RESEARCH ARTICLE

Recevied/ Geliş Tarihi: 11.01.2025
Accepted/ Kabul Tarihi: 30.03.2025
Published / Yayın Tarihi: 30.04.2025

Aydın Dental Journal - Volume **11** Issue **1** - April **2025** (41-55)

Aydın Dental Journal

Journal homepage: http://dergipark.ulakbim.gov.tr/adj
DOI: 10.17932/IAU.DENTAL.2015.009/dental_v011i1004

Comparison of Knowledge and Awareness Status of Senior Dental and Medical Students About MRONJ: A Cross-Sectional Study

Diş Hekimliği ve Tıp Fakültesi Öğrencilerinin MRONJ Hakkında Bilgi ve Farkındalık Durumlarının Karşılaştırılması: Kesitsel Çalışma

Selin Gaş[1*], Emine Öğüt[2], Erdinç Sulukan[3], Hümeyra Kocaelli Arıkan[4], Firdevs Şenel Veziroğlu[5]

ABSTRACT

Objective: Medication-related osteonecrosis of the jaw (MRONJ), a condition that can be managed and prevented through effective collaboration between dental and medical professionals, is a rare yet potentially serious disease. This study aimed to assess the knowledge and awareness of Turkish dental and medical school students regarding MRONJ.

Materials and Methods: A cross-sectional study was conducted among 254 dental and 234 medical students. Data were collected using an electronic and paper-based self-administered structured modified questionnaire consisting of five sections. SPSS Version 23 (IBM Corporation, Armonk, NY, USA) was utilized, with a significance level set at $p<0.05$.

Results: Both dental and medical students indicated that their curricula included courses on antiresorptive, antiangiogenic drugs, and the development of MRONJ associated with the use of these drugs. However, the level of knowledge and awareness among students in both groups regarding MRONJ was low. When comparing the awareness of MRONJ between medical and dental students, dental students (88.6%) exhibited a higher level than medical students (52.1%). Dental students also demonstrated greater awareness of the appropriate imaging techniques for diagnosing MRONJ compared to their medical counterparts ($p<0.05$). However, medical students' knowledge about dental approaches during bisphosphonate therapy was not as comprehensive as that of dental students.

Conclusion: Despite both dental and medical students having courses on MRONJ in their curriculum, their awareness and knowledge appear insufficient. This inadequacy may lead to misdiagnosis and inappropriate treatment modalities. Enhancing the quality and quantity of courses, with a focus on drugs inducing MRONJ and updated treatment protocols, could be proposed to address these issues.

Keywords: *Awareness, Dental Students, Knowledge, Medical Students, Osteonecrosis.*

ÖZET

Amaç: Antiresorptif, anti-anjiojenik ilaçların kullanımına bağlı gelişen çene kemik ölümü (MRONJ), diş ve tıp profesyonelleri arasındaki etkili işbirliği ile yönetilebilen ve önlenebilen nadir ancak potansiyel olarak ciddi bir durumdur. Bu çalışmanın amacı, Türk diş ve tıp fakültesi öğrencilerinin MRONJ hakkındaki bilgi düzeyini ve farkındalığını değerlendirmektir.

Gereç ve Yöntemler: 254 diş ve 234 tıp öğrencisi arasında kesitsel bir çalışma gerçekleştirildi. Veriler, beş bölümden oluşan bir elektronik ve kağıt tabanlı yapılandırılmış modifiye anket kullanılarak toplandı. Analizlerde SPSS Sürüm 23 (IBM Corporation, Armonk, NY, ABD) kullanıldı ve anlamlılık düzeyi $p<0.05$ olarak belirlendi.

Bulgular: Hem diş hem de tıp öğrencileri, müfredatlarının antiresorptif, anti-anjiojenik ilaçlar ve bu ilaçların kullanımına bağlı olarak gelişen MRONJ konulu dersleri içerdiğini belirtmişlerdir. Ancak, her iki grup öğrenci arasında MRONJ hakkındaki bilgi ve farkındalık düzeyi düşük bulunmuştur. Tıp ve diş hekimliği öğrencileri arasında MRONJ farkındalığı karşılaştırıldığında, diş hekimliği öğrencilerinin (%88,6), tıp öğrencilerine (%52,1) göre daha yüksek bir farkındalık düzeyine sahip olduğu gözlemlenmiştir. Diş hekimliği öğrencileri ayrıca, MRONJ teşhisi için uygun görüntüleme teknikleri konusunda tıp öğrencilerine göre daha fazla farkındalık göstermiştir ($p<0,05$). Tıp öğrencilerinin bifosfonat tedavisi almış veya almakta olan hastalarda diş tedavisi yaklaşımları konusundaki bilgisi, diş hekimliği öğrencilerinin bilgisi kadar kapsamlı bulunmamıştır.

Sonuç: Hem diş hem de tıp öğrencilerinin müfredatlarında MRONJ dersleri olmasına rağmen, farkındalık ve bilgilerinin yetersiz olduğu görülmektedir. Bu yetersizlik, yanlış teşhise ve uygun olmayan tedavi yöntemlerine yol açabilir. Bu sorunları ele almak için, MRONJ'a neden olan ilaçlar ve güncellenmiş tedavi protokollerine odaklanan derslerin kalitesini ve miktarını artırmak önerilebilir.

