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IZVORNI ZNANSTVENI RAD

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Dentists' Awareness of Medication-Related Osteonecrosis of the Jaw (Risk Factors, Drugs, and Prevention) in the Republic of Croatia

Znanje Doktora dentalne medicine o medikamentnoj osteonekrozi čeljusti (rizični čimbenici, lijekovi i prevencija) u Republici Hrvatskoj

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Abstract

Antiresorptive drugs (AR) have been used for many years in the treatment of various bone conditions such as osteoporosis, osteopenia, Paget's disease, bone metastases, multiple myeloma and the associated malignant hypercalcemia. As a side effect of AR therapy, medication-related osteonecrosis of the jaw, which affects the mandible more commonly than the maxilla, (MRONJ) has become an increased risk regarding patients' health and quality of life. The incidence of osteonecrosis has increased significantly in the last few years. One of the main methods of the disease prevention is the education of patients and doctors of dental medicine (DDMs). This is evidenced by the national program of information and prevention of antiresorptive therapy side effects, which was also the impetus for this study. **Purpose:** This study aims to test the knowledge of DDMSs on AR, especially on bisphosphonate (BF) therapy, MRONJ as well as on the risk factors of the disease itself. **Material and methods:** 458 DDMs from the Republic of Croatia participated in the survey and responded by an anonymous questionnaire to questions about the knowledge of AR/BF and the risk of MRONJ. **Results:** The results showed that 36.68% of DDMs do not know that MRONJ is the main complication of AR/BF therapy. The results are significantly different in terms of academic degree, specialization, workplace, and work experience. 60.26% of respondents do not know the main indications for AR/BF use, 53.26% do not know the factors affecting the onset of the disease, and 42.58% do not know which therapy is not recommended for patients on AR/BF therapy. 93.89% of respondents expressed the desire to educate on this issue. This current study was carried out to further investigate the pilot study findings which was conducted in the year 2015, but it had a significantly lower number of participants. **Conclusion:** This research suggests that further education of DDMS on this topic is necessary to prevent or to start early treatment of MRONJ.

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Introduction

Bisphosphonates (BF) are antiresorptive drugs (AR) that have been used for many years in the treatment of bone diseases such as osteoporosis, osteopenia, Paget's disease and in the treatment of malignancies such as multiple myeloma,

Uvod

Bifosfonati (BF) su antiresorptivni (AR) lijekovi koji se godinama primjenjuju u liječenju koštanih bolesti kao što su osteoporoza, osteopenija i Pagetova bolest te u liječenju malignih bolesti (multipli mijelom, koštane metatstatske bole-

bone metastatic diseases and malignant hypercalcemia (1,2). Although their positive therapeutic use is known for many years, it was only in 2003 that the side effects of their therapy, which is osteonecrosis of the jaw (3), were first mentioned in the literature. This specific, antiresorptive drugs-related form of osteonecrosis occurs primarily in the jaw bones, probably due to a combination of active remodeling, thin mucosa, susceptibility to infection, and it may affect the fibroblasts of the connective tissue (4).

In recent years, it has been described that new drugs can also cause MRONJ such as denosumab and romosozumab from the group of AR drugs, and bevacizumab, sunitinib, and sorafenib as part of antiangiogenic drugs (5). Due to the emergence of new drugs that can cause osteonecrosis, the previous name bisphosphonate osteonecrosis of the jaw (BRONJ) is not appropriate anymore, so the name is changed to medication-related osteonecrosis of the jaw (MRONJ).

The development of MRONJ is attributed to various factors, of which the most important is for those patients undergoing therapy with antiresorptive or antiangiogenic drugs. The type of administration of the drugs is also important. Intravenous administration of high-potency BFs used in malignancies carries a much higher risk of osteonecrosis than oral BFs, which are most commonly used in osteoporosis (5-9). The duration of therapy and higher doses of BF also pose a higher risk of developing osteonecrosis (10-11). Dental procedures also increase the development of osteonecrosis such as tooth extraction, placement of dental implants, periodontal and endodontic surgery (5,7,12-13), and concomitant bacterial contamination. Additional risks are older age (60 years and older), use of immunosuppressive drugs, anemia, corticosteroid use, renal failure, etc. (14-16).

For differential diagnosis of MRONJ, osteoradionecrosis as a consequence of radiation in the head and neck area, suppurative osteomyelitis following infection, various fibro-osseous lesions, alveolar sinusitis and chronic sclerosing osteitis should also be considered in the differential diagnostics (5).

The clinical picture of osteonecrosis can vary from small localized lesions involving no exposed necrotic bone tissue to exposed tissue of the entire jaw (5). A higher occurrence of osteonecrosis is present in the lower jaw (due to its poor blood circulation) and in places covered only with a thin mucosa (lingual side of the lower jaw, exostosis, torus) (13). Lesions may be present with or without signs of infection, while in the advanced stage they may spread to adjacent structures such as the mandibular canal or maxillary sinus (5).

MRONJ therapy is complex and unpredictable, and knowledge about this disease is essential for its prevention. Therefore, dentists must be familiar with this topic.

