Ann Med Res 2020;27(9):2421-7

Annals of Medical Research

DOI: 10.5455/annalsmedres.2020.03.259

Original Article

Medication-related osteonecrosis of the jaw: A survey of knowledge, practices and opinions of dentists

Onur Sahin

Deparment of Oral and Maxillofacial Surgery, Faculty of Dentistry, Izmir Katip Celebi University, Izmir, Turkey

Abstract

Aim: The aim of this study was to evaluate dentists on their knowledge on biphosphonates, medication related osteonecrosis of the jaw (MRONJ), and on the treatment approaches towards patients using bisphosphonates in the Faculty of Dentistry at İzmir Katip Çelebi University.

Material and Methods: This was a questionnaire-based cross-sectional study conducted on 97 dentists. The surveys consists of a total of 20 questions and four sections, with statistical analysis being used on the collected data. The Chi-square and Student-t tests were utilized to compare between the groups. The significance level was set at $p < 0.05$.

Result: There was no significant difference in terms of correct answers to the questions between the dentists with professional experience in surgical procedures (Group A), and the dentists without professional experience in surgical procedures (Group B) ($p > 0.05$). In the second part of the questionnaire, the dentists were asked various questions in order to measure their general knowledge regarding bisphosphonates and MRONJ. There was no significant difference between the groups in terms of correct answers ($p > 0.05$). In the third part of the questionnaire, surgical scenarios were presented to the dentists and generally, they preferred the option in which no procedure should be performed in patients who take intravenous (IV) bisphosphonates, regardless of the duration of use.

Conclusions: Increasing the awareness of medical practitioners, dentists, and patients in the use and side effects of bisphosphonates is important for preventing MRONJ. For this purpose, training strategies related to MRONJ should be established.

Keywords: Awareness; knowledge; medication related osteonecrosis of the jaw

INTRODUCTION

Bisphosphonates (BPs) are drugs that inhibit osteoclastic function and are non-metabolized analogues of endogenous pyrophosphonates (1). BPs, which can be taken oral or intravenous (IV) route and whose absorption takes place in the small intestine, pass through the systemic circulation quickly and are localized on the bone mineral surface, especially where osteoclastic activity is intense. The half-life of the bisphosphonates varies between 1-10 years (2). BPs generally act by inhibiting osteoclastic activity. At the same time, these drugs have been shown to suppress the bone turnover mechanism and inhibit the growth of mucous epithelial cells by inhibiting angiogenesis, thereby disrupting wound healing (3).

BPs is one of the most commonly used antiresorptive drugs to prevent skeletal complications of many diseases (4). BPs play an important role in the treatment of metastatic bone diseases and osteoporosis. It is used to reduce both serious complications such as hypercalcemia and pathological fractures, and to reduce complaints of pain thereby improving the quality of life in cancer patients with bone metastases (5).

Jaw bone osteonecrosis, which developed due to the use of bisphosphonate type drug, was first published by Marx in 2003 (6). However, until the report by The American Association of Oral and Maxillofacial Surgeons (AAOMS) was published in 2009, no universally accepted definition of bisphosphonate osteonecrosis had been presented. Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is defined as a necrotic bone area exposed for more than 8 weeks in the maxillofacial region without any history of radiotherapy in patients using bisphosphonates (7). In recent studies, antiresorptive and antiangiogenic drugs (Denosumab, Bevacizumab, Rituximab, Sunitinib and Raloxifene etc.) have been reported to cause BRONJ-like lesions and the last update published by AAOMS in 2014; recommended the use of the term ''medication related osteonecrosis of the jaw'' (MRONJ) (8).