Anahtar Kelimeler: *Farkındalık, Diş hekimliği öğrencileri, Bilgi, Tıp öğrencileri, Osteonekroz.*

[1]DDS, PhD, Assistant Professor, Department of Oral and Maxillofacial Surgery, School of Dentistry, Istanbul Gelisim University, Istanbul, Turkey
[2]DDS, Assistant Professor, Department of Oral and Maxillofacial Surgery, School of Dentistry, Istanbul Medipol University, Istanbul, Turkey
[3]DDS, Assistant Professor, Department of Oral and Maxillofacial Surgery, School of Dentistry, Beykent University, Istanbul, Turkey
[4]DDS, PhD, Associate Professor, Department of Oral and Maxillofacial Surgery, School of Dentistry, Istanbul University, Istanbul, Turkey
[5]DDS, PhD, Professor, Department of Oral and Maxillofacial Surgery, School of Dentistry, Beykent University, Istanbul, Turkey
***Corresponding Author:** Selin Gaş, e-mail: sgas@gelisim.edu.tr, **ORCID:** 0000-0002-3337-9403, Department of Oral and Maxillofacial Surgery, School of Dentistry, Istanbul Gelisim University, Istanbul, Turkey.

Introduction

Bisphosphonate-Related Osteonecrosis of the Jaw (BRONJ) was initially described by Marx in 2003.[1] Bisphosphonates, commonly prescribed for conditions such as bone metastases from various cancers, multiple myeloma, osteoporosis, and metabolic bone diseases, have been subject to updates in 2007, 2009, and 2014.[2] AAOMS (American Association of Oral and Maxillofacial Surgeons) acknowledged in 2014 that various drugs, including denosumab, sunitinib, sorafenib, sirolimus, etc., can also induce osteonecrosis of the jaw, leading to the broadened term Medication-Related Osteonecrosis of the Jaw (MRONJ). The most recent position paper was published in 2022.[3] The treatment of Osteonecrosis of the Jaws (ONJs) poses a significant challenge for clinicians, lacking a universally accepted standard.[4-6] Consequently, prevention becomes a crucial focus. Effective preventive strategies can mitigate risk factors.[7-9] Therefore, it is imperative to possess sufficient information about MRONJ and collaborate closely with clinicians.

While numerous studies in the literature evaluate the knowledge of healthcare professionals, dental and medical students regarding MRONJ[10-12], none compare the awareness and understanding of MRONJ between medical and dental school students. Given the pivotal role of physicians in preventing MRONJ and ensuring the proper management of patients prescribed antiresorptive or antiangiogenic drugs, the study aims to evaluate, measure, and compare the knowledge of dental and medical school students regarding MRONJ.

Materials and Methods

A cross-sectional observational study was conducted by the attendance of senior dental and medical students in Istanbul, Turkey between January 2022 and April 2022. Ethical approval was obtained from the Ethic Comittee of Institutional Review Board at Istanbul Medipol University (Ethical Desicion Number: 1349). A total of 488 participants, 254 dental students and 234 medical students, applied for a modified survey- a validated self-administered questionnaire-, published by Rosella in 2017.[13] The survey was composed of five section (Table 1).The knowledge and awareness of the students by evaluating 1-General demographic data 2-General information about antiresorptive and antiangiogenic durgs 3- Theraupatic use of antiantiresorptive and antiangiogenic drugs 4- Diagnosing osteonecrosis of the jaws and risk factors 5- Dental management of patients receiving BP therapy were examined.

Table 1. Dental and Medical Students' Knowledge of MRONJ

Section 1: Demographic Profile	Age	…….
	Gender	Male Female
	Name of college	…….
Section 2: General Knowledge of Antiresorptive/ Antiangiogenic Medications	Have you encountered any antiresorptive medications such as bisphosphonate related information during your study years?	Yes No
	Have you encountered any antiangiogenic medications related information during your study years?	Yes No
	Where have you heard about anti-resorptive medications?	Never heard of it University Mass media Scientific journals Medical meetings Other (……)
	Where have you heard about antiangiogenic medications?	Never heard of it University Mass media Scientific journals Medical meetings Other (……)

	Do you think it is important to ask if patients are using anti-resorptive medications?	Yes No
	Do you think it is important to ask if patients are using antiangiogenic medications?	Yes No
Section 3: Knowledge of Therapeutic Uses of Antiresorptive/Antiangiogenic Medications	What diseases are targeted by antiresorptive therapy? (it is possible to mark more than one choice):	Bone metastases Osteomyelitis Multiple myeloma Osteopetrosis Chondroblastoma Osteogenesis imperfekta Paget's disease of bone Osteopenia and osteoporosis Hypercalcemia of malignancy I don't know
	What diseases are targeted by anti-angiogenic therapy? (it is possible to mark more than one choice):	Elastofibromas Metastatic colorectal cancer Leiomyomas renal cell cancer Neuroendocrine tumor of the pancreas Multiple myeloma Granular cell tumors I don't know
	Mark the name of the antiresorptive drugs you are familiar with	Alendronate (Fosamax) Risedronate (Actonel) Ibandronate (Boniva) Neridronate (Nerixia) Pamidronate (Aredia) Zolendronate (Zometa) Tiludronate (Skelid) Denosumab (Prolia) I don't know of any antiresorptive drug
	Mark the name of the antiangiogenic drugs you are familiar with (it is possible to mark more than one choice):	Sunitib (Sutent) Sorafenib (Nexavar) Bevacizumab (Avastin) Sirolimus (Rapamune) I don't know of any anti-angiogenic drugs
	In what ways is antiresorptive drug therapy administered?	Only oral Only parenteral Both oral ve parenteral I don't know
	Does the use of antiresorptive/antiangiogenic drugs lead osteonecrosis of the jaws?	Yes No I don't know