The purpose of this study is to determine how doctors of dental medicine (DDM) are familiar with drugs that can cause MRONJ, with the indications for the use of individual drugs, and in general to collect information about their experience of treating the disease by themselves. To further raise awareness of MRONJ, all participant DDMs received a brochure as part of the national disease prevention program.

sti, maligna hiperkalcemija) (1, 2). Iako je njihova pozitivna terapijska primjena poznata već godinama, tek se 2003. u literaturi prvi put spominje nuspojava terapije, a to je medikamentna osteonekroza čeljusti (engl. *Medication Related Osteonecrosis of the Jaw* – MRONJ) (3). Taj specifični oblik osteonekroze prouzročen lijekovima pojavljuje se primarno u kostima čeljusti, vjerojatno zbog kombinacije aktivne remodelacije, podložnosti infekciji i tanke sluznice (4). Posljednjih se godina opisuju i drugi lijekovi koji nisu uvršteni u BF, ali također mogu izazvati osteonekrozu kao što su denosumab i romosozumab iz skupine AR lijekova, te bevacizumab, sunitinib i sorafenib kao lijekovi koji nisu uvršteni među AR lijekove (5). Zbog pojave novih lijekova koji mogu potaknuti osteonekrozu, dosadašnji naziv bisfosfonatna osteonekroza čeljusti (BRONJ) više nije primjeren, pa je promijenjen u medikamentna osteonekroza čeljusti (MRONJ).

Nastanak MRONJ-a ovisi o različitim čimbenicima, a najvažnija je terapija antiresorptivnim ili antiangiogenim lijekovima, način primjene lijeka, trajanje terapije te invazivnost stomatološkog zahvata. Intravenska primjena visokopotentnih BF-a koji se koriste u liječenju zloćudnih bolesti mnogo je rizičnija kad je riječ o osteonekrozi od oralnih BF-ova koji se najčešće propisuju za osteoporozu (5 – 9). Dugotrajnost terapije i veće doze AR-a također su rizičnije za pojavu osteonekroze (10 – 11). Razni stomatološki zahvati potenciraju nastanak osteonekroze poput vađenja zuba, ugradnje dentalnih implantata te parodontnih i endodontskih kirurških zahvata (5, 7, 12 – 13). Dodatni rizici su starija dob (60 i više godina), uporaba imunosupresivnih lijekova i kortikosteroida te anemija, insuficijencija bubrega i drugo (14 –16).

Za diferencijalnu dijagnozu MRONJ-a treba uzeti u obzir i drugi tip nekroze – osteoradionekrozu kao posljedicu zračenja u području glave i vrata, supurativni osteomijelitis, razne fibroosealne lezije, alveolarni sinusitis i kronični sklerozirajući osteitis (5).

Klinička slika osteonekroze može varirati od malih lokaliziranih lezija pa sve do zahvaćenosti cijele čeljusti (5). Češća je u donjoj čeljusti (zbog njezine slabije prokrvljenosti) i na mjestima koja su prekrivena tankom sluznicom (jezična strana donje čeljusti, egzostoza, torus) (13). Lezije mogu biti sa znakovima infekcije ili bez njih, a u uznapredovalom stadiju mogu se proširiti na susjedne strukture poput mandibularnog kanala ili maksilarnog sinusa (5).

Terapija MRONJ-a složena je i nepredvidiva, a poznavanje te bolesti prijeko je potrebno u njezinoj prevenciji. Zato liječnici i pacijenti moraju biti upoznati s tom temom.

Svrha ovog istraživanja jest ustanoviti koliko doktori dentalne medicine (DDM) znaju o lijekovima koji mogu prouzročiti MRONJ, o indikacijama o primjeni pojedinih lijekova te općenito o iskustvima u liječenju te bolesti. Nakon ispunjavanja upitnika svim sudionicima je podijeljena brošura pripremljena u sklopu nacionalnog programa prevencije bolesti u svrhu podizanja svijesti i informiranja o samoj bolesti.

Materials and methods

The research was conducted through an anonymous survey questionnaire distributed to DDMs throughout the Republic of Croatia in written and e-form. We followed up with non-responders by sending a reminder email 3-4 weeks after the initial email.

The research was approved by the Ethics Committee of the School of Dental Medicine, University of Zagreb, protocol number 05-PA-15-3 / 2017.

The questionnaire consisted of 21 questions divided into three parts. The first part included general data on respondents such as age, gender, work experience, location of business, counties of business and academic degree (postgraduate studies and area of specialty).

The second section contained information on the knowledge of BF and their risk for osteonecrosis (indications, risks, factors, type of procedure associated with osteonecrosis).

The third unit contained information on the treatment of MRONJ (knowledge of the factors that reduce the risk of osteonecrosis and treatment experience).

Materijal i metode

Istraživanje je provedeno na temelju anonimnoga anketnog upitnika koji je podijeljen doktorima dentalne medicine diljem Republike Hrvatske u pisanom i elektroničkom obliku. Liječnici koji nisu odgovorili na anketni upitnik poslan je podsjetnik poslije 3 do 4 tjedna.

Istraživanje je odobrilo Etičko povjerenstvo Stomatološkog fakulteta Sveučilišta u Zagrebu – broj protokola 05-PA-15-3 / 2017.

