



Awareness of Oral and Medical Healthcare Professionals in the Prevention, Diagnosis, and Management of Bisphosphonate-related Osteonecrosis of the Jaw

Bifosfonatlarla İlişkili Çene kemiği Nekrozunun Önlenmesi, Tanı ve Tedavisinde Diş ve Tıp Hekimlerinin Farkındalığı

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Abstract

Objective: The aim of this study was to evaluate the awareness and knowledge of oral and medical healthcare professionals regarding the prevention, diagnosis, and management of bisphosphonate-related osteonecrosis of the jaw (BRONJ).

Materials and Methods: Two surveys were conducted with oral and medical healthcare professionals to evaluate their knowledge and attitude about bisphosphonates and their experiences with BRONJ.

Results: A total of 385 oral and 119 medical healthcare responses were obtained. The level of knowledge of oral healthcare professionals who practiced for less than 10 years was significantly higher than that of those practicing for more than 10 years ($p<0.05$). Oral surgeons and periodontists had the highest level of knowledge ($p<0.05$). The knowledge level scores of the medical healthcare professionals exposed to the necrotic jaw during their careers were significantly higher than those who did not ($p<0.05$).

Conclusion: Within its limits, the knowledge of medical healthcare professionals was lower than expected. Knowledge of oral healthcare professionals was moderate, except for oral surgeons and periodontists. Multidisciplinary informative platforms between oral and medical healthcare professionals will benefit the management of potential risks and complications related to BPs.

Keywords: Bisphosphonate, bisphosphonate-related osteonecrosis of the jaw, awareness, survey

Öz

Amaç: Bu çalışmanın amacı, bifosfonatlarla ilişkili çene kemiği nekrozunun (BRONJ) önlenmesi, teşhisi ve tedavisi ile ilgili diş ve tıp hekimlerinin farkındalık ve bilgilerini değerlendirmektir.

Gereç ve Yöntemler: Diş ve tıp hekimlerine bifosfonatlar hakkındaki bilgi ve tutumlarını, BRONJ deneyimlerini ve farkındıklarını değerlendirmek için iki farklı anket uygulandı.

Bulgular: Toplam 385 diş hekimi ve 119 tıp hekimi anketi yanıtladı. On yıldan az süredir çalışan diş hekimlerinin bilgi düzeylerinin, 10 yıldan fazla çalışan diş hekimlerinden anlamlı olarak daha yüksek olduğu tespit edildi ($p<0,05$). Ağız ve çene cerrahları ve periodontologların en yüksek bilgi düzeyine sahip olduğu saptandı ($p<0,05$). Kariyerleri boyunca çene kemiği nekrozu ile karşılaşan tıp hekimlerinin bilgi düzeyi skoru, karşılaşmayanlara göre anlamlı olarak daha yüksek olarak bulundu ($p<0,05$).

Sonuç: Bu araştırmanın sınırları dahilinde, tıp hekimlerinin konu ile ilgili bilgisinin beklenenden daha düşük olduğu tespit edildi. Ağız ve çene cerrahları ve periodontologlar dışındaki diş hekimlerinin bilgisi orta düzeyde bulundu. Diş ve tıp hekimleri arasındaki multidisipliner bilgilendirici platformlar, bifosfonatlar ile ilgili potansiyel risk ve komplikasyonların yönetimi üzerinde faydalı bir etkiye sahip olacaktır.

Anahtar Kelimeler: Bifosfonat, bifosfonatlarla ilişkili çene kemiği nekrozu, farkındalık, anket

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Introduction

Bisphosphonates (BPs) are used to treat malignant bone diseases, prevent metastatic bone tumors, and prevent osteoporosis-related fractures in osteoporosis and osteopenia patients (1,2). Despite their beneficial effects, they have a severe side effect of bisphosphonate-related osteonecrosis of the jaw (BRONJ), defined as exposed necrotic bone at the maxillofacial region for more than 8 weeks (3). In 2014, as the second diagnostic criteria, bone that can be probed through an intraoral or extraoral fistula was also included (4). In recent years, due to the high number of osteonecrosis cases observed after the prescription of antiangiogenic and antiresorptive medications, the nomenclature was revised to medication-related osteonecrosis of the jaw (MRONJ) (2). A growing number of cancer and osteoporosis cases make this devastating clinical condition a potential complication for medical and oral healthcare professionals. Osteonecrosis lesions may occur spontaneously or after interventional approaches (5).

