

# Awareness of Medication Related Osteonecrosis of the Jaw among Dentist Working at Public Oral and Dental Health Care Centers in Ankara, Turkey

## Türkiye, Ankara’da Kamu Ağız ve Diş Sağlığı Merkezlerinde Çalışan Diş Hekimleri Arasında Çenenin İlaçla İlişkili Osteonekrozu Farkındalığı

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**ABSTRACT Objective:** Medication related osteonecrosis of the jaw (MRONJ) is a major complication of treatment with antiresorptive and antiangiogenic agents in the oral and maxillofacial region. This cross-sectional study aims to evaluate knowledge and awareness about MRONJ among dentists working in Ankara, Turkey. **Material and Methods:** A cross-sectional survey was carried out among dentists working at public oral and dental health care centers in Ankara. A questionnaire was designed to seek information about dentists’ demographic characteristics, their knowledge of the term “MRONJ”, of drugs that cause jaw osteonecrosis, of the risk factors of MRONJ and their attitudes and practices regarding MRONJ. A total of 325 dentists participated in the study. **Results:** More than half of the dentists in this study were unable to define osteonecrosis of the jaw. Most (61.2%) were able to identify bisphosphonates associated with MRONJ, but about 80% were unaware of antiangiogenic drugs and 93.5% of nuclear factor kappa B ligand inhibitors. Most dentists in the study were unaware of most of the main risk factors for MRONJ. Thirty-six percent of the dentists had received MRONJ training during their undergraduate education, but only 5.2% had been trained in the last five years. **Conclusion:** This study highlights a huge lack of knowledge and awareness about MRONJ among dentists in Turkey. There is a need to provide further education and training in order to improve dentists’ awareness of bisphosphonates and other medications that have the potential to cause osteonecrosis. Education of healthcare professionals and multidisciplinary cooperation can potentially improve patient safety and reduce the risk of developing MRONJ.

**ÖZET Amaç:** Çenenin ilaca bağlı osteonekrozu (MRONJ), oral ve maksillofasial bölgede antirezorptif ve antianjiyojenik ajanlarla tedavinin önemli bir komplikasyonudur. Bu kesitsel çalışma Türkiye, Ankara’daki diş hekimleri arasındaki MRONJ bilgi ve farkındalığını değerlendirmeyi amaçlamaktadır. **Gereç ve Yöntemler:** Ankara’da, kamu ağız ve diş sağlığı merkezlerinde çalışan diş hekimleri arasında kesitsel bir anket yapılmıştır. Diş hekimlerinin demografik özellikleri, “MRONJ” terimi, çene osteonekrozuna neden olan ilaçlar, MRONJ risk faktörleri, MRONJ ile ilgili tutum ve uygulamaları hakkında bilgi edinmek amacıyla bir anket tasarlanmıştır. Çalışmaya, toplam 325 diş hekimi katılmıştır. **Bulgular:** Bu çalışmada, diş hekimlerinin yarısından fazlası çenenin osteonekrozunu tanımlayamamıştır. Çoğu (%61,2) MRONJ ile ilişkili bifosfonatları tanımlayabilmiştir, ancak yaklaşık %80’i antianjiyojenik ilaçlardan ve %93,5’i nükleer faktör kapa B ligand inhibitörlerinden habersizdir. Çalışmada çoğu diş hekimi, MRONJ için ana risk faktörlerinin çoğunun farkında değildi. Diş hekimlerinin %36’sı lisans eğitimi sırasında MRONJ eğitimi almıştır, ancak son 5 yılda sadece %5,2’si eğitim almıştır. **Sonuç:** Bu çalışma, Türkiye’deki diş hekimleri arasında MRONJ hakkında büyük bir bilgi ve farkındalık eksikliğini vurgulamaktadır. Diş hekimlerinin, bisfosfonatlar ve çene nekrozuna neden olma potansiyeli olan diğer ilaçlarla ilgili farkındalıklarını artırmak için daha fazla eğitim ve öğretime ihtiyaç vardır. Sağlık profesyonellerinin eğitimi ve multidisipliner iş birliği potansiyel olarak hasta güvenliğini artırabilir ve MRONJ gelişme riskini azaltabilir.

**Keywords:** Medication related osteonecrosis of the jaw; antiresorptive drugs; antiangiogenic drugs; dentists

**Anahtar Kelimeler:** Çenenin ilaçlarla ilişkili osteonekrozu; antiresorptif ilaçlar; antianjiyojenik ilaçlar; diş hekimleri

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Bisphosphonates (BPs) are antiresorptive agents that have been used since the late 1960's to prevent bone loss.<sup>1</sup> However, the first case of BPs related to osteonecrosis of jaw (BRONJ) was published by Marx in 2003.<sup>2</sup> Numerous cases have since been reported in the literature.<sup>3-5</sup> In 2004, Novartis, the manufacturers of pamidronic acid and zoledronic acid, informed healthcare professionals that their labelling contained the risk of medication related osteonecrosis of the jaw (MRONJ). Other drugs such as denosumab and antiangiogenic agents have also been found to cause jaw osteonecrosis.<sup>6,7</sup> Therefore, the American Association of Oral and Maxillofacial Surgeons (AAOMS) changed the term from BRONJ to MRONJ.<sup>7</sup> MRONJ is described as an exposed bone or bone that can be probed with an intraoral or extraoral fistula in the maxillofacial region that has persisted for more than 8 weeks in a patient with a history of antiresorptive or antiangiogenic therapy and who has not received radiation therapy to the jaw or suffered an apparent metastatic disease of the jaw.<sup>8</sup>