Upitnik se sastojao od 21 pitanja koja su bila podijeljena u tri cjeline. U prvoj cjelini tražili su se opći podatci o ispitanicima kao što su dob, spol, radno iskustvo, mjesto rada, županija u kojoj se obavlja djelatnost i akademski stupanj obrazovanja (poslijediplomski studij i specijalizacija).

Druga cjelina sadržavala je informacije o poznavanju BF/AR-a i njihovu riziku za nastanak osteonekroze (indikacije, rizici, čimbenici, vrsta stomatološkog zahvata povezanog s osteonekrozom).

U trećoj cjelini bile su informacije o liječenju MRONJ-a (poznavanje čimbenika koji utječu na smanjenje rizika za na-

Table 1 Score scale for multiple-choice questions.
Tablica 1. Bodovna ljestvica za pitanja s više točnih odgovora

Number of questions • Broj pitanja	Number of correct answers • Broj točnih odgovora	Knows • Zna	Does not know • Ne zna
11	4	3-4	0-2
13	5	2-5	0-1
14	4	2-4	0-1
15	2	2	0-1
16	5	3-5	0-2

Table 2 Presentation of the results of the respondents according to the first group of questions.
Tablica 2. Prikaz rezultata ispitanika prema prvoj skupini pitanja

Category • Kategorija	Group • Skupina	Number of respondents • Broj ispitanika	Percentage • Postotak (%)
Sex • Spol	Female •Ženski	243	53.06
	Male • Muški	215	46.94
Average age • Prosječna dob	41.33 years • godina		
Average work experience • Prosječno radno iskustvo	25.2 years • godina		
Specialization • Specijalizacija	No specialization • Nema specijalizaciju	329	71.83
	Oral surgery • Oralna kirurgija	37	8.08
	Prosthodontics • Protetika	23	5.02
	Pedodontics •Pedodoncija	12	2.62
	Oral medicine • Oralna medicina	5	1.09
	Endodontics • Endodoncija	18	3.93
	Periodontists • Parodontologija	10	2.18
	Orthodontics • Ortodoncija	22	4.80
Postgraduate studies • Poslijediplomski studij	None • Nema	354	77.29
	Doctorate • Doktorat	49	10.70
	Master's Degree • Magisterij	47	10.26
	In process • U tijeku	8	1.75
Work • Djelatnost	Private practice • Vlastita praksa	174	37.99
	Health center • Dom zdravlja	172	37.55
	Polyclinic • Poliklinika	66	14.41
	Hospital • Bolnica	14	3.06
	Faculty • Fakultet	32	6.99

Table 3 DDMs' knowledge about the main complication of BF in the oral cavity by county.
Tablica 3. Znanje DDM- a o glavnoj komplikaciji BF/AR-a u usnoj šupljini po županijama

Counties • Županija	No DDM • Broj DDM-a	No (Figure 1) • Broj (slika 1.)	Know • Zna		Does not know • Ne zna	
			No • Broj	Prencentage • Postotak (%)	No • Broj	Prencentage • Postotak (%)
City of Zagreb • Grad Zagreb	148	1	125	84.46	23	15.54
Međimurje • Međimurska	30	2	18	60	12	40
Osijek-Baranja • Osječko-baranjska	29	3	16	55.17	13	44.83
Brod-Posavina • Brodsko-posavska	25	4	16	64	9	36
Primorje-Gorski Kotar • Primorsko-goranska	24	5	19	79.17	5	20.83
Split-Dalmatia • Splitsko-dalmatinska	20	6	11	55	9	45
Šibenik-Knin • Šibensko-kninska	19	7	8	42.11	11	57.89
Zadar • Zadarska	18	8	11	61.11	7	38.88
Bjelovar-Bilogora • Bjelovarsko-bilogorska	17	9	9	52.94	8	47.06
Krapina-Zagorje • Krapinsko-zagorska	16	10	5	31.25	11	68.75
Zagreb county • Zagrebačka	15	11	8	53.33	7	46.67
Sisak-Moslavina • Sisačko-moslavačka	15	12	7	46.67	8	53.33
Lika-Senj • Ličko-senjska	14	13	4	28.57	10	71.43
Požega-Slavonija • Požeško-slavonska	13	14	4	30.77	9	69.23
Istra • Istarska	13	15	10	76.92	3	23.08
Koprivnica-Križevci • Koprivničko-križevačka	10	16	1	10	9	90
Karlovac • Karlovačka	9	17	4	44.44	5	55.56
Virovitica-Podravina • Virovitičko-podravska	9	18	4	44.44	5	55.56
Vukovar-Srijem • Vukovarsko-srijemska	7	19	6	85.71	1	14.29
Varaždin • Varaždinska	4	20	4	100	0	0
Dubrovnik-Neretva • Dubrovačko-neretvanska	3	21	1	33.33	2	66.67