Section 4: Knowledge of Osteonecrosis of Jaw and Its Risk Factors	What is the correct definition of osteonecrosis of the jaw according to the American Association of Oral and Maxillofacial surgeons (AAOMS)?	a. Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 8 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents, and no history of radiation therapy to the jaws or obvious metastatic disease to the jaws.
		b. Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 4 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents, and no history of radiation therapy to the jaws or obvious metastatic disease to the jaws.
		c. Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 8 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents, and a medical history of radiation therapy to the jaws or obvious metastatic disease to the jaws.
		d. Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 4 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents and, a medical history of radiation therapy to the jaws or obvious metastatic disease to the jaws.
		e. I don’t know.
	Which imaging methods can be used in osteonecrosis of the jawbone? (You can mark more than one option.)	Scintigraphy Dental volumetric tomography Magnetic resonance imaging Panoramic radiography Periapical radiography No idea
	Which of the following are the risk factors related to osteonecrosis of the jaw? (You can mark more than one option.)	Tobacco Antibiotic therapy Alcohol Application way Hypertension Treatment time Hyperlipidemia Steroid therapy Total dose of drug administered Microtrauma No idea

Do you think patients should be checked by the dentist before starting an IV bisphosphonates treatment?	Yes No I don't know

Chi-Square Analysis: Comparison of dental and medical students`general knowledge about antiresorptive\antiangiogenic drugs, *p < 0.05

Statistical Analysis

A power analysis was performed and it was found that 340 samples produces a two-sided 95% confidence interval with a width equal to 0.220 when the sample correlation is 0.050. SPSS Version 23 (IBM Corporation, Armonk, NY, USA) was used for analysis. A Chi-square test was used to compare the categorical variables between groups. Probability of less than 0.05 (P < 0.05) was accepted as statistically significant.

Results

Among 254 dental students, 145 were females (57.1%) and 109 were males (42.9%); 234 medical students, 120 were females (51.9%) and 114 were males (48.7%). The general demographic characteristics of the students participating in the study were shown in Table 2 for the first section.

Table 2. General Demographic Characteristics of the Students

		Dental Students		Medical Students		p
		N	%	N	%	
Age	21-22	96	37.8	20	8.5	0.001
	23-24	131	51.6	126	53.8	
	>25	27	10.6	88	37.6	
	Total	254	100	234	100	
Gender	Male	109	42.9	114	48.7	0.116
	Female	145	57.1	120	51.3	
	Total	254	100	234	100	

Chi-Square Analysis: General Demographic Characteristics of the Students ,*p < 0.05

As shown in Table 3, while 95.3% of dental students and 76.1% of medical students stated that they had encountered antiresorptive drugs, it is observed that the number of students encountering antiangiogenic drugs has decreased statistically significantly (dental students: 76.7%; medical students: 68.3%). When both antiangiogenic and antiresorptive drugs were compared, the awareness of dental students was statistically higher than that of medical students (p<0.05). 92.9% of dental students reported that they first heard about drugs such as bisphosphonates in their curriculum, while this rate was 79.5% for medical students. 3.1% of dental students stated that they have never heard of antiresorptive drugs, whereas this rate was 17.9% for medical students (p<0.05). The majority of dental (82.3%) and medical (83.3%) students encountered information regarding antiangiogenic medications at the university. While the rate of dental students who have never heard of antiangiogenic drugs was 15.4%, this rate was 16.2% among medical students. The majority of medical (93.2%) and dental students (96.1%) reported that it is important to ask whether antiresorptive and antiangiogenic drugs are used in their patients.

Table 3. Comparison of General Knowledge About Antiresorptive/Antiangiogenic Drugs

		Dental Students	Medical Students		p
Have you encountered any antiresorptive medications such as bisphosphonate related information during your study years?	Yes	242 (95.3%)	178 (76.1%)	420 (86.1%)	0.001
Where have you heard about antiresorptive medications?	University	238 (93.7%)	186 (79.5%)	424 (86.9%)	0.001
	Never heard	8 (3.1%)	42 (17.9%)	50 (10.2%)	
	Scientific journals	5 (2.0%)	3 (1.3%)	8 (1.6%)	
	Scientific meetings	2 (0.8%)	2 (0.9%)	4 (0.8%)	
	Others	1 (0.4%)	0 (0.0%)	1 (0.2%)	
Have you encountered any antiangiogenic medications related information during your study years?	Yes	195 (76.7%)	160 (68.3%)	355 (71.2%)	0.001
Where have you heard about antiangiogenic medications?	University	210 (82.7%)	195 (83.3%)	404 (82.8%)	0.585
	Never heard	39 (15.4%)	38 (16.2%)	77 (15.8%)	
	Scientific meetings	1 (0.4%)	0 (0.0%)	1 (0.2%)	
	Media	3 (1.2%)	1 (0.4%)	4 (0.8%)	
	Others	1 (0.4%)	0 (0.0%)	1 (0.2%)	
Do you think it is important to ask if patients are using anti-resorptive medications?	Yes	244 (96.1%)	218 (93.2%)	462 (94.7%)	0.110
Do you think it is important to ask if patients are using antiangiogenic medications?	Yes	229 (90.2%)	212 (90.6%)	441 (90.4%)	0.496

Chi-Square Analysis: Comparison of General Knowledge About Antiresorptive/Antiangiogenic Drugs, *p < 0.05