Many factors such as therapeutic indication, drug type and duration, local factors, demographic, systemic and genetic

Received: 23.03.2020 **Accepted:** 21.08.2020 **Available online:** 22.09.2020
Corresponding Author: Onur Sahin, Deparment of Oral and Maxillofacial Surgery, Faculty of Dentistry, Izmir Katip Celebi University, Izmir, Turkey **E-mail:** onursahin43@hotmail.com

factors were mentioned in determining the incidence of MRONJ (9). Local etiological factors that are effective in the development of MRONJ are defined as dentoalveolar surgical procedures, anatomical factors, dentures and accompanying local intraoral inflammatory diseases (8). A large-scale review by Filleul et al. concluded that tooth extraction was the main triggering factor in 67% of MRONJ cases (10). Tooth extraction is a predisposing factor between 52% and 61% in MRONJ formation (11). The incidence of developing osteonecrosis after tooth extraction is reported as 0.5% in patients using oral BPs, while it is reported between 1.6% and 14.8% in patients using BPs via IV route (12). These studies clearly show that tooth extraction is an important risk factor to consider in the development of MRONJ. In addition, Marx et al. reported that periodontitis was present in 84% of patients with BRONJ, dental caries in 29%, gingival abscess in 13%, recent canal treatment in 11% and the presence of anatomical differences in the mandible (6).

In the light of this information regarding MRONJ and its applications in dentistry, it is important for dentists to have awareness and knowledge on subjects such as bisphosphonates, MRONJ development and treatment. The aim of this present study was to evaluate dentists' knowledge on biphosphonates and MRONJ, and the treatment approaches towards patients using bisphosphonates at the various departments in our faculty.

MATERIAL and METHODS

This study is a cross-sectional based survey that was conducted over a period of 3 months and was approved by the Non-Interventional Clinical Studies Institutional Review Board of İzmir Katip Çelebi University (IRB No:345). This study has been carried out in accordance with the guidelines regarding the Helsinki Human Rights Act. Potential participants were defined as dentists who received a PhD in the field or are undergoing specialty training at the various departments of Faculty of Dentistry, İzmir Katip Çelebi University. The participating dentists were asked fill out survey forms which were distributed and collected by hand, upon completion. In this study, the questionnaire developed by Albussain et al., which is in line with the 2009 principles of the Oral and Maxillofacial Surgery Association, was used following the review of the related literature and similar studies (13).

The surveys consist of a total of 20 questions and four sections. The participants were split into two groups, with the first being a group of 38 residents with professional experience in surgical procedures (Oral and Maxillofacial Surgery, Periodontology) (Group A) and the second a group of 59 residents without professional experience in surgical procedures (Restorative Dentistry, Endodontics, Pediatric Dentistry, Oral and Maxillofacial Radiology, Orthodontics and Prosthodontics) (Group B). The answers given by the residents to the questions provided in the survey were identified with numbers and percentages and recorded for use in statistical evaluations which were performed using SPSS 21.0 (Statistical Package for the Social Sciences, Chicago, IL, USA). All categorical variables are presented as percentages and continuous variables are presented as mean and standard deviation. Chi-square test was used to calculate categorical variables and Student-t test was used to calculate quantitative variables. All data were evaluated at a significance level of $p < 0.05$.

RESULTS

The study included 32 dentists aged 24-25 years, 62 dentists aged 26-30 years, 2 dentists aged 31-35 years, and 1 dentist 36-years-old. Of the 97 dentists, 53 (54.63%) are female and 44 (45.37%) are male. The majority of the physicians (49.48%) participating in the study have a duration of 3-5 years as a dentist (Table 1).

Table 1. Description of the dentists participating in the survey

	N(%)
Age (yr)	
23-24	32 (32.9)
25-30	62 (63.9)
31-35	2 (2.1)
>35	1 (1.1)
Gender	
Female	53 (54.63)
Male	44 (45.37)
Working years as a dentist (yr)	
1-2	32 (32.9)
3-5	48 (49.48)
6-10	14 (14.52)
>10	3 (3.1)