BPs are used for osteoporosis, metastases of solid tumour bone, cancer-associated hypercalcaemia, Paget's disease and multiple myeloma.<sup>9</sup> Several hypotheses have been suggested for action mechanisms of BPs, involving the inhibition of osteoclast activity or the reduction of osteoclast numbers.<sup>10-12</sup> In addition, some sources assert that BPs can inhibit angiogenesis.<sup>13,14</sup> Denosumab, which has two commercial trade names, Prolia and Xgeva, is a fully human monoclonal antibody against the nuclear factor kappa B ligand (RANKL) receptor activator and inhibits osteoclastic bone resorption. Denosumab, an antiresorptive drug, is approved for use in both osteoporosis and bone-related malignancies. Bevacizumab and sunitinib have been licensed for use in carcinomas of renal cells, neuroendocrine tumours and gastrointestinal tumours, and inhibit angiogenesis.<sup>13,14</sup>

The main risk factor for the development of MRONJ is dental extraction.<sup>15</sup> The risk of MRONJ in patients receiving intravenous (IV) BPs for cancer therapy is higher than for those receiving oral or IV medication for osteoporosis. Furthermore, antiresorptive drug therapy administered for more than four years and/or with the concomitant of corticosteroids

also related to a higher risk.<sup>8</sup> The precision incidence and prevalence rates of MRONJ are uncertain, with different literature reports. The reported prevalence of MRONJ in cancer patients using antiresorptive or antiangiogenic medications is 1% and in patients treated with osteoporosis using antiresorptive medicines it is 0.01-0.1%.<sup>16</sup> AAOMS states that the incidence ranges from 0.004 to 0.1%.<sup>8</sup> However, MRONJ is difficult to treat and can lead to significant patient morbidity.<sup>17</sup>

MRONJ is a growing problem, as prescription levels of MRONJ-related drugs have risen notably in recent years and are expected to increase further. In 2015, the European Medicines Agency recommended that prescribers issue patient prompting cards explaining the risk of MRONJ associated with their BP medications.<sup>18</sup> The clinical guidelines published through the Scottish Dental Clinical Effectiveness Programme suggest that dental treatment is required before medicines are started and should be thoroughly evaluated by dentists.<sup>19</sup> Clinical guidelines recommend that patients be in optimal oral health as close as possible to the time at which they start MRONJ related medications.<sup>20</sup> Many studies have identified decreases in MRONJ incidence rates using adequate dental screening and preventive care.<sup>21,22</sup> In fact, prevention of MRONJ as much as possible is a far better option than treating it.<sup>23</sup> The success of preventive approaches is specifically associated with awareness of the main risk factors. Vescovi et al. reported that, in 567 cases of MRONJ, 63.8% were related to prior dentoalveolar surgery.<sup>24</sup> Surprisingly, 71.1% of dentists in their study were not aware that dentoalveolar surgery was a major trigger for osteonecrosis in patients receiving BPs.<sup>25</sup> Hence, awareness of MRONJ is critical for dentists because of their role in dentoalveolar surgery such as dental extraction. There has been no comprehensive study to investigate the level of knowledge about MRONJ among dentists in Turkey. This cross-sectional study aims to fill this gap.

## MATERIAL AND METHODS

This study was approved by the ethics committee of the Faculty of Medicine, Afyonkarahisar Health Sciences University (2019/3-56) and all participants

signed an informed consent agreement. The study was undertaken in accordance with the principles of Helsinki Declaration. All dentists working in public oral and dental health care centers in Ankara were planned to be included in the study. Specialist dentists were excluded from the study. Ankara is the second largest city and capital of the country, situated in a central region. There are ten public oral and dental health centres in Ankara and approximately 700 dentists work in these centers. The study was carried out in seven of these centres, including all dentists working in the centres. Three oral and dental health care centres were excluded from the study because they did not give permission for the research, owing to patient density. Permission for the study was obtained from the Ministry of Health, Ankara Provincial Health Directorate (23 May 2019-4120). In addition, permission and approval were obtained from the administration of each of the participating oral and dental health centres in Ankara.

A questionnaire was designed to seek information about dentists' demographic characteristics, their knowledge of the term "MRONJ", of drugs that cause jaw osteonecrosis, of the risk factors of MRONJ and their attitudes and practices regarding MRONJ. The validity and reliability of the questions were confirmed by the pre-test method with a pilot group of 25 dentists. Dentists working in the oral and dental health centres were visited and their consent was obtained for the survey. The questionnaires were administered face to face to 370 dentists. All the data were analysed separately by an oral surgeon. The validity criterion was that all the questions in the questionnaire were read and answered. Therefore, uncompleted surveys and/or surveys in which half or fewer of the questions were filled in were considered invalid. Both descriptive and analytical statistical measurements were used to define the main variables included in each section of the questionnaire, using the Statistical Package for Social Sciences (SPSS-version 22) software (SPSS Inc., Chicago, IL).