Medical healthcare professionals are the first link in the chain of events, and they should warn patients about BRONJ. Awareness of oral and medical healthcare professionals about BRONJ is paramount in the prevention, early detection, diagnosis, and management of these cases. Therefore, this study evaluated oral and medical healthcare professionals' knowledge, awareness, and attitude regarding BPs and BRONJ.

Materials and Methods

This observational cross-sectional study was conducted between September 2018 and January 2019. Two different surveys were applied to oral and medical healthcare professionals. According to the sample size calculation, the estimated participation numbers were 379 and 110 for oral and medical healthcare professionals, respectively. A pilot study was performed to ensure the survey's feasibility and validity. The questionnaire applied by Alhussain et al. (6) and El Osta et al. (7) was used for oral and medical healthcare professionals surveys, respectively.

The survey for oral healthcare professionals comprised three sections. The first section included questions about professional experience and demographic data, the second focused on perceptions about BRONJ, and the third assessed knowledge acquisition. The survey for medical healthcare professionals consisted of three sections and included 20 questions. The first section gathered data on demographic and professional characteristics; the second collected information about the number of BPs prescribed monthly and the name/form/duration of the recommended BPs; and the third comprised 30 sub-questions that evaluated the experience and knowledge of professionals. The highest score that could be obtained was 29 and 30 points in oral and medical healthcare professionals surveys, respectively. A higher score indicates a higher level of knowledge.

Correct response rates of less than 25%, 25-50%, 50-75%, and more than 75% were considered weak, moderate, good, and excellent, respectively.

This study was approved by the Ethics Committee of İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine (decision no: A-19, date: 05.06.2018).

Statistical Analysis

The data were collected via a web-based program (Survey Monkey, US). Normality was checked with the Shapiro-Wilks test. Intergroup differences were evaluated by Kruskal-Wallis, One-Way ANOVA, and Student's t-test. Mann-Whitney was used to determine the groups that caused the difference, and significance was assessed at $p < 0.05$. Statistical analyses were conducted using SPSS Statistics 22 software (SPSS IBM, Turkey).

Results

A total of 485 dentists registered with the Turkish Dental Association responded to the survey. Due to missing answers and abandoning the test, 100 participants were excluded. A total of 200 medical health professionals working at the İstanbul University Institute of Oncology and Cerrahpaşa Medical Faculty participated in the survey and related to the abovementioned problems; 119 responded to surveys included in the study.

The average knowledge score for oral healthcare professionals was 14.25 ± 6.39 . The knowledge of oral healthcare professionals is presented in Table 1, and the knowledge score by gender, age, specialization status, type of specialty, and duration of work in Table 2. General dentists had significantly lower total knowledge scores than specialists ($p = 0.000$; $p < 0.05$). Among the specialties, oral and maxillofacial surgeons had significantly higher total knowledge scores than others ($p < 0.05$). Additionally, the total knowledge scores of the group with a professional practice duration of 1-5 years were significantly higher than those of groups with a longer duration of work ($p < 0.05$) (Table 2).

The average knowledge score for medical healthcare professionals was 19.29 ± 6.83 . Correct response rates related to BRONJ are presented in Table 3. Medical healthcare professionals' knowledge score according to demographic and professional characteristics is shown in Table 4. The knowledge level scores of the medical healthcare professionals who spent more than 51% of the day on academic work were found to have significantly higher scores than those who spent less than 25% ($p = 0.025$; $p < 0.05$). Medical healthcare professionals' knowledge scores according to the answers given to the questions about the use of BPs are shown in Table 5. The knowledge scores of medical healthcare professionals who prescribed BPs were found to be significantly higher than those who did not ($p = 0.009$; $p < 0.05$).