The responses given by physicians for the treatment options according to the stages of the use of bisphosphonates, routes of administration and MRONJ are shown in Table 2. The correct answers are indicated by an asterisk (*). When dentists were asked about diseases requiring using bisphosphonates, 84.5% indicated osteoporosis, 78.4% bone metastases, 53.7% multiple myeloma and 40.2% osteitis deformans; 9,2% answering diabetes and 5,1% hypertension. When asked about the intake methods of bisphosphonates, 91.7% of residents answered IV ,76.2% orally, and 4.1% "not sure", with 26.8% indicating that the answer was Intramuscular (IM) which was incorrect. When asked about correct treatment options during the high risk phase of MRONJ, 43.2% answered that there is no need for treatment and 86.5% indicated that "patient education" would be required. In the Stage 0 of MRONJ, the correct responses, patient education and the treatment of symptoms options were marked as 91.7% and 50.5%, respectively. The correct response for Stage 1, patient education, the treatment of symptoms and mouthwash options were 88.6%, 76.2% and 60.8%, respectively. The correct responses for Stage 2 were the patient education, treatment of symptoms, mouthwash, and antibiotic treatment. The correct response rate in Stage 2 was 83.5%, 73.1%, 69.1%, 81.4%, respectively. For Stage 3 the correct answers were; patient education marked as 79.3%, treatment of symptoms 86.5%, use of mouthwash 63.9%, antibiotics 91.7% and surgical debridement 77.3%.

Table 2. Frequency of responses to the questions measuring participants' general knowledge about MRONJ

	N(%)
Knowledge Q1: indication for bisphosphonates use	
Osteoporosis*	82 (84.5)
Osteoitis deformans*	39 (40.2)
Diabetes	9 (9.2)
Bone metastates*	76 (78.4)
Multiple myeloma*	52 (53.7)
Hypertension	5 (5.1)
Knowledge Q2: bisphosphonate route of administration	
Oral*	
Intravenous*	
Intramuscular	
Not sure	
Knowledge Q3-Q7: selected treatment for MRONJ stages	
At risk	
No treatment*	42 (43.2)
Patient education*	84 (86.5)
Treat symptoms	36 (37.1)
Mouth rinse	62 (63.9)
Antibiotics	19 (19.5)
Surgical debridement	9 (9.2)
Stage 0	
No treatment	31 (31.9)
Patient education*	89 (91.7)
Treat symptoms*	49 (50.5)
Mouth rinse	66 (68.1)
Antibiotics	21 (21.6)
Surgical debridement	11 (11.3)
Stage 1	
No treatment	27 (27.8)
Patient education*	86 (88.6)
Treat symptoms*	74 (76.2)
Mouth rinse*	59 (60.8)
Antibiotics	44 (45.3)
Surgical debridement	16 (16.4)
Stage 2	
No treatment	23 (23.7)
Patient education*	81 (83.5)
Treat symptoms*	71 (73.1)
Mouth rinse*	67 (69.1)
Antibiotics*	79 (81.4)
Surgical debridement	37 (38.1)
Stage 3	
No treatment	17 (17.5)
Patient education*	77 (79.3)
Treat symptoms*	84 (86.5)
Mouth rinse*	62 (63.9)
Antibiotics*	89 (91.7)
Surgical debridement*	75 (77.3)

MRONJ: Medication-related osteonecrosis of the jaw
Q: Question *: Correct answers

In the third part of the questionnaire, dental procedures required by patients were presented and dentists were asked to mark the procedures that can be performed in accordance with the duration and route of the bisphosphonate use. The answers given are shown in Table 3 and the correct answers are shown with an asterisk (*). When asked about simple tooth extraction the answer included, patients who have oral bisphosphonate use under 3 years can be treated, those who use bisphosphonate for more than 3 years can be treated after 3 months break, and those who use IV bisphosphonate can be operated independently of their duration, and their marking rates are 62.8, 43.2%, 14.4% and 5.1% respectively. When asked about complicated tooth extractions, 55.6% of residents selected the correct response which was that "it can be performed in patients using oral bisphosphonates for less than 3 years." Other responses included, "in those who use bisphosphonates for more than three years, the procedure can be done after 3 months", and "those who use IV bisphosphonate can be treated independently of their duration", with the correct responses being marked as 39.1%, 5.1% and 3.1%, respectively. Correct answers for impacted tooth extraction were also the same as in the other types of tooth extractions, and the marking rates of these responses were found to be 40.2%, 31.9%, 4.1%, 2.1%, respectively. The other procedure which was provided was related to dental implant treatment in patients taking bisphosphonates. Answers included, "those who had been using oral bisphosphonates for under three years" and "those who used it for more than 3 years", with the correct answer being treatment after a 3-month break, were marked as 50.5% and 37.1%, respectively. Correct answers for "periodontal surgery and endodontic surgery can be performed in patients who have used oral bisphosphonates for less than 3 years", "those who use bisphosphonates for more than 3 years can be treated after a 3 month break", and "those who use IV bisphosphonates can be operated on independent of the duration". The marking rates of these responses were 53.7%, 40.2%, 24.7% and 11.3% for periodontal surgery, and 42.3%, 38.1%, 17.5% and 9.2% for endodontic surgery, respectively.