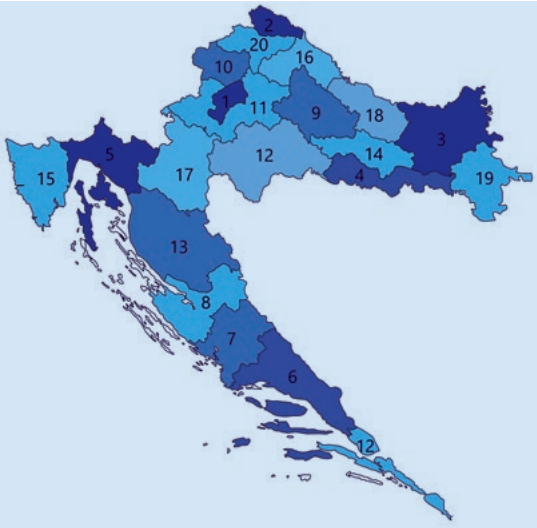

Figure 1 Map of counties in Croatia. See table 3 for numbers
Slika 1. Karta županija u Republici Hrvatskoj – pogledati tablicu 3. za brojeve

In the second and third units, multiple-choice answers to the questions are offered. Five questions (11, 13, 14, 15, 16) had more than one correct answer. Questions with multiple correct answers were scored as follows: +1 point for the correct answer, and -1 point for the incorrect answer. Based on the total number of points, the researchers determined two groups according to the point scale for individual questions: "KNOWS" and "DOES NOT KNOW". (Table 1.) Each question with more correct answers offered the possibility to complete the answer "I AM NOT SURE" or "I AM NOT FAMILIAR WITH THIS ISSUE", which in that case would be classified as the answer "I DON'T KNOW".

U drugoj i trećoj cjelini trebalo je zaokružiti točan odgovor između više ponuđenih. Za pet pitanja (11, 13, 14, 15, 16) mogło se odabrati više točnih odgovora. Pitanja s više točnih odgovora bodovana su na sljedeći način: +1 bod za točan odgovor i -1 bod za netočan odgovor. Na temelju ukupnoga broja bodova istraživači su, prema bodovnoj ljestvici za pojedina pitanja, odredili dvije skupine: „ZNA" i „NE ZNA". (tablica 1.) Svako pitanje s više točnih odgovora nudilo je mogućnost dopunjavanja odgovora „NISAM SIGURAN" ili „NISAM OBAVIJEŠTEN O TOM PROBLEMU", što bi u tom slučaju bilo klasificirano kao odgovor „NE ZNA".

Results

The questionnaire was distributed to a total number of 951 participants out of which 504 responded. 46 questionnaires were not usable, so they were discarded. Finally, the study involved 458 (48.2%) DDM from all over the Republic of Croatia, of which 233 (50.9%) were female and 215 (49.1%) were male. The average age of the respondents is 41.33 years with an average work experience of 25.2 years. Respondents were classified according to specialization, academic degree, work experience, and county. Tables 1 and 2 show the results of the respondents from the first group of questions.

Table 3 and Figure 1 show DDM's general knowledge about the main complication (osteonecrosis of the jaw) of BF in the oral cavity by county. The highest number of participants who offered correct answers was in the city of Zagreb, but also the highest number of incorrect answers was in the city of Zagreb as well, which can be explained by the highest number of participants in this region since it is the most populated region in Croatia.

Table 4 shows DDM's knowledge of the main complication of bisphosphonate therapy, MRONJ. The table also categorizes DDMs by specialization, level of academic education, place of employment, and work experience.

Rezultati

Upitnik je proslijeđen ukupno 951 sudioniku od kojih je 504 odgovorilo. Odbačeno je 46 upitnika jer nisu bili potpuni. Konačno, u istraživanju je sudjelovalo 458 (48,2 %) doktora dentalne medicine iz cijele Republike Hrvatske, od kojih 233 (50,9 %) žene i 215 (49,1 %) muškaraca. Prosječna dob bila je 41,33 godine s prosječnim radnim iskustvom od 25,2 godine. Ispitanici su razvrstani prema specijalizaciji, akademskom stupnju, radnom iskustvu i županiji. U tablici 1. i 2. nalaze se rezultati ispitanika iz prve skupine pitanja.

Tablica 3. i Slika 1. prikazuje znanje doktora dentalne medicine o glavnoj komplikaciji AR terapije (osteonekroza čeljusti) u usnoj šupljini po županijama. Najveći broj sudionika koji su dali točne, ali i netočne odgovore, bio je u gradu Zagrebu, što se može objasniti najvećim brojem sudionika u toj regiji jer je najnaseljenija u Republici Hrvatskoj.

Tablica 4. pokazuje znanje doktora dentalne medicine o glavnoj komplikaciji terapije bisfosfonatima – MRONJ-u. Tablica također kategorizira liječnike prema specijalizaciji, stupnju akademskog obrazovanja, mjestu rada i radnome iskustvu.

Rezultati pokazuju da 36,68 % svih ispitanika ne zna da je MRONJ glavna komplikacija BF/AR terapije.