The level of knowledge of the therapeutic usage of antiresorptive and antiangiogenic medications was demonstrated in Table 4 for the third section. Medical students were more familiar with all the mentioned antiresorptive drugs than dental students. While Zolendronate (Zometa) was the most heard antiresorptive drug, Tiludronate (Skelid) was the least heard antiresorptive drug for both groups. Similar to previous results, all antiangiogenic drugs were mostly known by medical students. Dental students knew less about antiresorptive and antiangiogenic drugs than medical students. Among the therapeutic uses of antiresorptive therapy, osteopenia and osteoporosis were the most commonly recognized among dental students (77.6%) and medical students (80.8%). The second most well-known disease was bone metastases (69.7% of dental students, 76.5% of medical students). None of the dental students were able to identify elastofibroma, metastatic colorectal cancer, leiomyoma, and renal cell cancer, while a few medical students (3.4%) identified these diseases ($p<0.05$). When the routes of administration were questioned, few dental students (20.5%) and medical students (19.2%) reported that they had no idea ($p>0.05$). The majority of dental students (73.6%) and medical students (78.2%) stated that these drugs are administered to patients by both oral and parenteral routes ($p>0.05$). Most dental students (88.6%) knew that antiresorptive/antiangiogenic drugs could cause osteonecrosis of the jaw. However, more than half of the medical students (52.1%) had no idea about this topic.

Table 4. Comparison of the therapeutic use of drugs

		FACULTY		Total	p
		Dental Faculty	Medical Faculty		
In which diseases is antiresorptive drug therapy indicated? (You can check multiple options.)	Elastofibroma	0 (0.00%)	8 (3.4%)	8 (1.6%)	0.843
	Bone metastases	177 (69.7%)	179 (76.5%)	356 (73.0%)	0.816
	Multiple myeloma	107 (42.1%)	158 (67.5%)	165 (33.8%)	0.002
	Osteogenesis imperfecta	136 (53.5%)	153 (65.4%)	289 (59.2%)	0.121
	Osteomyelitis	119 (46.9%)	48 (20.5%)	167 (34.2%)	0.001
	Osteopenia and osteoporosis	197 (77.6%)	189 (80.8%)	376 (77.0%)	0.964
	Osteopetrosis	69 (27.2%)	126 (53.8%)	195 (40.0%)	0.001
	Paget's disease	98 (38.6%)	82 (35.0%)	180 (36.9%)	0.910
	Chondroblastoma	42 (16.5%)	83 (35.5%)	125 (25.6%)	0.002
	Metastatic colorectal cancer	0 (0.0%)	8 (3.4%)	8 (1.6%)	0.132
	Leiomyoma	0 (0.0%)	8 (3.4%)	8 (1.6%)	0.132
	Renal cell carcinoma	0 (0.0%)	8 (3.4%)	8 (1.6%)	0.132
	No idea	23 (9.1%)	0 (0.0%)	25 (5.1%)	0.371
In which diseases is antiangiogenic drug therapy indicated? (You can check multiple options.)	Elastofibroma	53 (20.9%)	68 (29.1%)	121 (24.8%)	0.265
	Leiomyoma	52 (20.8%)	69 (29.5%)	121 (24.8%)	0.214
	Metastatic colorectal cancer	85 (33.5%)	136 (58.1%)	221 (45.3%)	0.001
	Multiple myeloma	81 (31.9%)	120 (51.3%)	201 (41.2%)	0.002
	Neuroendocrine tumor of the pancreas	65 (25.6%)	32 (13.7%)	97 (19.9%)	0.007
	Renal cell carcinoma	86 (33.9%)	116 (49.6%)	202 (41.4%)	0.009
	Granular cell tumor	59 (23.2%)	14 (6%)	73 (15%)	0.001
	No idea	124 (48.8%)	29 (12.4%)	153 (31.3%)	0.001
Please indicate the antiresorptive drugs that are actively prescribed today. (You can check multiple options.)	Alendronate (Fosamax)	92 (36.2%)	177 (75.6%)	269 (55.1%)	0.001
	Denosumab (Prolia)	80 (31.5%)	174 (74.4%)	254 (52.0%)	0.001
	Ibandronate (Boniva)	63 (24.8%)	89 (38.0%)	152 (31.1%)	0.283
	Neridronate (Nerixia)	23 (9.1%)	79 (33.8%)	102 (20.9%)	0.001
	Pamidronate (Aredia)	69 (27.2%)	152 (65.0%)	221 (45.3%)	0.001
	Risendronate (Actonel)	41 (16.1%)	123 (52.6%)	164 (33.6%)	0.001
	Tiludronate (Skelid)	31 (12.2%)	48 (20.5%)	79 (16.2%)	0.217
	Zolendronate (Zometa)	135 (53.1%)	188 (80.3%)	323 (66.2%)	0.135
	No idea	81 (31.9%)	18 (7.7%)	99 (20.3%)	0.001
	Sorafenib (Nexavar)	44 (17.3%)	144 (61.5%)	188 (38.5%)	0.001
	Sunitinib (Sutent)	40 (15.7%)	154 (65.8%)	194 (39.8%)	0.001
	No idea	182 (71.7%)	52 (22.2%)	234 (48.0%)	0.001
Please indicate the antiangiogenic drugs that are actively prescribed today. (You can check multiple options.)	No idea	52 (20.5%)	45 (19.2%)	97 (19.9%)	0.249
	Oral and parentheral	187 (73.6%)	183 (78.2%)	370 (75.8%)	
	Only oral	12 (4.7%)	4 (1.7%)	16 (3.3%)	
	Only parentheral	3 (1.2%)	2 (.9%)	5 (1.0%)	
Do the use of antiresorptive/antiangiogenic drugs cause osteonecrosis in the jaws?	Yes	225 (88.6%)	112 (47.9%)	337 (69.1%)	0.001
	No idea	23 (9.1%)	122 (52.1%)	145 (29.7%)	
	No	6 (2.4%)	0 (0.0%)	6 (1.2%)	