In the fourth part of the questionnaire, the dentists were asked if they knew whether other drugs other than bisphosphonates cause jaw bone osteonecrosis, whether they knew that the term MRONJ was used instead of the term BRONJ, do you feel comfortable treating patients with MRONJ with their current knowledge, where they had obtained the first information about BRONJ was asked (Table 4). 62.8% of dentists answered "No" to the question of "Do you know that other drugs besides bisphosphonates cause osteonecrosis?" 71.1% of the dentists answered "No" to the question of "Do you know that term MRONJ is used instead of BRONJ?". To the question of "Do you feel comfortable treating patients with MRONJ with your current knowledge?"

Table 3. Frequency of management plans for the 6 scenario procedures differing by route and duration of BP administration

	Perform Scenario Procedure,(%)	Discontinue BP for 3 moi Then perform scenario procedure, (%)	Do not Perform Scenario procedure, (%)	Refer %
Scenario 1: simple tooth extraction				
Oral BP ≤3 year	61 (62.8)*	24 (24.8)	4 (4.1)	8 (8.3)
Oral BP >3 year	32(32.9)	42 (43.2)*	16 (16.5)	7 (7.4)
IV BP ≤3 year	14 (14.4)*	52 (53.6)	24 (24.6)	7 (7.4)
IV BP > 3 year	5 (5.1)*	19 (19.6)	40 (41.2)	33 (34.1)
Scenario 2: complicated tooth extraction				
Oral BP ≤3 year	54 (55.6)*	19 (19.6)	11 (11.4)	13 (13.4)
Oral BP >3 year	29 (29.9)	38 (39.1)*	22 (22.7)	8 (8.3)
IV BP ≤3 year	5 (5.1)*	39(40.2)	39 (40.2)	14 (14.5)
IV BP > 3 year	3 (3.1)*	21 (21.7)	56(57.8)	17 (17.4)
Scenario 3: impacted tooth extraction				
Oral BP ≤3 year	39 (40.2)*	22 (22.7)	24 (24.8)	12 (12.3)
Oral BP >3 year	28 (28.9)	31 (31.9)*	27 (27.9)	11 (11.3)
IV BP ≤3 year	4 (4.1)*	29 (29.9)	46 (47.4)	18 (18.6)
IV BP > 3 year	2 (2.1)*	26 (26.9)	51 (52.4)	18 (18.6)
Scenario 4: implant placement				
Oral BP ≤3 year	49 (50.5)*	21 (21.6)	13 (13.4)	14 (14.5)
Oral BP >3 year	25 (25.8)	36 (37.1)*	17 (17.4)	19 (19.7)
IV BP ≤3 year	11 (11.3)	19 (19.7)	43 (44.3)*	24 (24.7)
IV BP > 3 year	6 (6.2)	17 (17.4)	59 (60.9)*	15 (15.5)
Scenario 5: periodontal surgery				
Oral BP ≤3 year	52 (53.7)*	31 (31.9)	5 (5.2)	9 (9.2)
Oral BP > 3 year	32 (32.9)	39 (40.2)*	14(14.5)	12 (12.4)
IV BP ≤3 year	24 (24.7)*	35 (36.1)	28 (28.9)	10 (10.3)
IV BP > 3 year	11 (11.3)*	26 (26.7)	41 (42.3)	19 (19.7)
Scenario 6: endodontic surgery				
Oral BP ≤3 year	41 (42.3)*	28 (28.8)	19 (19.7)	9 (9.2)
Oral BP > 3 year	32 (32.9)	37 (38.1)*	21 (21.6)	7 (7.4)
IV BP ≤3 year	17 (17.5)*	33 (34.1)	36 (37.1)	11 (11.3)
IV BP > 3 year	9 (9.2)*	26 (26.9)	41 (42.2)	21 (21.7)