Table 4 Does the DDM know which the main complication of the application of BF in the oral cavity is - analysis according to the years of graduation, areas of specialization, postgraduate studies and working area.
Tablica 4. Znanje DDM-a o glavnoj komplikaciji primjene BF/AR-a u usnoj šupljini – analiza prema godini stjecanja diplome, područjima specijalizacije, postdiplomskom studiju te mjestu obavljanja djelatnosti

	Knows • Zna		Does not know • Ne zna	
	Number • Broj	Percentage • Postotak (%)	Number • Broj	Percentage • Postotak (%)
All (458) • Svi (458)	290	63.32	168	36.68
Specialization • Specijalizacija				
No specialization • Nema specijalizaciju	195	59.27	134	40.73
Oral surgery • Oralna kirurgija	33	89.19	4	10.81
Prosthodontics • Protetika	17	73.91	6	26.09
Pedodontics • Pedodoncija	8	66.66	4	33.33
Oral medicine • Oralna medicina	3	60.00	2	40.00
Endodontics • Endodoncija	13	72.22	5	27.78
Periodontics • Parodontologija	5	50.00	5	50.00
Orthodontics • Ortodoncija	17	77.27	5	22.73
Postgraduate studies • Poslijediplomski studij				
None • Nema poslijediplomski studij	207	58.47	146	41.53
Master's Degree • Magisterij	33	70.21	14	29.79
Doctorate • Doktorat	43	87.6	6	12.24
In process • U tijeku	7	87.50	1	12.50
Workplace • Mjesto obavljanja djelatnosti				
Private practice • Vlastita praksa	97	56.07	76	43.93
Health center • Dom zdravlja	90	52.33	82	47.67
Polyclinic • Poliklinika	60	90.91	6	9.09
Hospital • Bolnica	13	92.86	1	7.14
Faculty • Fakultet	30	93.75	2	6.25
Work experience • Radno iskustvo				
Up to 5 years • Do 5 godina	103	86.55	16	13.45
6-10 years • 6-10 godina	68	72.34	26	27.66
11-15 years • 11-15 godina	46	68.66	21	31.34
16-20 years • 16-20 godina	35	56.45	27	43.55
21 and more years • 21 i više godina	38	33.33	76	66.67

The results show that 36.68% of all subjects do not know that MRONJ is a main complication of BF therapy.

Tables 5 and 6 show the knowledge of all respondents and respondents of oral surgery specialists about the knowledge of complications of BF therapy, risks, factors, and types of dental procedures that lead to an increased risk for the development of osteonecrosis of the jaw.

The study found that: 39.74% of DDMs know the indications for the use of AR/BF. 67.57% of DDMs know that the main indication for the use of AR/BF therapy is osteoporosis, 41.92% know that AR is also indicated in bone metastases, while only 23.80% of DDMs managed to mention multiple myeloma as an indication; oral surgeons, as physicians who primarily treat patients with osteonecrosis, have shown better knowledge. 72.97% of oral surgeons know the indications for the use of AR/BF therapy. 72.97% point out that the BF/AR therapy is indicated for bone metastases, 67.57% for osteoporosis, and 56.76% state multiple myeloma as an indication for this therapy; 49.13% of DDMs do not know which way to administer AR/BF therapy or that it carries a higher risk of developing osteonecrosis. Only 13.51% of oral surgery specialists do not know the same data; 66.16% of respondents do not know whether bisphosphonate therapy should be discontinued before invasive dental surgery, while 75.68% of oral surgery specialists are aware

U tablicama 5. i 6. prikazano je znanje svih ispitanika i ispitanika specijalista oralne kirurgije o poznavanju komplikacija BF/AR terapije, rizicima, čimbenicima i vrstama stomatoloških zahvata koji povećavaju rizik od nastanka osteonekroze čeljusti.

Studija je pokazala sljedeće: 39,74 % doktora dentalne medicine zna indikacije AR/BF terapije. Njih 67,57 % zna da je glavna indikacija za primjenu terapije AR/BF osteoporoza, 41,92 % zna da je AR indiciran i u slučaju metastaza u kostima, a samo je 23,80 % spomenulo multipli mijelom kao indikaciju za BF/AR terapiju. Oralni kirurzi kao liječnici koji primarno liječe bolesnike s osteonekrozom pokazali su bolje znanje. Tako 72,97 % oralnih kirurga poznaje indikacije za primjenu AR/BF terapije. Njih 72,97 % ističe da je BF/AR terapija indicirana za koštane metastaze, 67,57 % za osteoporozu, a 56,76 % kao indikaciju za tu terapiju navodi multipli mijelom. Ali 49,13 % doktora dentalne medicine ne zna na koji način primijeniti AR/BF terapiju ili da to potiče pojavu osteonekroze. Samo 13,51 % specijalista oralne kirurgije ne zna te podatke, 66,16 % ispitanika ne zna treba li prekinuti terapiju bisfosfonatima prije invazivne dentalne kirurgije, a 75,68 % specijalista oralne kirurgije svjesno je toga. Čimbenike za smanjenje komplikacija točno je označilo 30,57 % doktora dentalne medicine. Veće znanje pokazali su oralni kirurzi. Glavnu komplikaciju AR/BF terapije točno

Table 5 Analysis of questions from the DDM knowledge questionnaire - knowledge of the complications of BF therapy, risks, factors, and types of dental procedures - included all respondents.
Tablica 5. Analiza pitanja iz upitnika o znanju DDM-a – poznavanje komplikacija BF/AR terapije, rizika, čimbenika i vrsta stomatološkog zahvata; obuhvaćeni su svi ispitanici

