
- [4] Allen MR. Recent advances in understanding bisphosphonate effects on bone mechanical properties. *Curr Osteoporos Rep* 2018; 16(2):198-204. <https://doi.org/10.1007/s11914-018-0430-3>
- [5] Dell'aquila E, Armento G, Iuliani M, Simonetti S, D'Onofrio L, Zeppola T, et al. Denosumab for cancer-related bone loss. *Expert Opin Biol Ther* 2020; 20(11):1261-74. <https://doi.org/10.1080/14712598.2020.1814731>
- [6] Endo Y, Kumamoto H, Nakamura M, Sugawara S, Takano-Yamamoto T, Sasaki K, et al. Underlying mechanisms and therapeutic strategies for Bisphosphonate-Related Osteonecrosis of the Jaw (BRONJ). *Biol Pharm Bull* 2017; 40(6):739-50. <https://doi.org/10.1248/bpb.b16-01020>
- [7] Farrier AJ, Sanchez Franco LC, Shoab A, Gulati V, Johnson N, Uzoigwe CE, et al. New anti-resorptives and antibody mediated anti-resorptive therapy. *Bone Joint J* 2016; 98-B(2):160-5. <https://doi.org/10.1302/0301-620X.98B2.36161>
- [8] Aldhalaan NA, Baqais A, Al-omar A. Medication-related osteonecrosis of the jaw: a review. *Cureus* 2020; 12(2):6944. <https://doi.org/10.7759/cureus.6944>
- [9] Giudice A, Antonelli A, Chiarella E, Baudi F, Barni T, Di Vito A. The case of medication-related osteonecrosis of the jaw addressed from a pathogenic point of view. innovative therapeutic strategies: focus on the most recent discoveries on oral mesenchymal stem cell-derived exosomes. *Pharmaceuticals* 2020; 13(12):423. <https://doi.org/10.3390/ph13120423>
- [10] Voss PJ, Steybe D, Poxleitner P, Schmelzeisen R, Munzenmayer C, Fuellgraf H, et al. Osteonecrosis of the jaw in patients transitioning from bisphosphonates to denosumab treatment for osteoporosis. *Odontology* 2018; 106(4):469-80. <https://doi.org/10.1007/s10266-018-0362-5>
- [11] Vallina C, Ramírez L, Torres J, Casañas E, Hernández G, López-Pintor RM. Osteonecrosis of the jaws produced by sunitinib: a systematic review. *Med Oral Patol Oral Cir Bucal* 2019; 24(3):e326-e338. <https://doi.org/10.4317/medoral.22858>
- [12] Maluf G, Caldas RJ, Fregnani ER, da Silva Santos PS. A rare case of bevacizumab-related osteonecrosis of the jaw associated with dental implants. *Int J Implant Dent* 2019; 5(1):34. <https://doi.org/10.1186/s40729-019-0188-0>
- [13] Hasegawa T, Kawakita A, Ueda N, Funahara R, Tachibana A, Kobayashi M, et al. A multicenter retrospective study of the risk factors associated with medication-related osteonecrosis of the jaw after tooth extraction in patients receiving oral bisphosphonate therapy: can primary wound closure and a drug holiday really prevent MRONJ? *Osteoporos Int* 2017; 28(8):2465-73. <https://doi.org/10.1007/s00198-017-4063-7>
- [14] Wick A, Bankosegger P, Otto S, Hohlweg-Majert B, Steiner T, Probst F, et al. Risk factors associated with onset of medication-related osteonecrosis of the jaw in patients treated with denosumab. *Clin Oral Investig* 2022; 26(3):2839-52. <https://doi.org/10.1007/s00784-021-04261-4>
- [15] Nicolatou-Galitis O, Schiodt M, Mendes RA, Ripamonti C, Hope S, Drudge-Coates L, et al. Medication-related osteonecrosis of the jaw: definition and best practice for prevention, diagnosis, and treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2019; 127(2):117-35. <https://doi.org/10.1016/j.oooo.2018.09.008>
- [16] Song M. Dental care for patients taking antiresorptive drugs: a literature review. *Restor Dent Endod* 2019; 44(4):e42. <https://doi.org/10.5395/rde.2019.44.e42>

- [17] Kim HY. Review and update of the risk factors and prevention of antiresorptive-related osteonecrosis of the jaw. *Endocrinol Metab* 2021; 36(5):917-27. <https://doi.org/10.3803/EnM.2021.1170>
- [18] Dimopoulos MA, Kastiris E, Bamia C, Melakopoulos I, Gika D, Roussou M, et al. Reduction of osteonecrosis of the jaw (ONJ) after implementation of preventive measures in patients with multiple myeloma treated with zoledronic acid. *Ann Oncol* 2009; 20(1):117-20. <https://doi.org/10.1093/annonc/mdn554>