BP: Bisphosphonate; IV: Intravenous; *: Correct Answers

Table 4. Frequency of responses to questions on knowledge acquisition

	N (%)
Q 1: Do you know that other drugs besides bisphosphonates cause osteonecrosis?	
Yes	36 (37.2)
No	61 (62.8)
Q 2: Do you know that in terminology, MRONJ is used instead of BRONJ?	
Yes	28 (28.9)
No	69 (71.1)
Q 3: Do you feel comfortable treating patients with MRONJ with your current knowledge?	
Yes	12 (12.4)
Could use minor supplementation	14 (14.5)
Not sure	27 (27.8)
No	44 (45.3)
Q 4: Where did you first learn about BRONJ?	
Undergraduate education	78 (80.4)
Journal articles	8 (8.1)
Internet	5 (5.1)
Scientific meetings	4 (4.3)
Continuing education courses	2 (2.1)

MRONJ: Medication related osteonecrosis of the jaw
BRONJ: Bisphosphonates related osteonecrosis of the jaw

45.3% of dentists answered ''No'', with 27.8% indicating that they were "Not Sure" if they are comfortable while treating BRONJ patients. When asked where they received information on BRONJ for the first time, most of the residents indicated the undergraduate education option (80.4%).

There was no significant difference in terms of correct answers to the questions between the genders and between specialist groups performing surgical procedures and the non-surgical groups (p> 0.05). In the second part of the questionnaire, questions regarding biphosphonates and BRONJ were asked in order to measure their general knowledge on the subject. There was no significant difference between the groups in terms of correct answers (p> 0.05). In the third part of the questionnaire, surgical scenario questions were asked clinically. Generally, dentists preferred the option that no procedure is performed in patients who use IV bisphosphonates, regardless of duration of use. When the answers given to the clinical scenario questions were compared, significantly more correct answers were obtained in the group of dentists performing surgical procedures (p: 0.039).

DISCUSSION

Although clinical and experimental research has been conducted since the first report of BRONJ, information on the treatment and prognosis of the disease is still limited. Therefore, it is critical for medical professionals and dentists to evaluate oral health and dental risk factors before, during and after application of bisphosphonates. Today, the best precaution for MRONJ treatment is to prevent it from occurring at all (14). For this purpose, it is recommended that practitioners follow up with patients diagnose the early clinical and radiological signs and prefer endodontic treatment instead of extraction (15). The amount of existing knowledge of dentists concerning anti-resorptive drug use, questioning whether these drugs are being used by patients while taking their history, and possessing a sold theoretical and practical infrastructure about jaw bone osteonecrosis caused by the drug are extremely effective in preventing these complications. Vescovi et al. reported that 63.8% of 567 MRONJ cases occurred due to a previous dentoalveolar procedure (16). For this purpose, in our cross-sectional study, it was designed to evaluate the knowledge, practice and opinions of dentists about patients using bisphosphonates and other antiresorptive drugs.

In this current study, when dentists were asked about the diseases in which bisphosphonates were used, the options of osteoporosis (84.5%) and bone metastases (78.4%), which were highly accurate, were selected. In the study of Hajmohammadi et al. with 116 dentists, when the diseases using bisphosphonates were asked; 64.7% of participants marked osteoporosis treatment, 53.4% marked bone metastases (17). In the study of Lima et al., it was determined that 65.4% of the dentists did not know the diseases which indicated use of bisphosphonates (18). Comparing these data with previous studies, it was observed that the dentists who participated in our study had more information concerning the indications of bisphosphonates. However, it should be taken into consideration that the dentists participating in our study are young and have a specialist level or PhD education.