Chi-Square Analysis: Comparison of the therapeutic use of drugs *p < 0.05

In the fourth part of the survey, only half of the dental students (52%) and medical students (49.1%) chose the correct definition of MRONJ (Table 5). When asked about the appropriate imaging technique to diagnose MRONJ, the awareness of dental students was higher than that of medical students (77.6%-45.3%). Dental students were more familiar when panoramic and periapical radiography were of concern (77.6%, 45.3%). Among risk factors for MRONJ, the total dose of drug administered was the most recognized one by dental (77.6%) and medical (82.9%) students. This was followed by the duration of treatment and smoking, respectively (Table 5). Almost all dental students (95.7%) argued that patients should be checked by a dentist before starting iv bisphosphonate therapy, with a significantly higher rate compared to medical students (84.6%).

Table 5. Knowledge of Risk Factors Related to Osteonecrosis of the Jaw

		Dental Students	**Medical Students**		**p**
What is the correct definition of osteonecrosis of the jaw according to the American Association of Oral and Maxillofacial surgeons (AAOMS)?	Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 8 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents, and no history of radiation therapy to the jaws or obvious metastatic disease to the jaws.	35 (13.8%)	43 (18.4%)	78 (16.0%)	0,001
	Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 4 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents, and no history of radiation therapy to the jaws or obvious metastatic disease to the jaws.	132 (52.0%)	115 (49.1%)	247 (50.6%)	
	Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 8 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents, and a medical history of radiation therapy to the jaws or obvious metastatic disease to the jaws.	30 (11.8%)	23 (9.8%)	53 (10.9%)	
	Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 4 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents and, a medical history of radiation therapy to the jaws or obvious metastatic disease to the jaws.	27 (10.6%)	4 (1.7%)	31 (6.4%)	
	I don't know	30 (11.8%)	49 (20.9%)	79 (16.2%)	

Which imaging methods can be used in osteonecrosis of the jawbone? (You can mark more than one option.)	Dental volumetric tomography	187 (73.6%)	178 (76.1%)	365 (74.8%)	0.996
	Magnetic resonance imaging	110 (43.3%)	81 (34.6%)	191 (39.1%)	0.173
	Panoramic radiography	197 (77.6%)	94 (40.2%)	291 (59.6%)	0.001
	Scintigraphy	95 (37.4%)	110 (47.0%)	205 (42.0%)	0.114
	Periapical radiography	115 (45.3%)	39 (16.7%)	154 (31.6%)	0.001
	I don't know	16 (6.3%)	38 (16.2%)	54 (11.1%)	0.187
Which of the following are the risk factors related to osteonecrosis of the jaw? (You can mark more than one option.)	Alcohol	140 (55.1%)	132 (56.4%)	272 (55.7%)	0.962
	Microtrauma	137 (53.9%)	101 (43.2%)	238 (48.8%)	0.035
	Antibiotic therapy	56 (22.0%)	66 (28.2%)	122 (25.0%)	0.248
	Hypertension	57 (22.4%)	80 (34.2%)	137 (28.1%)	0.017
	Steroid therapy	137 (53.9%)	173 (73.9%)	310 (63.5%)	0.001
	Treatment time	182 (71.7%)	161 (68.8%)	343 (70.3%)	0.164
	Total dose of drug administered	197 (77.6%)	194 (82.9%)	391 (80.1%)	0.344
	Tobacco	168 (66.1%)	161 (68.8%)	329 (67.4%)	0.942
	Administration way	148 (58.3%)	82 (35.0%)	230 (47.1%)	0.001
	Hyperlipidemia	48 (18.9%)	79 (33.8%)	127 (26.0%)	0.001
	I don't know	23 (9.1%)	36 (15.4%)	59 (12.1%)	0.129
Do you think patients should be checked by the dentist before starting an IV bisphosphonates treatment?	Yes	243 (95.7%)	198 (84.6%)	441 (90.4%)	0.001
	No	2 (0.8%)	6 (2.6%)	8 (1.6%)	
	I don't know	9 (3.5%)	30 (12.8%)	39 (8.0%)	

Chi-Square Analysis: Knowledge of Risk Factors Related to Osteonecrosis of the Jaw,*$p < 0.05$

The fifth section of the survey, shown in Table 6, was about dental management of patients receiving bisphosphonate therapy. When the management of patients under iv BP therapy was of concern, 79.5% of dental students and 41.0% of medical students stated that invasive dental treatment is not safe and should not be performed ($p<0.05$). However, most medical students (56.4%) have no knowledge on the subject, which raises the suspicion of inadequacy of education. However, concerning the indication of invasive dental treatment for patients under oral BP therapy for less than 4 years without risk factors, 18.4% of dental students indicated it as unsafe, whereas the percentage was 9.4% for medical students ($p<0.05$). While 66.5% of dental students and 16.2% of medical students stated that being associated with a risk factor for less than 4 years made dental treatments unsafe in these patients ($p<0.05$), 60.2% of dental students and 16.7% of medical students argued that dental treatments could not be performed in patients who had been using oral bisphosphonates for more than 4 years ($p<0.05$).