Table 1. Oral healthcare professionals' BRONJ knowledge

		n	%
Diseases	Osteoporosis	364	94.5
	Osteitis deformans	119	30.9
	Diabetes mellitus	3	0.8
	Bone metastasis	317	82.3
	Multiple myeloma	254	66
	Hypertension	-	-
Bisphosphonate route	Oral	371	96.4
	IV-intravenous	334	86.8
	IM-intramuscular	45	11.7
	Not sure	17	4.4
Data requested for intervention	CTX	225	58.4
	Complete blood count	24	6.2
	aPTT	8	2.1
	HbA1c	4	1
	Glycemic index	1	0.3
	No idea	123	31.9
Known bisphosphonate drugs	Zometa®	252	65.5
	Nidilat®	22	5.7
	Fosamax®	262	68.1
	Prolia®	39	10.1
	Boniva®	194	50.4
	Aredia®	140	36.4
	Osteo bi-flex®	31	8.1
	Protelos®	20	5.2
Frequency of BRONJ following oral bisphosphonate use	Common	134	34.8
	Very common	14	3.6
	Rare	50	13
	Very rare	109	28.3
	Exceptional	51	13.2
	I don't know	27	7
Frequency of BRONJ following IV bisphosphonate use	Common	132	34.3
	Rare	3	0.8
	Very rare	35	9.1
	Exceptional	95	24.7
	I don't know	120	31.2
Number of patients with BRONJ symptoms (min-max, mean ± SD)		0-100	2.17±8.3
Number of patients using oral bisphosphonates (min-max, mean ± SD)		0-100	4.72±10.76
Number of patients using IV bisphosphonate (min-max, mean ± SD)		0-70	2.6±7.19
min-max: Minimum-maximum, SD: Standard deviation, CTX: C-terminal telopeptide, BRONJ: Bisphosphonate-related osteonecrosis of the jaw, The correct answers are written in bold			

Discussion

The present study aimed to evaluate the knowledge of oral and medical healthcare professionals about BP usage and BRONJ as its side effect. The oral healthcare professionals survey aimed at assessing the knowledge about BRONJ covered several key aspects. Most oral healthcare professionals know that BP is prescribed for osteoporosis and bone metastases but less for other indications. Similar results were observed in literature (8-10). Besides, in a study, 65.4% of oral healthcare professionals could not define the indications of BPs (11). Similar to the literature, the most familiar BP was alendronate, followed by zoledronic acid and ibandronate, and the least was

pamidronate in this study (12). On the contrary, in another study, most responders were unaware of alendronate, zoledronic acid, and risedronate sodium (13). Obtaining a complete medical history of the patient and knowing about the information received is undeniably essential to prevent BRONJ. To date, limited data is available for suggesting C-terminal telopeptide (CTX) as a diagnostic marker for high-risk group definition of BRONJ before invasive dental treatments (14,15). Since there is no clear-cut consensus about the topic, 58.4% of participants considered obtaining CTX levels.

In this study, similar to the literature, specialists had higher knowledge scores than general dentists, and oral and maxillofacial surgeons demonstrated significantly higher

Table 2. Oral healthcare professionals' total knowledge score by gender, age, specialization status, type of specialty and duration of work

		Total knowledge score
		Mean ± SD
Gender	Female	14.76±6.59
	Male	13.68±6.12
	p ¹	0.097
Age	23-34	15.74±6.55*
	35-44	13.03±5.39
	45-54	11.74±5.86
	55-64	11.4±5.12
	p ²	0.000*
Specialization status	No	12.96±5.65
	Yes	17.93±6.94*
	p ¹	0.000*
Specialty	Oral and maxillofacial surgery	22.39±4.78*
	Oral and maxillofacial radiology	15.5±6.36
	Endodontics	15±6.96
	Oral implantology	19.5±4.04
	Orthodontics	8.67±3.32
	Pedodontics	14.14±7.4
	Periodontology	16.78±6.72
	Prosthetic dentistry	14.33±6.76
	Restorative dentistry	16.2±3.9
	p ²	0.000*
Profession practice (year)	1-5	15.65±6.53*
	6-10	16.04±6.41*
	11-20	12.47±5.55
	>20	11.8±5.57
	p ²	0.000*