When dentists were questioned on treatment options according to the stages of BRONJ in line with the guidelines of the American Oral and Maxillofacial Surgery Association; most of the dentists marked patient education (informing patients on the importance of oral care and giving oral hygiene education) in the early stages of the disease, treating the symptoms and mouthwash options, and in the advanced stages, they chose the antibiotic option. In the study of Alhussain et al., participants preferred less aggressive approaches at early stages, while marking antibiotic use and surgical debridement options for the advanced stages of the disease (13). The answers provided by the dentists in the study were found to be largely compatible with the correct answers.

In the third part of the questionnaire, the dentists participating in the study were asked about the procedure and the duration of the bisphosphonate intake for 6 different surgical applications. Participants gave more accurate answers to the scenarios in which patients have used oral BPs for less than 3 years. However, when concerning those who had used BP orally for more than 3 years or those who received BP via IV route were more likely to respond incorrectly about the surgical applications. This shows that although the participants had sufficient information about the use of bisphosphonates, they do not have sufficient information about how to perform these procedures in their clinical practice. In clinical scenario questions, participants had increased referral rates in patients using IV bisphosphonates. In the study of Alhussain et al., dentists mostly preferred to direct patients who had used bisphosphonates for more than 3 years and patients using IV bisphosphonates to a specialist. In addition, as the complexity of the surgery to be performed increased, the referral rates of dentists increase as well (13). In the study of Gonzales et al., it was determined that dentists tend to avoid invasive procedures and refer patients to another dentist (19). In our study, it was observed that dentists performing surgery answered clinical scenario questions correctly at a significantly higher rate (p< 0.05).

80.5% of the dentists who participated in our study stated that they received the first information about BRONJ during their undergraduate education. In the study of De Lima et al., 35.6% of dentists received their knowledge about bisphosphonates during the undergraduate period (18). In the study of Alhussain et al., physicians with an age range of 45-54 years were reported to have a statistically significantly lower knowledge score than other age groups (13). This shows that with the increase in the use of bisphosphonates and the rate of development of BRONJ, this issue is included in the curriculum and especially

newer graduates have more knowledge on this subject. In this study, we attribute the higher rate of correct answers compared to other studies in the literature to the lower average age of the participants and to the participants having a PhD or specialist level education.

The answers given to the questions that if they knew whether other drugs besides bisphosphonates cause the jaw bone osteonecrosis and if they knew whether MRONJ was used instead of BRONJ in terminology, were largely "no". We think that the lack of information on this subject should be updated with the courses given at the undergraduate level.

In the literature, there is a consensus among dentists on the need to expand MRONJ prevention training (20-22). It is important that dentists have sufficient knowledge about MRONJ. However, it is a fact that many patients do not have sufficient information about the drugs they use. In this group of patients, effective communication and close cooperation between medical practitioners and dentists should be essential.

CONCLUSION

There are a limited number of studies in the literature regarding the knowledge of dentists about bisphosphonates and MRONJ. Existing studies were carried out by asking different questions to different groups (dentists, specialist dentists, dentistry students). Therefore, the fact that we could not compare the data of this study with the previous studies and that the data were regional is the limitation of our study. The results of current study show that although the majority of the dentists have knowledge about bisphosphonates and MRONJ, they do not find themselves sufficient to treat patients using bisphosphonates. It also shows that they do not have sufficient knowledge about the updated current terminology and on antiresorptive and antiangiogenic drugs other than and bisphosphonate. Given the difficulty of the treatment process of the disease, the best measure for MRONJ treatment is to be protected from the disease before it occurs. This will be possible by increasing the awareness of medical practitioners, dentists and patients about the use and side effects of bisphosphonates. For this purpose, training strategies related to MRONJ should be established.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: This study was reviewed and approved by Katip Celebi University Non-Interventional Clinical Studies Institutional Review Board, Turkiye (No:345).