## RESULTS

The study was carried out in 7 oral and dental health care centers in Ankara since 3 oral and dental health

centers did not give permission for the survey. Questionnaires were distributed to 370 dentists working in these centers and asked to be answered within ten minutes. 33 dentists did not participate in the survey, and 12 questionnaires were excluded from the study because fewer than half were answered. Three hundred and 25 valid questionnaires were finally obtained from dentists with a response rate of 87.84% (Figure 1).

### SOCIODEMOGRAPHIC CHARACTERISTICS

Some of the demographic features of the participants are summarised in Table 1. Most of the participants in this study were male, aged 35 years or older, and about one-third of the participants had more than 20 years of clinical experience.

### DEFINITION OF MEDICATION RELATED OSTEONECROSIS OF THE JAW

Table 2 shows the dentists' knowledge about the term MRONJ: 11% of the dentists stated that they were now hearing the term MRONJ for the first time, 15.7% had heard it before but did not know what it was, 47.1% knew a little and 25.2% knew enough. When asked "Which of the following criteria should be met in order to define a case as MRONJ?", the dentists answered as follows: "Current or previous treatment with antiresorptive or antiangiogenic agents" (39.7%), "exposed bone, or bone that can be probed through an extra-oral or intra-oral fistula in the maxillofacial region that has persisted for more than 8 weeks" (38.8%), "no history of radiation therapy to the jaws" (28.6%), "no obvious metastatic tumour to the jaw" (15.7%). 48.3% of the participants stated that they are not sure.

### ANTIRESORPTIVE AND ANTIANGIOGENIC DRUGS THAT CAUSE MEDICATION RELATED OSTEONECROSIS OF THE JAW

Table 3 shows the number and percentage distribution of dentists' responses to questions about antiresorptive and antiangiogenic drugs that cause MRONJ. Regarding such drugs, dentists correctly answered as follows: "BPs" (61.2%), "antiangiogenic drugs" (20.3%) and "RANKL inhibitors" (6.5%). When asked "Which drug group does denosumab be-

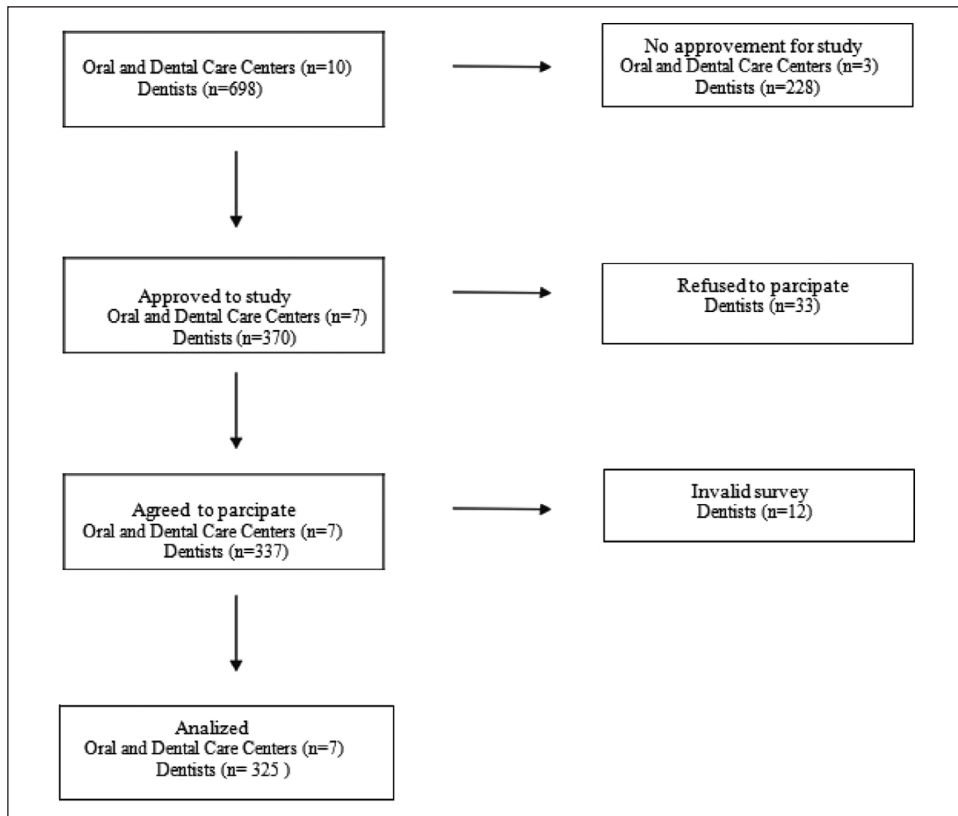


FIGURE 1: Flow chart of the study.

long to?”, only 2.8% of the dentists gave the correct answer, “RANKL inhibitors”. Others wrongly answered “BPs” (27.7%) and “antiangiogenic drugs” (2.8%). Regarding the indications for the use of BPs, dentists correctly answered “osteoporosis” (54.8%), “bone metastases of malignant tumours” (28.9%), “Paget’s disease” (16.6%), “multiple myelomas” (15.2%) and “osteogenesis imperfecta” (10.2%). Regarding routine applications of BPs, dentists correctly answered “oral” (39.1%) and “IV” (28.9%).