¹Student t-test, ²One-way ANOVA test, *p<0.05, SD: Standard deviation

Table 3. Medical healthcare professionals' BRONJ knowledge		
	Correct responses	
	n	%
Criteria for diagnosis of BRONJ-clinical conditions (n=97)		
Exposed bone that has not healed in the maxillofacial region for 8 weeks	75	77.3
No local signs of malignancy in the affected area	29	29.9
No history of radiotherapy on the affected area	16	16.5
Using oral and/or iv bisphosphonates	88	90.7
Having used oral and/or iv bisphosphonates in the past	76	78.4
Absence of necrotic bone or non-specific clinical signs and symptoms may be observed in BRONJ	62	63.9
BRONJ can be observed without infection and pain	58	59.8
Pathological fracture, extra-oral fistula and osteolysis are complications of BRONJ	70	72.2
The diagnosis of BRONJ is generally clinical	62	63.9
Predisposing risk factors in BRONJ (n=94)		
Age >65	75	79.8
Chemotherapy	67	71.3
Dentoalveolar surgery	75	79.8
Comorbidity (anemia, diabetes, kidney failure)	75	79.8
Corticosteroid therapy	84	89.4
Duration of bisphosphonate usage	84	89.4
Oral and/or dental problems can be observed during bisphosphonate usage	81	86.2
Genetic factors	53	56.4
Effect of bisphosphonate	84	89.4
Tobacco usage	65	69.1
IV bisphosphonate usage	75	79.8
Participation in the following statements about the role of diagnostic methods in BRONJ management (n=94)		
There is a little need for diagnostic imaging in patients with clear clinical findings of BRONJ	33	35.1
Panoramic and conventional radiography does not show characteristic findings in the early stages of the disease	41	43.6
Biopsy is recommended only if bone metastasis is suspected	53	56.4
Participation in the following statements in the treatment and prevention of BRONJ (n=94)		
Recovery is often difficult	72	76.6
Temporarily or permanently discontinuing bisphosphonate use is effective in BRONJ management	65	69.1
Surgical treatment turns out the clinical picture of BRONJ more difficult	32	34.0
BRONJ treatment is mainly medical	35	37.2
The effectiveness of additional treatments has not yet been proven	40	42.6
Minimally invasive dental treatments are recommended in patients using bisphosphonates	66	70.2
Prevention of BRONJ is very important	80	85.1
BRONJ: Bisphosphonate-related osteonecrosis of the jaw		

knowledge than other specialty groups (16,17). The Korean group associated their result with the greater experience of oral and maxillofacial surgeons face with BRONJ and their further rate of medication history taking (16). On the contrary, in a survey any differences were not observed in the total knowledge score of responders depending on their area of expertise, which was attributed to the low turnout among specialists (18). In this study, oral healthcare professionals with more than 10 years of experience had a lower level of knowledge score when compared to less

experience. Similarly, oral healthcare professionals under 30 years of age and recent graduates elucidated better knowledge scores reported about bone resorption inhibitors and BRONJ (18).

In the medical healthcare professionals survey, 76.1% mentioned osteoporosis in terms of therapeutic indication of BP, similar to other studies (19,20). The specialty of the medical healthcare professionals included in the studies can be considered as the reason for these results. As stated in the literature, although the osteoporosis indication is known

Table 4. Evaluation of the knowledge scores of medical healthcare professionals according to demographic and professional characteristics

		Knowledge score		p-value
		Mean ± SD	Median	
Academic degree	Professor	21.5±5.72	22	0.752
	Associate professor	21.4±5.4	21.5	
	Specialist	19.32±6.36	20	
	Research assistant	18.66±7.37	21	
Area of expertise	Internal medicine	21.63±5.61	22	0.108
	Physical therapy and rehabilitation	17.13±6.56	20.5	
	Hematology	18.09±7.96	19	
	Oncology	22.27±4.13	21	
	Orthopedics	19.55±7.58	22	
Age	<30	19.06±6.8	21	0.771
	30-50	18.97±7.47	19	
	>50	21.36±4.13	22	
Gender	Female	18.61±6.6	21	0.310
	Male	19.69±6.98	21	
Profession practice (year)	<5	19.02±7.34	22	0.184
	5-9	17.31±6.51	18.5	
	≥10	20.59±6.14	21	
Daily patient number	<10	20.33±2.66	20.5	0.322
	10-20	18.26±7.09	19	
	>20	19.63±7.01	22	
Clinical practice time (%)	<25%	18.73±7.02	21	0.771
	25-50%	21.17±5.11	21	
	51-75%	20.33±7.11	21	
	>75%	19.14±7.35	22	
Research activities (%)	<25%	18.51±7.06	21	0.037*
	25-50%	22.14±4.74	21.5	
	>51%	24.75±2.5	24.5	