REFERENCES

1. Migliorati CA, Woo SB, Hewson I, et al. A systematic review of bisphosphonate osteonecrosis (bon) in cancer. Support Care Cancer 2010;18:1099-106.
2. Diel IJ, Bergner R, Grötz KA. Adverse effects of bisphosphonates: current issues. J Support Oncol 2007;5:475-82.
3. Holtmann H, Lommen J, Kübler NR, et al. Pathogenesis of medication-related osteonecrosis of the jaw: a comparative study of in vivo and in vitro trials. J Int Med Res 2018;46:4277-96.
4. Gutta R, Louis P. Bisphosphonates and osteonecrosis of the jaws: Science and rationale. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;104:186-93.
5. Assael LA. Oral bisphosphonates as a cause of bisphosphonate-related osteonecrosis of the jaws: clinical findings, assessment of risks and preventive strategies. J Oral Maxillofac Surg 2009;67:35-43.
6. Marx RE. Pamidronate (Aredia) and zoledronate (Zometa) induced avascular necrosis of the jaws: a growing epidemic. J Oral Maxillofac Surg 2003;61:1115-7.
7. Ruggiero SL, Dodson TB, Assael LA, et al. American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaw-2009 update. Aust Endod J 2009;35:119-30.
8. Ruggiero SL, Dodson TB, Fantasia J, et al. Medication-Related Osteonecrosis of the Jaw—2014 Update. J Oral Maxillofac Surg 2014;72:1938-56.
9. Sahin O, Odabasi O, Aliyev T, et al. Risk factors of medication-related osteonecrosis of the jaw: a retrospective study in a Turkish subpopulation. J Korean Assoc Oral Maxillofac Surg 2019;45:108-15.
10. Filleul O, Crompot E, Saussez S. Bisphosphonate-induced osteonecrosis of the jaw: a review of 2,400 patient cases. J Cancer Res Clin Oncol 2010;136:1117-24.
11. Otto S, Tröltzsch M, Jambrovic V, et al. Tooth extraction in patients receiving oral or intravenous bisphosphonate administration: a trigger for BRONJ development? J Craniomaxillofac Surg 2015;43:847-54.
12. Yamazaki T, Yamori M, Ishizaki T, et al. Increased incidence of osteonecrosis of the jaw after tooth extraction in patients treated with bisphosphonates: a cohort study. Int J Oral Maxillofac Surg 2012;41:1397-403.
13. Alhussain A, Peel S, Dempster L, et al. Knowledge, practices, and opinions of ontario dentists when treating patients receiving bisphosponates. J Oral Maxillofac Surg 2015;73:1095-105.
14. El-Rabbany M, Sgro A, Lam DK, et al. Effectiveness of treatments for medication-related osteonecrosis of the jaw: A systematic review and meta-analysis. J Am Dent Assoc 2017;148:584-94.
15. Dereci O, Orhan EO, Irmak O, et al. The effect of the duration of intravenous zolendronate medication on the success of non-surgical endodontic therapy: a retrospective study. BMC Oral Health 2016;16:9.
16. Vescovi P, Campisi G, Fusco V, et al. Surgery-triggered and non surgery-triggered Bisphosphonate-related Osteonecrosis of the Jaws (BRONJ): a retrospective analysis of 567 cases in an Italian multicenter study. Oral Oncol 2011;47:191-4.

17. Hajmohammadi E, Sattarzadeh S, Amani F. Knowledge rate of dentists regarding dental consideration of bisphosphonate drug user patients. J Res Med Den Sci 2015;3:194-8.
18. de Lima PB, Brasil VL, de Castro JF, et al. Knowledge and attitudes of Brazilian dental students and dentists regarding bisphosponate-related osteonecrosis of the jaw. Support Care Cancer 2015;23:3421-6.
19. Gonzales CB, Young V, Ketchum NS, et al. How concerns for bisphosphonate- induced osteonecrosis of the jaw affect clinical practice among dentists: a study from the South Texas Oral Health Network. Gen Dent 2015;63:61-7.
20. Escobedo M, García-Consuegra L, Junquera S, et al. 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;119:395-400.
21. Al-Samman AA, Al-Ani RS. Across-sectional survey on medication-related osteonecrosis of the jaws' knowledge and awareness in a sample of dental society. J Craniomaxillofac Surg 2019;47:926-31.
22. Sturrock A, Preshaw PM, Hayes C, et al. General dental practitioners' perceptions of, and attitudes towards, improving patient safety through a multidisciplinary approach to the prevention of medication-related osteonecrosis of the jaw (MRONJ): a qualitative study in the North East of England. BMJ Open 2019;9:e029951.