Table 6. Knowledge of Dental Management in Patients Undergoing Bisphosphonate Therapy According to Dental and Medical Students

		Dental Students	Medical Students		p
Can invasive dental treatments be performed safely to patients during an intravenous bisphosphonate drug therapy?	Yes	29 (11.4%)	6 (2.6%)	35 (7.2%)	0.001
	No	202 (79.5%)	96 (41.0%)	298 (61.1%)	
	I don't know	23 (9.1%)	132 (56.4%)	155 (31.8%)	
Can invasive dental treatments be performed safely to patients using oral bisphosphonates for <4 years without risk factors?	Yes	164 (64.4%)	104 (44.4%)	268 (54.4%)	0.001
	No	46 (18.4%)	23 (9.4%)	69 (14.4%)	
	I don't know	44 (17.4%)	107 (45.4%)	151 (30.4%)	
Can invasive dental treatments be performed safely to patients using oral bisphosphonates for <4 years with risk factors?	Yes	45 (17.7%)	55 (23.5%)	100 (20.5%)	0.001
	No	169 (66.5%)	38 (16.2%)	207 (42.4%)	
	I don't know	40 (15.7%)	141 (60.3%)	181 (37.1%)	
Can invasive dental treatments be performed safely to patients using oral bisphosphonates for >4 years?	Yes	50 (19.7%)	30 (12.8%)	80 (16.4%)	0.001
	No	153 (60.2%)	39 (16.7%)	192 (39.3%)	
	I don't know	51 (20.1%)	165 (70.5%)	216 (44.3%)	
Would you like to know more about osteonecrosis of the jaws associated with the use of antiresorptive/antiangiogenic drugs?	Yes	242 (95.3%)	127 (54.3%)	369 (75.6%)	0.001
	No	12 (4.7%)	107 (45.7%)	119 (24.4%)	

Chi-Square Analysis: Knowledge of Dental Management in Patients Undergoing Bisphosphonate Therapy According to Dental and Medical Students,*$p < 0.05$

Discussion

In the literature, several studies regarding the knowledge of MRONJ by dentists and dental students can be found.[10,13,14] Nevertheless, the knowledge of osteonecrosis by medical students that are going to become doctors is crucial. There is only one study which reported the awareness about MRONJ among medical students.[15]

MRONJ is a potentially serious adverse event in patients with cancer and bone diseases who have been receiving antiresorptive or antiangiogenic drugs. It can cause painful bone exposure in maxilla and mandible. Having sufficient information about MRONJ is essential for improving treatment outcomes, reducing drug-related complications, and thus increasing the quality of life of patients. Although several studies in the literature have investigated MRONJ awareness in dentists and other healthcare professionals[16,17], few studies have evaluated the knowledge levels of dental and medical school students.[13,15] To the best of our knowledge, there has been no study comparing the knowledge levels of dental and medical school students. As a result of the study conducted by Almousa et al.[11] with the dental students, almost one third of the students stated that they did not receive any information about antiresorptive and antiangiogenic drugs during their undergraduate years. Unlike the previous study, in the current study, almost all of the dental students received information about antiresorptive drugs during their undergraduate years, while much less of the students in the medical school stated that they encountered this information compared to the dental students. In both groups, less of the participants in the study stated that they encountered information about antiangiogenic drugs. The difference between the knowledge levels of this drugs may be related to the subsequent reflection in the literature of antiangiogenic drugs causing osteonecrosis of the jaw. In Italy, Franchi et al.[15] measured the knowledge level of MRONJ in medical students and observed that they did not have sufficient knowledge. They reported that there was an increase in the knowledge awareness about MRONJ among the students who were in the 6th year of medical school compared to those in the 5th year, and they argued that the reason for this was the increase in the number of patients and practical experience in the last years of the students.

Due to the increasing incidence of MRONJ, there is a consensus among dentists to raise awareness of MRONJ and increase the training necessary to prevent it. However, the prescription of drugs that cause MRONJ by medical doctors necessitates the need for medical doctors to have sufficient knowledge about MRONJ.[18-21]

In their study, Escobeto et al.[14] found that senior dental students had a higher case resolution rate compared to dentists with private practice. López-Jornet et al.[22], compared the knowledge of BRONJs among students and dentists in Spain. Unlike with the previous study results, they reported that the dentists' knowledge of BRONJs was higher than that of the students. In the present study, it was observed that dental students had more knowledge about MRONJ than medical students.

In the current study, Turkish dental and medical students, with the majority of the participants could not recognize the generic and brand names of antiresorptive and antiangiogenic medication. Several studies in the literature have reported the similiar results with our study.[10,13,20] In the study of de Lima et al.[20], the majority of dentists and dental students could not classify these drugs and could not recognize their commercial brand names. This result made us think that the generic and brand names of MRONJ-related drugs were not emphasized enough during university years and were not included in the education curriculum. In the present study, Zolendronate (Zometa) was the most frequently known antiresorptive medication, followed by Alendronate (Fosamax) and Denosumab (Prolia) in both groups. Similiar to our study results, Almousa et al.[10] found that mentioned three medications were the most known ones. But in their study, Alendronate was the most recognized medication. S. Franchi et al.[15] reported that among Italian medical students which showed that the majority of the participants lacked knowledge regarding antiangiogenic medications caused MRONJ. Similiar findings were found in the current study. Medical students recognized both antiangiogenic drugs and antiresorptive drugs statistically less than the dental students. In both groups, antiangiogenic drugs were recognized less frequently than antiresorptive drugs. We hypothesize that this is due to the later realization that antiangiogenic drugs cause osteonecrosis of the jaw. When we investiagted the studies in the literature, including the present study, we observe that healthcare professionals do not have enough knowledge about antiresorptive and antiangiogenic drugs. In order to make the correct diagnosis of the disease and to reduce the possibility of getting osteonecrosis of the jaw, it is necessary to increase the relevant trainings in all health fields, especially in dentistry.