Number of questions and keywords from the question • Br. pitanja i ključne riječi iz pitanja	Answers to the questions in percentages and the number of DDMs who have chosen the listed answer • Odgovori na pitanja u postotcima i broju DMD-a koji su izabrali navedeni odgovor			
11. Indications for the use of BF • Indikacije za primjenu BF-a	Knows • Zna	Does not know • Ne zna		
	182 39.74%	276 60.26%		
Diseases for which BF is applied • Bolesti za koje se primjenjuju BF	Osteoporosis • Osteoporoza	Multiple myelom • Multipli mijelom	Bone metastases • Koštane metastaze	
	286 62.45%	109 23.80%	192 41.92%	
12. Method of BF administration and risk of osteonecrosis • Način primjene BF/AR-a i rizik od nastanaka osteonekroze	po.	iv.	Equally • Podjednako	Does not know • Ne zna
	23 5.02%	174 37.99%	30 6.55%	225 49.13%
13. Factors influencing the occurrence of osteonecrosis • Čimbenici koji utječu na pojavu osteonekroze	Knows • Zna	Does not know • Ne zna		
	214 46.72%	244 53.26%		
14. Association of dental procedures with the risk of osteonecrosis • Povezanost stomatološkog zahvata s rizikom od nastanka osteonekroze	Knows • Zna	Does not know • Ne zna		
	263 57.42%	195 42.58%		
Type of dental procedure • Vrsta stomatološkog zahvata	Extraction • Ekstrakcija	Implant placement • Ugradnja implantata		
	220 48.03%	217 47.38%		
15. The need to discontinue BF th. Before an invasive procedure • Potreba za prekidom BF/AR terapije prije invazivnog zahvata	Knows • Zna	Does not know • Ne zna		
	155 33.84%	303 66.16%		
16. Procedures to reduce the risk of complications • Postupci za smanjenje rizika od nastanka komplikacija	Knows • Zna	Does not know • Ne zna		
	140 30.57%	318 69.43%		

of this issue. Complication reduction factors were accurately indicated by 30.57% DDM`s. Greater knowledge was shown by oral surgeons. The main complication of AR/BF therapy is precisely determined by 63.32% DDMs, equal representation of responses in physicians with and without specialization: 59.27% without specialization, 89.19% oral surgery specialists, 73.91% prosthodontics specialists, 50.00% periodontology specialists. The degree of academic education also correlates with the number of correct answers. Doctors with a Ph.D. (87.76%), a Master's Degree (70.21%), and doctors who are currently in postgraduate studies (87.50%) show better knowledge than doctors who have not done postgraduate studies (58.47%). Considering the working place, DDMs employed in a polyclinic, hospital, or School of Dental Medicine answered the question about the main complication of AR/BF therapy more accurately. More than 90% answered correctly; DDM`s knowledge of AR/BF is inversely proportional to work experience. 86.55% of DDMs with less than five years of work experience correctly answered the question about the main complication of AR/BF therapy, while only 33.33% of DDMs with more than 21 years of work experience answered the same question correctly; 57.42% of DDM`s do not know which procedures should not be performed on patients under AR/BF therapy, and on-

je odredilo 63,32 % doktora dentalne medicine i bila je podjednaka zastupljenost odgovora kod liječnika sa specijalizacijom i bez nje: 59,27 % bez specijalizacije, 89,19 % specijalista oralne kirurgije, 73,91 % specijalista protetike i 50,00 % specijalista parodontologije; S brojem točnih odgovora korelira i stupanj akademske naobrazbe. Liječnici s doktoratom (87,76 %) i magisterijem (70,21 %) te oni trenutačno na poslijediplomskom studiju (87,50 %), pokazali su bolje znanje od liječnika koji nisu završili poslijediplomski studij (58,47 %). S obzirom na mjesto obavljanja djelatnosti, na pitanje o glavnoj komplikaciji AR/BF terapije točnije su odgovorili liječnici zaposleni u poliklinici, bolnici ili na Stomatološkom fakultetu. Više od 90 % odgovorilo je točno. Znanje doktora dentalne medicine o AR/BF-u obrnuto je proporcionalno s radnim iskustvom. Na pitanje o glavnoj komplikaciji AR/BF terapije točno je odgovorilo 86,55 % liječnika s manje od pet godina radnog staža, dok je na isto pitanje točno odgovorilo samo 33,33 % njih s više od 21 godine staža. Istaknimo da 57,42 % doktora dentalne medicine ne zna koji se zahvati ne bi trebali obavljati pacijentima na AR/BF terapiji, a samo 20,97 % takve bi pacijente uputilo specijalistu. Dodajmo da 10,81 % oralnih kirurga uspješno liječi komplikacije, a 40,54 % djelomično uspješno. Ispitanici su dosad imali 291 pacijenta s osteonekrozom, u prosjeku 0,64 po liječniku. Od njih