For gender Mann-Whitney U test, for other parameters Kruskal-Wallis test was used, *p<0.05, SD: Standard deviation, BRONJ: Bisphosphonate-related osteonecrosis of the jaw

Table 5. Medical healthcare professionals' knowledge scores according to the answers given to the questions about the use of bisphosphonates

		Knowledge score		p-value
		Mean ± SD	Median	
Bisphosphonate prescription	Yes	20.06±6.33	22	¹ 0.009*
	No	15.07±8.09	19	
Number of newly prescribed bisphosphonates per month	<5	20.69±5.23	21	² 0.941
	6-10	18.69±8.32	22	
	>10	20.73±4.86	22	
Number of patients using bisphosphonates coming to the clinic (monthly)	0	17.90±8.63	20,5	² 0.149
	<5	17.13±7.99	20,5	
	6-10	19.56±5.85	20	
	>10	21.55±5.55	22	
Encounter with exposed necrotic jaw during medical career	Yes	20.78±5.74	22	¹ 0.082
	No	18.25±7.28	20	
Condition of treating exposed necrotic jaw during medical career	Yes	20.83±7.0	22	¹ 0.267
	No	19.13±6.75	21	
Awareness of the effect of bisphosphonates on osteonecrosis of the jawbone	Yes	19.29±6.83	21	
	No			

¹Mann-Whitney U test, ²Kruskal-Wallis test, *p<0.05, SD: Standard deviation

to be high by medical healthcare professionals working in general clinical areas, specialties such as oncology and radiotherapy, responsible for the follow-up of cancer patients, had more knowledge about other indications.

In this study, a high percentage of awareness was observed about BRONJ as a side effect of BPs (82.4%) in medical healthcare professionals. Even though there seems to be a basic awareness of BRONJ, there are knowledge gaps and a need for additional education (21). Although in this study specialty of medical professionals was not significantly associated with a high knowledge score similar to Kim et al. (19), in other studies, specialty types, especially ear, nose, and throat specialists, oncologists, and physicians who counteracted with cancer patients had higher knowledge scores (7,20). Despite medical healthcare professionals' experience not contributing to the knowledge scores in this study, the highest level of awareness was observed in the group with more than 20 years of work experience in Kim et al.'s (19) study. Miranda-Silva et al. (20) reported that professionals with 5-10 years and less than 5 years of training presented significantly higher knowledge scores. In recent years, medical healthcare professionals have encountered patients using BP and have BRONJ in increasing frequencies, which may affect the relationship between experience and knowledge. Accordingly, in this study, the knowledge level scores of the medical healthcare professionals exposed to the necrotic jaw during their career were significantly higher than those who did not face

this clinical condition (p<0.05). Most medical healthcare professionals who participated in this study (82.1%) could not entirely identify the BRONJ with the defined clinical criteria. Since medical healthcare professionals are one part of the equilibrium for BRONJ management, emphasis should be given to continuous professional training strategies.

A possible limitation of this study is that only Turkish oral and medical healthcare professionals were included. Therefore, the conclusions drawn from this study can only be generalized to Turkey.

BPs were included in the core basic education of Dentistry a long time ago. For this reason, dentists are expected to graduate with knowledge about the subject. This may explain differences in the responses to knowledge questions among oral and medical healthcare professionals. With the increase in the use of BP, the incidence of its side effects has also increased, and oral and medical healthcare professionals now encounter BRONJ patients more often. Understandably, healthcare professionals are more likely to encounter this situation and know more about the subject.

Conclusion

The information gathered from this study highlights the approach of oral and medical healthcare professionals to BRONJ and the need for additional training or guidelines to ensure that patients receive scientifically evidence-

based treatments. Prevention remains the most critical aspect of the management, and AAOMS re-emphasizes the importance of a multidisciplinary approach to treating patients receiving antiresorptive therapies. As stated, a continuous effort is needed to educate patients and oral and medical healthcare professionals and the coordinated work of the oral and medical healthcare professionals has the utmost importance.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine (decision no: A-19, date: 05.06.2018).

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Authorship Contributions

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