20% of the sample in both groups did not have any idea of the question, that is "In which ways is antiresorptive drug therapy administered?". Approximately 75% of both groups gave the response, oral and parenteral. This question was not included in any of the survey studies conducted in the literature. The purpose of measuring the answers given to this question is that the route of administration of the drug is also effective in the spread and speed of osteonecrosis of the jaw. The physician's knowledge of this situation will be an important factor in taking the necessary precautions.

Only half of the students who participated in the survey in both groups knew the definition of MRONJ correctly. While 20.9% of medical students declared that they had no idea, this rate was 11% among dental students. These results are alarming. Curriculum changes are required to increase awareness of MRONJ in both of the schools, especially in medical schools. In contrast, Rugieiro et al.[2] and Rosella et al.[13] observed that most of the dental students participating in the studies could not know the correct definition of MRONJ. Lack of information on the definition of MRONJ may lead to delayed diagnosis in people who may develop MRONJ and, accordingly, to an increased risk of other complications that may affect quality of life.

When asked about the imaging methods that can be used in the diagnosis of MRONJ, the majority of dental students answered panoramic radiography (77.6%) and dental volumetric tomography (73.6%), while the majority of medical students (76.1%) answered dental volumetric tomography. However, medical school students thought that MRONJ could be diagnosed with panoramic and periapical radiography at a lower rate compared to dental school students. This results make us think that there are deficiencies in our health education system. Courses in medical and dental faculties should be coordinated and joint courses should be available when necessary. Radiological

imaging methods are very important in the early diagnosis of MRONJ.[23,24] In many cases, early diagnosis can be determined only by radiological evaluation. However, imaging methods have not been questioned in any study evaluating MRONJ awareness in the literature. For this reason, we wanted to measure the knowledge level of students in dentistry and medical faculties in Turkey about imaging methods. As a result, we observed that the students did not have sufficient knowledge level.

When the question about possible risk factors for MRONJ was evaluated, the most of the participants in our study stated that the total dose of drug was risk factor, while more than 50% stated that alcohol, steroid treatment, tobacco use and duration of treatment were risk factors. It is a known fact that the increase in the dose of drug administered and the duration of treatment also increase the risk of osteonecrosis.[25] The answers of the participants in our study were insufficient. However, compared to the study by Almousa et al.[10], the participants in the present study were found to more knowledgable about risk factors. The majority of the participants, especially almost all of the dental students, asked, "Should patients be checked by dentists before starting iv bisphosphonate therapy?" when asked the question, answered yes. Similarly, Almousa et al.[10] stated that the dentists and dental students participating in the study answered yes to this question. Franchi et al.[15], in their study, similar to the present study, medical students are aware that patients should go to a dentist before starting bisphosphonate therpy. Another common point in the mentioned three studies is that the iv route of administration carries a greater risk for MRONJ than the oral route.

It is known that the risk of developing osteonecrosis is minimal if bisphosphonates are used orally for less than 4 years.[2] Administration of the drug intravenously or subcutaneously increases the risk of osteonecrosis. In our study, while 79.5% of dental students stated that invasive dental treatments could not be performed while using iv bisphosphonates, less than half of the medical school students stated the same answer. Unfortunately, 56.4% of the medical students stated that they did not have any idea about this subject. These results are worrying. Some precautions should be taken. Especially in medical faculties, more documents on the subject should be presented to students. "Can invasive dental treatments be performed in individuals who have been using oral bisphosphonates for less than 4 years and have no risk factors?" While only 64.4% of dental students answered yes to the question, the rate of the medical school students was 44.4%. Almost half of the medical students declared that they had no idea about this subject. However, there are few students who declare that they have no idea about the subject among the students of the dental school. Almousa et al.[10] reported similar results in their study. These results suggest that the participants in both studies did not have enough knowledge about MRONJ and the disease could not be managed properly.

"Can invasive dental treatments be performed safely to patients using oral bisphosphonates for <4 years without risk factors, and in patients who have used oral bisphosphonates for more than 4 years?" The answers given to the questions are not satisfactory for both groups. Especially the majority of medical students stated that they had no idea about this issue. Similarly, Almousa et al.[10] and López-Jornet et al.[22] in their study, they observed that both dentists and dental students did not have a good command of the dental treatment approach in patients who used or were using bisphosphonates. The present study results showed that despite the existence of guidelines both groups (students and practising dentists) had confused ideas as to how to carry out invasive dental treatment (extraction of teeth) in cases of patients taking bisphosphonates.[22]

A clinician should know the drugs associated with MRONJ, have knowledge of the risk factors and dental approach when MRONJ occurs. It is also important that medical doctors and dentists cooperate in order to manage MRONJ and improve patients' quality of life. Almost all of the dental students participating in our study stated that they were willing to learn more about MRONJ regarding the use of antiresorptive and antiangiogenic drugs. Unfortunately, only 54.3% of medical school students were found to be eager

to gain knowledge. For the ideal maintenance of MRONJ in the future, due attention should be paid to the issue in all fields of health, especially in medical faculties today. Necessary training should be provided.

Conclusion

For all the sections in the survey, the level of knowledge is insufficient in dental students, especially medical students. Although medical students have more incomplete information, they are also not willing to have more information. This situation is threatening. Based on our study results, we can say that some courses should be common in medical and dental schools, the importance of consultation should be emphasized and it should be taught that working in cooperation is important. Necessary seminars should be given, case reports should be presented and workshops should be organized to correct the lack of knowledge about MRONJ.

Ethical Approval

The necessary ethical approval for this study was obtained from Istanbul Medipol University Institutional Review Board and Ethics Committee (Ethical approval no: 1349).

Conflict of interest

The authors have no conflict of interest to declare.