Table 6 Analysis of questions from the DDM knowledge questionnaire - knowledge of complications of BF therapy, risks, factors, and types of dental procedures - only specialists in oral surgery are included.
Tablica 6. Analiza pitanja iz upitnika o znanju DDM-a – poznavanje komplikacija BF/AR terapije, rizika, čimbenika i vrsta stomatološkog zahvata; obuhvaćeni su samo specijalisti oralne kirurgije

Number of questions and keywords from the question • Br. Pitanja i ključne riječi iz pitanja	Answers to the questions in percentages and the number of DDMs who have chosen the listed answer • Odgovori na pitanja u postotcima i broju DDM-a koji su izabrali navedeni odgovor			
11. Indications for the use of BF • Indikacije za primjenu BF-a	Knows • Zna	Does not know • Ne zna		
	27 72.97%	10 27.03%		
Diseases for which BF is applied • Bolesti za koje se primjenjuju BF/AR	Osteoporosis • Osteoporoza	Multiple myelom • Multipli mijelom	Bone metastases • Koštane metastaze	
	25 67.57%	21 56.76%	27 72.97%	
12. Method of BF administration and risk of osteonecrosis • Način primjene BF/AR-a i rizik od nastanaka osteonekroze	*po.*	*iv.*	Equally • Podjednako	Does not know • Ne zna
	0 0%	30 81.08%	2 5.41%	5 13.51%
13. Factors influencing the occurrence of osteonecrosis • Čimbenici koji utječu na pojavu osteonekroze	Knows • Zna	Does not know • Ne zna		
	28 75.68%	9 24.32%		
14. Relationship between dental procedure and risk for the development of osteonecrosis • Povezanost stomatološkog zahvata s rizikom od nastanka osteonekroze	Knows • Zna	Does not know • Ne zna		
	31 83.78%	6 16.22%		
Type of dental procedure • Vrsta stomatološkog zahvata	Extraction • Ekstrakcija	Implant placement • Ugradnja implantata	Subgingival scaling • Subgingivno uklanjanje kamenca	
	29 78.38%	29 78.38%	7 18.92%	
15. The need to discontinue BF th. Before an invasive procedure • Potreba za prekidom BF terapije prije invazivnog zahvata	Knows • Zna	Does not know • Ne zna		
	28 7568%	9 24.32%		
16. Procedures to reduce the risk of complications • Postupci za smanjenje rizika od nastanka komplikacija	Knows • Zna	Does not know • Ne zna		
	26 70.27%	11 29.73%		

ly 20.97% of DDMs would refer such patients to a specialist; 10.81% of oral surgeons successfully treat complications, and 40.54% of oral surgeons partially successfully treat complications. It was recorded that 291 patients with osteonecrosis were treated, averaging 0.64 per physician. Of these, 144 were treated by oral surgery specialists, 3.89 per oral surgeon; 69.43% of DDMs claim that in the last 5 years, they have not taken any course on this issue because it was not organized. 6.77% of DDMs are not interested in this topic. 93.89% of respondents would like to know more.

Discussion

The incidence of MRONJ in recent years has increased significantly (9,17-25). Constant education of both patients and therapists is necessary with an accent on prevention and early detection of complications caused by these drugs.

In 2015, a pilot study was conducted on the knowledge of DDMs on the side effects of BF therapy in the Republic of Croatia (26). The results (26) showed that 44.1% of the DDMs did not know that osteonecrosis was the main complication of BF therapy. For these reasons, a study collected information on knowledge of DDMs about AR/BF drugs and side effects of the therapy from the entire territory of the Republic of Croatia to obtain representative data on this topic, which was achieved given the response percentage of the questionnaire.

The study showed that 36.68% of DDMs did not know that osteonecrosis was a major complication of BF therapy. Results vary significantly by academic degree, specialization, place of work, county, and work experience. These results are consistent with the results of many publications ranging from 16.67% - 59.5 % (22-24,27-33). Various publications exclude oral surgeons from research because it is assumed that they deviate from the average with their knowledge (26). The study compared knowledge about BF, osteonecrosis, and disease treatment between oral surgeons and other DDMs and showed that the results differed significantly, which is consistent with many publications (24,27). If specialists from various branches of dental medicine are excluded from the research, 40.73% of the DDMs do not know that osteonecrosis is the main complication of BF therapy.

In the study, subjects encountered 291 osteonecroses, averaging 0.64 per physician. It is a worrying fact that 60.26% of respondents do not know the main indications for the use of BF, 53.26% do not know the factors that influence the onset of the disease and 42.58% do not know which procedures are not recommended for patients on BF therapy. Dentoalveolar surgery is a major risk factor for the development of MRONJ. This data states that DDM education on detailed anamnesis, BF recognition, risk assessment of the disease and the recognition of the disease itself is extremely important.

The length of work experience was shown to be a major factor in recognizing and being informed about the disease. The most correct answers were given by DDMs with less than 5 years of work experience due to the fact that they have been increasingly informed about this topic during their studies in recent years, while the least correct answers were given by

su 144 liječena kod specijalista oralne kirurgije, njih 3,89 po oralnom kirurgu. Uz to, 69,43 % doktora dentalne medicine tvrdi da u posljednjih 5 godina nisu pohađali ni jedan tečaj o toj temi jer nije bio organiziran. Za tu temu nije zainteresirano 6,77 % liječnika, a njih 93,89 % željelo bi znati više o toj problematici.