During anamnesis, the patient generally refers to the brand name of the product rather than to the name of the medicine used. Thus, a lack of knowledge of the commercial brand names of medications makes it hard to assess the risk for MRONJ accurately. To test dentists’ awareness of drug names, an open-ended question was asked: “Which of the drugs here listed could cause MRONJ (active substancetrade name)?” Only 47 dentists (14.46%) were able to cite at least one drug name. The drugs named by the dentists were Fosamax, Zometa, Bonviva and Actonel.

**TABLE 1:** Sociodemographic characteristics of the participants.

Demographic data	Number (n)	Percentage (%)
<b>Age</b>		
25-34 years old	96	29.5
35-44 years old	118	36.3
45-54 years old	90	27.7
55 years old ≤	21	6.5
<b>Gender</b>		
Male	124	39.2
Female	201	61.8
<b>Working experience</b>		
1-5 years	51	15.7
6-10 years	42	12.9
11-15 years	78	24.0
15-20 years	58	17.8
20 years and more	96	29.5
Total	325	100

Some dentists cited the following active drug ingredients; zoledronat (zoledronic acid), alendronate (alendronic acid) and pamidronate.

**TABLE 2:** Dentists' knowledge about the term "medication related osteonecrosis of the jaw".

Questions	Answers	Number (n)	Percentage (%)
1. Have you ever heard of the concept of medication related osteonecrosis of the jaw (MRONJ)?	I hear that first time	36	11.1
	I heard it, but I don't know what it is	51	15.7
	I know a little	153	47.1
	I know enough	85	25.2
2. According to the American Association of Oral and Maxillofacial Surgeons (AAOMS), what criteria should it meet to define a case as MRONJ? (You can select multiple options)	Current or previous treatment with antiresorptive or antiangiogenic agents	129	39.7
	Exposed bone, or bone that can be probed through an extra-oral or intra-oral fistula in the maxillofacial region that persistent for more than 8 weeks	126	38.8
	No history of radiation therapy to the jaws	93	28.6
	No obvious metastatic tumor to the jaws	51	15.7
	I am not sure	157	48.3

MRONJ: Medication related osteonecrosis of the jaw; AAOMS: Association of Oral and Maxillofacial Surgeons.

**TABLE 3:** Dentists' knowledge about drugs that cause osteonecrosis in the jaws.

Questions	Answers	(n)	(%)
1. Which of the following drugs are drugs that cause MRONJ? (You can select more than one option)	Bisphosphonates	199	61.2*
	Antidiabetics	3	0.9
	Antiangiogenic drugs	66	20.3*
	Antihypertensives	0	0
	RANKL inhibitors	21	6.5*
	I am not sure	120	36.9
2. Which drug group of denosumab is?	Bisphosphonates	90	27.7
	RANKL inhibitors	9	2.8*
	Antiangiogenic drugs	9	2.8
	I am not sure	217	66.8
3. What are the indications for the use of bisphosphonates? (You can select more than one option)	Osteoporosis	178	54.8*
	Paget's disease	54	16.6*
	Osteogenesis imperfecta	33	10.2*
	Multiple myeloma	51	15.7*
	Bone metastases of malignant tumors	94	28.9*
	I am not sure	120	36.9
4. What are the routine applications of bisphosphonates? (You can select more than one option)	Oral	127	39.1*
	Intramuscular (IM)	36	11.1
	Intravenous (IV)	94	28.9*
	I am not sure	168	51.7
5. Write down what you know from drugs that may cause MRONJ (active substance or trade name):	.....		

\*: Correct answers

MRONJ: Medication related osteonecrosis of the jaw; RANKL: Nuclear factor kappa B ligand; IV: Intravenous; IM: Intramuscular.

**RISK FACTORS OF MEDICATION-RELATED OSTEONECROSIS OF THE JAW**

The success of preventive intervention is specifically connected to the awareness of significant risk factors.

Figure 2 shows the distribution of correct answers of dentists with respect to risk factors for MRONJ. Regarding risk factors, dentists correctly answered chemotherapy (66.8%), smoking (55.7%), poor oral



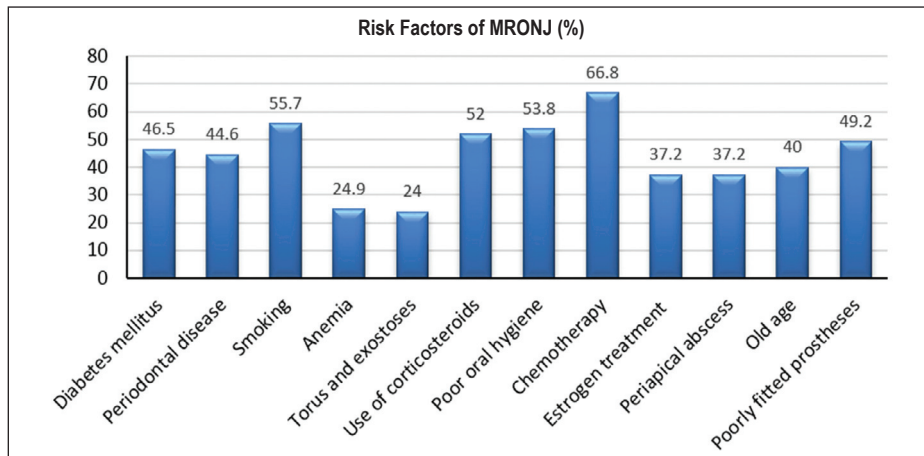


FIGURE 2: Distribution of accurate answers about risk factors of medication related osteonecrosis of the jaw.