Sources of Funding

No funding was received for this study.

Author Contributions

Idea/Concept: S.G, E.Ö, E.S, H.K.A, F.Ş.V Design: S.G, E.S, H.K.A, F.Ş.V Control/ Supervision: S.G, H.K.A, F.Ş.V Literature Review: S.G, E.Ö, E.S., H.K.A, F.Ş.V Data Collection and/or Processing: S.G, E.Ö, E.S, F.Ş.V Analysis and/or Interpretation: S.G, E.Ö, E.S, H.K.A, F.Ş.V Writing the Article: S.G, E.Ö, E.S, H.K.A, F.Ş.V Critical Review: S.G, E.Ö, E.S, H.K.A, F.Ş.V.

References

1. Marx RE. Pamidronate (Aredia) and zoledronate (Zometa) induced avascular necrosis of the jaws: a growing epidemic. J Oral Maxillofac Surg. 2003;61:1115-7.
2. Ruggiero SL, Dodson TB, Fantasia J, 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.
3. Ruggiero SL, Dodson TB, Aghaloo T, Carlson ER, Ward BB, Kademani D. American Association of Oral and Maxillofacial Surgeons' Position Paper on Medication-Related Osteonecrosis of the Jaws-2022 Update. J Oral Maxillofac Surg. 2022;80(5):920-43.
4. Hess LM, Jeter JM, Benham-Hutchins M, Alberts DS. Factors associated with osteonecrosis of the jaw among bisphosphonate users. Am J Med. 2009;121:475–83.
5. Mercer E, Norton T, Woo S, Treister N, Dodson TB, Solomon DH. Ninety-one osteoporosis patients affected with bisphosphonaterelated osteonecrosis of the jaw: a case series. Calcif Tissue Int. 2013;93:241–8.
6. Hallmer F, Bjørnland T, Nicklasson A, Becktor JP, Andersson G. Osteonecrosis of the jaw in patients treated with oral and intravenous bisphosphonates: experience in Sweden. Oral Surg Oral Med Oral Pathol Oral Radiol. 2014;118:202–8.
7. Vandone AM, Donadio M, Mozzati M, 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.
8. Abu-Id MH, Warnke PH, Gottschalk J, et al. "Bis-phossy jaws"- high and low risk factors for bisphosphonate-induced osteonecrosis of the jaw. J Craniomaxillofac Surg. 2008;36(2):95-103.
9. Bauer JS, Beck N, Kiefer J, Stockmann P, Wichmann M, Eitner S. Awareness and education of patients receiving bisphosphonates. J Craniomaxillofac Surg. 2012;40:277–82.
10. Almousa MA, Alharbi GK, Alqahtani AS, Chachar Y, Alkadi L, Aboalela A. Dental practitioners' and students' knowledge of medication related osteonecrosis of the jaw (MRONJ). Saudi Pharm J. 2021;29:96-103.
11. El Osta L, El Osta B, Lakiss S, Hennequin M, El Osta N. Bisphosphonate-related osteonecrosis of the jaw: awareness and level of knowledge of Lebanese physicians. Support Care Cancer. 2015;23:2825-31.
12. Acharya S, Patil V, Ravindranath V, Kudva A, Nikhil K. Medication-related osteonecrosis of the jaw: knowledge and perceptions of medical professionals on the usage of bone modifying agents and dental referrals. J Med Life. 2022;15:368-73.
13. Rosella D, Papi P, Pompa G, Capogreco M, De Angelis F, Di Carlo S. Dental students' knowledge of medication-related osteonecrosis of the jaw. Eur J Dent. 2017;11:461-8.
14. 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;119:395-400.
15. 15. Franchi S, Brucoli M, Boffano P, Dosio C, Benech A. Medical students' knowledge of medication related osteonecrosis of the jaw. J Stomatol Oral Maxillofac Surg. 2020;121:344-6.
16. Miranda-Silva W, Montezuma MA, Benites BM, Bruno JS, Fonseca FP, Fregnani ER. Current knowledge regarding medication-related osteonecrosis of the jaw among different health professionals. Support Care Cancer. 2020;28:5397-404.
17. Yamori M, Tamura M, Mikami M, et al. Differences in the Knowledge and Experience of Physicians and Dentists About Medication-Related Osteonecrosis of the Jaw in Osteoporotic Patients. Int Dent J. 2021;71(4):336-42.

18. Yoo JY, Park YD, Kwon YD, Kim DY, Ohe JY. Survey of Korean dentists on the awareness of bisphosphonate-related osteonecrosis of the jaws. J Investig Clin Dent. 2010;1:90-5.
19. 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;222:121-5.
20. de Lima PB, Brasil VL, de Castro JF, 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.
21. 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;73:1095-105.
22. López-Jornet P, Camacho-Alonso F, Molina-Miñano 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;16:878-82.
23. Moreno-Rabié C, Gaêta-Araujo H, Oliveira-Santos C, Politis C, Jacobs R. Early imaging signs of the use of antiresorptive medication and MRONJ: a systematic review. Clin Oral Investig. 2020;24:2973-89.
24. Wongratwanich P, Shimabukuro K, Konishi M, et al. Do various imaging modalities provide potential early detection and diagnosis of medication-related osteonecrosis of the jaw? A review. Dentomaxillofac Radiol. 2021;50:20200417.
25. Henry DH, Costa L, Goldwasser F, et al. Randomized, double-blind study of denosumab versus zoledronic acid in the treatment of bone metastases in patients with advanced cancer (excluding breast and prostate cancer) or multiple myeloma. J Clin Oncol. 2011;29(9):1125-32.