- [19] Yarom N, Shapiro CL, Peterson DE, Van Poznak CH, Bohlke K, Ruggiero SL, et al. Medication-related osteonecrosis of the jaw: MASCC/ISOO/ASCO clinical practice guideline. *J Clin Oncol* 2019; 37(25):2270-90. <https://doi.org/10.1200/JCO.19.01186>
- [20] Maluf G, Caldas RJ, Silva Santos PS. Use of leukocyte- and platelet-rich fibrin in the treatment of medication-related osteonecrosis of the jaws. *J Oral Maxillofac Surg* 2018; 76(1):88-96. <https://doi.org/10.1016/j.joms.2017.06.004>
- [21] Di Fede O, Canepa F, Panzarella V, Mauceri R, Del Gaizo C, Bedogni A, et al. The Treatment of Medication-Related Osteonecrosis of the Jaw (MRONJ): a systematic review with a pooled analysis of only surgery versus combined protocols. *Int J Environ Res Public Health* 2021; 18(16):8432. <https://doi.org/10.3390/ijerph18168432>
- [22] Monteiro L, Vasconcelos C, Pacheco JJ, Salazar F. Photobiomodulation laser therapy in a Lenvatinib-related osteonecrosis of the jaw: a case report. *J Clin Exp Dent* 2021; 13(6):e626-9. <https://doi.org/10.4317/jced.58323>
- [23] Almeida MVDC, Moura AC, Santos L, Gominho L, Cavalcanti UDNT, Romeiro K. Photodynamic therapy as an adjunct in the treatment of medication-related osteonecrosis of the jaw: a case report. *J Lasers Med Sci* 2021; 12:e12. <https://doi.org/10.34172/jlms.2021.12>
- [24] Hayashida S, Soutome S, Yanamoto S, Fujita S, Hasegawa T, Komori T, et al. Evaluation of the Treatment Strategies for Medication-Related Osteonecrosis of the Jaws (MRONJ) and the factors affecting treatment outcome: a multicenter retrospective study with propensity score matching analysis. *J Bone Miner Res* 2017; 32(10):2022-9. <https://doi.org/10.1002/jbmr.3191>
- [25] De Lima PB, Brasil VL, De Castro JF, 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; 23(12):3421-6. <https://doi.org/10.1007/s00520-015-2689-6>
- [26] R Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing 2022. Available from: <https://www.R-project.org/> [Accessed on February 9, 2023]
- [27] Paredes L, Gonçalves LS, Miranda AMMA, Netto JNS, Perez DEC, Pires FR. Knowledge of dental professionals and dental students on bisphosphonates and bisphosphonate-associated osteonecrosis of the jaws. *Res Soc Dev* 2022; 11(9):e16211931553. <https://doi.org/10.33448/rsd-v11i9.31553>
- [28] Marlière DAA, Costa TE, Junqueira RB, Barbosa SM, Asprino L, Chaves Netto HDM. Knowledge and clinical behavior on antiresorptivemedications and osteonecrosis of the jaws: a cross-sectional study. *RGO* 2019; 67:e20190058. <http://doi.org/10.1590/1981-863720190005820190018>
- [29] Vinitzky-Brener I, Ibáñez-Mancera NG, Aguilar-Rojas AM, Álvarez-Jardón AP. Knowledge of bisphosphonate-related osteonecrosis of the Jaws among Mexican dentists. *Med Oral Patol Oral Cir Bucal* 2017; 22(1):e84-e87. <https://doi.org/10.4317/medoral.21433>
- [30] Dahlgren M, Wexell CL. Uncertainty managing patients treated with antiresorptive drugs: a cross-sectional study of attitudes and self-reported behavior among dentists in Sweden. *Acta Odontol Scand* 2020; 78(2):109-17. <https://doi.org/10.1080/00016357.2019.1655586>
- [31] 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; 72(10):1938-56. <https://doi.org/10.1016/j.joms.2014.04.031>
- [32] Tanna N, Steel C, Stagnell S, Bailey E. Awareness of medication related osteonecrosis of the jaws (MRONJ) amongst general dental practitioners. *Br Dent J* 2017; 222(2):121-5. <https://doi.org/10.1038/sj.bdj.2017.79>
- [33] Alqhtani NR, Almalki AK, Zuhair FA, Alenazi AA, Nabhan AB, Alqahtani M. Knowledge, attitude, and management of general dentist toward medication-related osteonecrosis of the jaws. *J Pharm Bioallied Sci* 2020; 12(Suppl 1):S151-S154. [https://doi.org/10.4103/jpbs.JPBS\\_47\\_20](https://doi.org/10.4103/jpbs.JPBS_47_20)
- [34] Escobedo M, García-Consuegra L, Junquera S, Olay S, Ascani G, Junquera L. Medication-related osteonecrosis of the jaw: A survey of knowledge, attitudes, and practices among dentists in the principality of Asturias (Spain). *J Stomatol Oral Maxillofac Surg* 2018; 119(5):395-400. <https://doi.org/10.1016/j.jormas.2018.04.008>