hygiene (53.8%), the use of corticosteroids (52.0%), poorly fitted prostheses (49.2%), diabetes mellitus (46.5%), periodontal disease (44.6%), old age (40.0%), periapical abscess (37.2%), oestrogen treatment (37.2%), anaemia (24.9%) and torus and exostoses (24.0%).

Figure 3 shows the distribution of numbers and percentages of dentists' correct responses to statements about the risk factors of MRONJ. Among the respondents, 34.5% knew that those patients who use oral BPs have a lower risk of MRONJ than those who use IV BPs, and 47.5% were aware that, when the treatment period lasts longer than four years, the risk of MRONJ related to oral BPs increases; 29.5% were aware that the risk of osteonecrosis increases if the

C-terminal cross-linking telopeptide is below normal (<100 pg/mL); 41.8% were aware that the incidence of MRONJ in the lower jaw is higher than in the upper jaw and 45.2% of dentists were aware that a drug holiday in patients receiving oral BPs may reduce the risk of osteonecrosis.

### MANAGEMENT OF MEDICATION-RELATED OSTEONECROSIS OF THE JAW

Table 4 illustrates the attitudes of dentists towards MRONJ. 44.6% of the dentists enquired whether their patients were taking antiresorptive or antiangiogenic drugs when recording anamnesis. While 21.5% of the dentists claimed they could easily distinguish drug-induced osteonecrosis seen in jaws

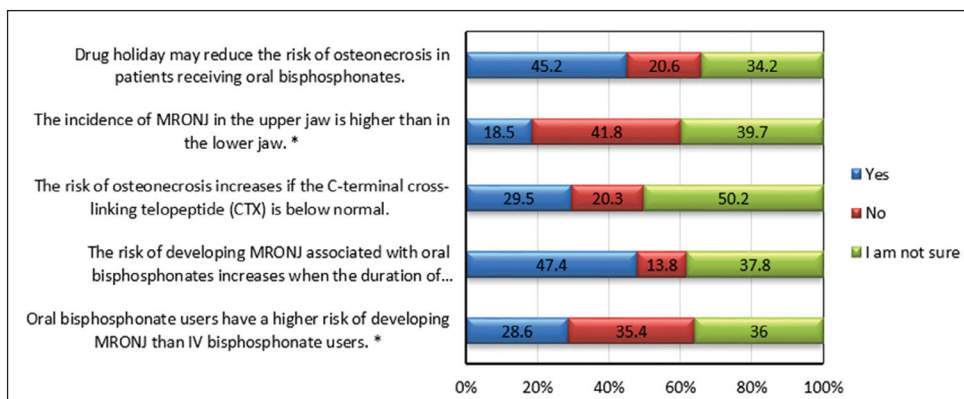


FIGURE 3: Dentists' knowledge about risk situations of medication related osteonecrosis of the jaw.

\*:Wrong expressions

**TABLE 4:** Attitude and practices of dentists about medication related osteonecrosis of the jaw.

Questions	Yes	No
1. Do you inquire whether your patients are taking antiresorptive or antiangiogenic drugs when taking anamnesis?	145 (44.6%)	180 (55.4%)
2. Have you ever met an MRONJ patient in the clinic?	61 (18.8%)	264 (81.2%)
3. Can you easily distinguish drug-induced osteonecrosis seen in the jaws from other similar pathologies in the clinic?	70 (21.5%)	255 (78.5%)
4. Did MRONJ develop after tooth extraction in your patients?	3 (0.9%)	322 (99.1%)
5. Did you receive MRONJ training during the undergraduate education period of the faculty of dentistry?	118 (36.3%)	207 (63.7%)
6. Did you receive any training about MRONJ in the last 5 years?	17 (5.2%)	305 (94.8%)
7. Would you like to train about MRONJ?	220 (67.7%)	105 (32.3%)

MRONJ: Medication related osteonecrosis of the jaw.

from other similar pathologies, only 18.8% had encountered an MRONJ case before in the clinic. Only three dentists (0.9%) reported patients who had developed MRONJ after tooth extraction. The study showed that 36.3% of the dentists had received training on MRONJ during their undergraduate education in the faculty of dentistry, but only 5.2% of the dentists had received such training in the last five years, whereas 7.7% stated that they wished to receive training on MRONJ.

## DISCUSSION

MRONJ is an increasing problem, since the prescribing rates of MRONJ-related drugs have increased dramatically. MRONJ has a harmful impact on the quality of life of patients, involving considerable physical, psychological and social consequences. MRONJ is a significant disease requiring sophisticated management, and preventive care strategies are critical because of the associated difficulties in the treatment of jaw osteonecrosis.<sup>8</sup> It is important to increase the awareness and knowledge of MRONJ among dentists, in medical specialisms such as orthopedics and oncology and in patients using the medicines in question. The present study was carried out to evaluate the awareness and knowledge of MRONJ among dentists in Turkey.

Antiresorptive and antiangiogenic drugs are frequently prescribed for the treatment of metabolic bone diseases such as osteopenia and osteoporosis, Paget's disease, malignant hypercalcaemia, multiple myeloma and prostate and breast cancer by many medical disciplines such as orthopaedics and oncology.<sup>26,27</sup> In this study, with regard to indications for the use of BPs, 54.8% of dentists knew about osteoporosis and 28.9% knew about bone metastases of malignant tumours. Lopez et al. reported that most of the dentists were not aware of the indications for BPs.<sup>28</sup> Fewer than half of the dentists knew that BPs were routinely taken orally (39.1%) and intravenously (28.9%). Most dentists (61.2%) were able to recognize MRONJ-related BPs but their knowledge of other drugs involved was limited. Similarly, in Ontario, Canada, Alhussain et al. found that 60% of dentists surveyed had adequate knowledge of BP-related osteonecrosis.<sup>29</sup> In addition, 50% of dentists did not feel confident treating patients using BPs, and 23% claimed to follow published guidelines referring to surgical treatment.

Recent evidence has shown that many antiresorptive and antiangiogenic drugs that are not limited to BPs may cause MRONJ. In the present study, approximately 80% of the dentists were unaware of antiangiogenic drugs and 93.5% were unaware of RANKL inhibitors. Only nine dentists (2.8%) knew

that denosumab was a RANKL inhibitor. These findings are consistent with those of Tanna et al., who reported that more than 90% of general dental practitioners did not know drugs other than BPs related to MRONJ, and, similarly, only 2% of the dentists were aware that denosumab could cause osteonecrosis of the jaw.<sup>30</sup> Escobedo et al. reported that 38.5% of the dentists in Spain were unaware of the implications of denosumab in osteonecrosis of the jaw.<sup>31</sup>

Dentoalveolar surgeries, periodontal diseases and denture use represent the local risk factors for MRONJ.<sup>32</sup> Factors associated with medicine, such as the form of BP, length of treatment and mode of administration, are also among the risk factors, as well as local factors. Moreover, there are also many comorbidity systemic risk factors such as diabetes and anaemia. It is therefore important for dentists to be trained to patients with antiresorptive drugs before and during treatment. Most dentists in the study were unaware of the main risk factors for MRONJ. Generally, however, fewer than half of the participants answered questions about risk factors of MRONJ correctly. Only 34.5% of dentists were aware that IV BPs present a higher risk for MRONJ than oral BPs, although 47.4% were aware of the increased risk when oral BPs were used in treatment for more than four years.

In this study, 11.1% of the dentists stated that they had heard the term “MRONJ” for the first time, 47.1% knew a little about it and 25.2% said they knew enough. In fact, more than half of the dentists in this study were unfamiliar with the definition of MRONJ. Vinitzky-Brener et al. reported that, although 40.5% of participants claimed to be familiar with the term “BPs-related osteonecrosis”, only three (0.7%) actually demonstrated adequate knowledge in this field.<sup>33</sup> In a study among Mexican dentists, 99.3% did not have the correct information with which to diagnose, prevent and treat MRONJ. In research conducted in Korea, more than half of the dentists (56.5%) had simply heard of BRONJ, but their clinical implementation was inadequate.<sup>25</sup> It is crucial to understand why knowledge of this topic among dentists in Turkey is so poor. The present

study showed that 36.3% of the dentists had been trained on MRONJ as undergraduates but only 5.2% had been trained in the last five years. In 2003, when the first BRONJ case was reported, this topic was put into the curriculum in subsequent years in Turkey. Approximately 70% of the participants had undergone 10 or more years of study, so most can not have received adequate training about MRONJ during their undergraduate studies. In addition, dentists working in public oral and dental health centres have a low level of interest and participation in scientific courses and meetings to improve their knowledge and skills. Unfortunately, postgraduate training in Turkey is not mandatory and there is no incentive to perform it. Practical measures such as the provision of free lectures and seminars and workshops can, therefore, be taken to improve dentists’ awareness of MRONJ.<sup>34</sup>

Most patients do not have adequate knowledge of the medications they take. Bauer et al. indicated that only 32% of patients taking IV BPs and 17% of patients taking oral BPs were aware of the risk of MRONJ.<sup>35</sup> The present study reveals that 55.4% of the dentists do not enquire whether their patients are taking antiresorptive or antiangiogenic drugs when recording anamnesis. Yoo et al. reported that 33.3% of Korean dentists did not include intake of antiresorptive medicines in preoperative patient anamnesis.<sup>25</sup> The authors found that most of the dentists were not aware of the guidelines of the AAOMS.

Patients should be fully informed by the doctor and pharmacist about the risk of MRONJ when starting drug treatment. Masson et al. reported that only 11.8% of general medical practitioners and 9.7% of pharmacists recommended that patients inform their dentist they were using a BP.<sup>36</sup> Patients who come to a dentist for treatment are mostly unaware of the risk of MRONJ. Sometimes patients may not supply practitioners with enough information about the diseases they have experienced or drugs taken, etc. Dentists should be able to access all of the patient’s medical records through the national network information system. Sharing medical records with dentists may save dentists’ clinical time and minimize patient risk. It is important for



dentists to engage directly and closely with other healthcare professionals such as medical doctors and pharmacists, to improve patient health. More focus on oral health education in the training of other health professionals could potentially improve collaboration between the dentistry and medical professions.<sup>20</sup>

## CONCLUSION

This study highlights that there is a need to ensure onward training in order to increase Turkish dentists' awareness of BPs and other drugs that have the potential to cause osteonecrosis. In Turkey, detailed national guidelines are needed to help dentists make decisions. Continuous education programmes should be organized to contribute to the professional development of dentists and their participation should be encouraged. Dentists need to work closely with the physicians who prescribe these drugs so that they are aware of the potential risks and are informing their patients accordingly. Also, dentists should be able to access all of the patient's medical records through the national network information system. Education and effective multidisciplinary collaboration potentially

enhances patients' safety and can decrease their risk of developing MRONJ.

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## Conflict of Interest

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

## Authorship Contributions

*This study is entirely author's own work and no other author contribution.*

## REFERENCES

- Nakatsuka K. [Development of bisphosphonates]. *Nihon Rinsho*. 2003;61(2):219-25. [\[PubMed\]](#)
- Marx RE. Pamidronate (Aredia) and zoledronate (Zometa) induced avascular necrosis of the jaws: a growing epidemic. *J Oral Maxillofac Surg*. 2003;61(9):1115-7. [\[Crossref\]](#) [\[PubMed\]](#)
- Leite AF, Figueiredo PT, Melo NS, Acevedo AC, Cavalcanti MG, Paula LM, et al. Bisphosphonate-associated osteonecrosis of the jaws. Report of a case and literature review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006;102(1):14-21. [\[Crossref\]](#) [\[PubMed\]](#)
- Melo MD, Obeid G. Osteonecrosis of the jaws in patients with a history of receiving bisphosphonate therapy: strategies for prevention and early recognition. *J Am Dent Assoc*. 2005;136(12):1675-81. [\[Crossref\]](#) [\[PubMed\]](#)
- Ruggiero SL, Mehrotra B, Rosenberg TJ, Engroff SL. Osteonecrosis of the jaws associated with the use of bisphosphonates: a review of 63 cases. *J Oral Maxillofac Surg*. 2004;62(5):527-34. [\[Crossref\]](#) [\[PubMed\]](#)
- Papapoulos S, Chapurlat R, Libanati C, Brandi ML, Brown JP, Czerwiński E, et al. Five years of denosumab exposure in women with postmenopausal osteoporosis: results from the first two years of the FREEDOM extension. *J Bone Miner Res*. 2012;27(3):694-701. [\[Crossref\]](#) [\[PubMed\]](#) [\[PMC\]](#)
- Christodoulou C, Pervena A, Klouvas G, Galani E, Falagas ME, Tsakalos G, et al. Combination of bisphosphonates and antiangiogenic factors induces osteonecrosis of the jaw more frequently than bisphosphonates alone. *Oncology*. 2009;76(3):209-11. [\[Crossref\]](#) [\[PubMed\]](#)
- Ruggiero SL, Dodson TB, Fantasia J, Goodday R, Aghaloo T, Mehrotra B, et al; American Association of Oral and Maxillofacial Surgeons. 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. Erratum in: *J Oral Maxillofac Surg*. 2015;73(7):1440. Erratum in: *J Oral Maxillofac Surg*. 2015;73(9):1879. [\[Crossref\]](#) [\[PubMed\]](#)
- Wooltorton E. Patients receiving intravenous bisphosphonates should avoid invasive dental procedures. *CMAJ*. 2005;172(13):1684. [\[Crossref\]](#) [\[PubMed\]](#) [\[PMC\]](#)
- Baron R, Ferrari S, Russell RG. Denosumab and bisphosphonates: different mechanisms of action and effects. *Bone*. 2011;48(4):677-92. [\[Crossref\]](#) [\[PubMed\]](#)
- Lacey DL, Boyle WJ, Simonet WS, Kostenuik PJ, Dougall WC, Sullivan JK, et al. Bench to bedside: elucidation of the OPG-RANK-RANKL pathway and the development of denosumab. *Nat Rev Drug Discov*. 2012;11(5):401-19. [\[Crossref\]](#) [\[PubMed\]](#)
- Russell RG, Watts NB, Ebetino FH, Rogers MJ. Mechanisms of action of bisphosphonates: similarities and differences and their potential influence on clinical efficacy. *Osteoporos Int*. 2008;19(6):733-59. [\[Crossref\]](#) [\[PubMed\]](#)

13. Allen MR, Burr DB. The pathogenesis of bisphosphonate-related osteonecrosis of the jaw: so many hypotheses, so few data. *J Oral Maxillofac Surg.* 2009;67(5 Suppl):61-70. [[Crossref](#)] [[PubMed](#)]
14. Landesberg R, Woo V, Cremers S, Cozin M, Marolt D, Vunjak-Novakovic G, et al. Potential pathophysiological mechanisms in osteonecrosis of the jaw. *Ann N Y Acad Sci.* 2011;1218:62-79. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
15. Bernardi S, Di Girolamo M, Necozione S, Continenza MA, Cutilli T. Antiresorptive drug-related osteonecrosis of the jaws, literature review and 5 years of experience. *Musculoskelet Surg.* 2019;103(1):47-53. [[Crossref](#)] [[PubMed](#)]
16. Oral Health Management of Patients at Risk of Medication-Related Osteonecrosis of the Jaw. *Dental Clinical Guidance.* 2017. [[Link](#)]
17. Sturrock A, Preshaw PM, Hayes C, Wilkes S. Perceptions and attitudes of patients towards medication-related osteonecrosis of the jaw (MRONJ): a qualitative study in England. *BMJ Open.* 2019;3;9(3):e024376. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
18. Further measures to minimise risk of osteonecrosis of the jaw with bisphosphonate medicine. *European Medicines Agency.* Accessed December 27, 2019. [[Link](#)]
19. Oral health management of patients at risk of medication-related osteonecrosis of the jaw. Accessed December 27, 2019. [[Link](#)]
20. Sturrock A, Preshaw PM, Hayes C, Wilkes S. 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;17;9(6):e029951. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
21. Dimopoulos MA, Kastiritis 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 zolendronic acid. *Ann Oncol.* 2009;20(1):117-20. [[Crossref](#)] [[PubMed](#)]
22. Vandone AM, Donadio M, Mozzati M, Ardine M, Polimeni MA, Beatrice S, et al. Impact of dental care in the prevention of bisphosphonate-associated osteonecrosis of the jaw: a single-center clinical experience. *Ann Oncol.* 2012;23(1):193-200. [[Crossref](#)] [[PubMed](#)]
23. El-Rabbany M, Sgro A, Lam DK, Shah PS, Azarpazhooh A. Effectiveness of treatments for medication-related osteonecrosis of the jaw: a systematic review and meta-analysis. *J Am Dent Assoc.* 2017;148(8):584-94.e2. [[Crossref](#)] [[PubMed](#)]
24. Vescovi P, Campisi G, Fusco V, Mergoni G, Manfredi M, Merigo E, 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(3):191-4. [[Crossref](#)] [[PubMed](#)]
25. Yoo JY, Park YD, Kwon YD, Kim DY, Ohe JY. Survey of Korean dentists on the awareness on bisphosphonate-related osteonecrosis of the jaws. *J Investig Clin Dent.* 2010;1(2):90-5. [[Crossref](#)] [[PubMed](#)]
26. Conte-Neto N, Bastos AS, Spolidorio LC, Marcantonio RA, Marcantonio E Jr. Oral bisphosphonate-related osteonecrosis of the jaws in rheumatoid arthritis patients: a critical discussion and two case reports. *Head Face Med.* 2011;27;7:7. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
27. Arantes HP, Silva AG, Lazaretti-Castro M. Bisphosphonates in the treatment of metabolic bone diseases. *Arq Bras Endocrinol Metabol.* 2010;54(2):206-12. [[Crossref](#)] [[PubMed](#)]
28. López-Jornet P, Camacho-Alonso F, Molina-Mi-ano F, Gomez-Garcia F. Bisphosphonate-associated osteonecrosis of the jaw. Knowledge and attitudes of dentists and dental students: a preliminary study. *J Eval Clin Pract.* 2010;16(5):878-82. [[Crossref](#)] [[PubMed](#)]
29. Alhussain A, Peel S, Dempster L, Clokie C, Azarpazhooh A. Knowledge, practices, and opinions of ontario dentists when treating patients receiving bisphosphonates. *J Oral Maxillofac Surg.* 2015;73(6):1095-105. [[Crossref](#)] [[PubMed](#)]
30. 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;27;222(2):121-5. [[Crossref](#)] [[PubMed](#)]
31. Escobedo M, Garcia-Consuegra L, Junquera S, Olay S, Ascani G, Junquera L, 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(5):395-400. [[Crossref](#)] [[PubMed](#)]
32. Ruggiero SL, Dodson TB, Assael LA, Landesberg R, Marx RE, Mehrotra B, et al; American Association of Oral and Maxillofacial Surgeons. American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaws—2009 update. *J Oral Maxillofac Surg.* 2009;67(5 Suppl):2-12. [[Crossref](#)] [[PubMed](#)]
33. Vinitzky-Brener I, Ibaez-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;1;22(1):e84-e7. [[PubMed](#)] [[PMC](#)]
34. 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. [[Crossref](#)] [[PubMed](#)]
35. Bauer JS, Beck N, Kiefer J, Stockmann P, Wichmann M, Eitner S, et al. Awareness and education of patients receiving bisphosphonates. *J Craniomaxillofac Surg.* 2012;40(3):277-82. [[Crossref](#)] [[PubMed](#)]
36. Masson DR, Callaghan EO, Seager M. The knowledge and attitudes of north wales health-care professionals to bisphosphonate associated osteochemonecrosis of the jaws. *Journal of Disability and Oral Health.* 2009;10(4):175-83. [[Link](#)]