Rasprava

Incidencija nastanka MRONJ-a posljednjih je godina u znatnom porastu (9,17 – 25). S obzirom na osnovnu bolest i odgovarajuću BF/AR terapiju koja je jedan od glavnih čimbenika rizika za nastanak osteonekroze, potrebna je stalna edukacija pacijenta i terapeuta u obliku prevencije i ranog otkrivanja bolesti

U 2015. godini provedeno je u jednoj hrvatskoj županiji pilot-istraživanje o tome poznaju li doktori dentalne medicine nuspojave terapije BF-om (26). Rezultati (26) su pokazali da 44,1 % liječnika nije znalo da je osteonekroza glavna komplikacija te terapije. Zato je pokrenuto istraživanje o informiranosti, odnosno koliko doktori dentalne medicine iz cijele zemlje znaju o BF/AR-u i nuspojavama terapije kako bi se dobila reprezentativna slika o navedenoj tematici.

Studija je pokazala da 36,68 % doktora dentalne nije znalo da je osteonekroza glavna komplikacija BF/AR terapije. Rezultati se značajno razlikuju, ovisno o akademskom stupnju, specijalizaciji, mjestu rada, radnom iskustvu i županiji. Ti su rezultati u skladu s rezultatima u mnogim publikacijama u rasponu od 16,67 % do 59,5 % poznavanja spomenute terapije i osteonekoze (22 – 24, 27 – 33). U raznim publikacijama oralni kirurzi isključeni su iz istraživanja jer se pretpostavlja da svojim znanjem odskaču od prosjeka (26). U istraživanju se usporedilo znanje o BF/AR-u, osteonekrozi i liječenju bolesti između oralnih kirurga i ostalih doktora dentalne medicine te se pokazalo da se rezultati znatno razlikuju, što je u skladu s mnogim publikacijama (24, 27). Ako se iz istraživanja isključe specijalisti raznih grana dentalne medicine, 40,73 % doktora dentalne medicine ne zna da je osteonekroza glavna komplikacija BF terapije.

U istraživanju su se ispitanici susreli s 291 osteonekrozom, prosječno 0,64 po liječniku. Zabrinjava podatak da 60,26 % ispitanika ne zna koje su glavne indikacije za primjenu BF/AR-a, 53,26 % ne zna glavne čimbenike koji utječu na nastanak bolesti, a 42,58 % ne poznaje koji se zahvati ne preporučuju za pacijente na spomenutoj terapiji. Pokazalo se da je dentoalveolarna kirurgija glavni čimbenik rizika za razvoj MRONJ-a. Ti podatci pokazuju da je iznimno važna edukacija doktora dentalne medicine o detaljnoj anamnezi, prepoznavanju BF/AR-a, procjeni rizika za nastanak bolesti te radi prepoznavanja bolesti.

Radno iskustvo pokazalo se kao glavni čimbenik za prepoznavanje i informiranost o bolesti. Najviše točnih odgovora dali su liječnici s manje od 5 godina radnog staža s obzirom na to da su posljednjih godina sve više informirani o toj temi

Appendix
Anonymous questionnaire on the side effects of bf/ar therapy in the oral cavity
BIPHOSPHONATE (ANTIRESORPTIVE) THERAPY IN DENTAL MEDICINE

Q1 sex m f

Q2 year of birth:

Q3 year of graduation:

Q4 have you specialized in something?
A) no
B) yes (name of specialization))

Q5 have you completed postgraduate studies?
A) i haven't
B) specialist postgraduate study (master's degree)
C) doctoral postgraduate studies

Q6 which county do you work in as a doctor of dental medicine?

Q7 in which institution do you perform the job of dental medicine doctor?
A) own practice
B) health center
C) polyclinic
D) hospital
E) faculty

Q8 did you gain knowledge about the application of biphosphonate (antiresoptive) therapy during your education?
A) yes
B) no

Q9 do you know the main complications of biphosphonate (antiresoptive) application in the oral cavity?
A) subperiosteal and central osteoma of the jaw
B) generalized periodontitis and gingivitis
C) osteonecrosis of the jaw
D) dry or burning mouth syndrome
E) i don't know

Q 10 have you encountered complications of biphosphonate therapy during your work?
A) yes
B) no
C) i'm not sure

Q11 circulate the indications of biphosphonate (antiresorptive) use known to you (multiple answers):
A) osteoarthritis
B) osteoporosis
C) metastatic prostate cancer
D) systemic erythematic lupus
E) multiple myeloma
F) diabetes mellitus
D) anemia
H) metastatic breast cancer
I) multiple sclerosis
J) addison's disease
K) i am not aware of this issue

Q12 higher risk for complications in the oral cavity causes:
A) oral administration of bisphosphonates
B) intravenous application of biphosphonate
C) equally (irrespective of the method of application)
D) i'm not sure

Q13 which factors affect the complication of complications caused by biphosphontic drugs? (More answers)
A) age of 60 and over
B) artificial heart valves
C) corticosteroid therapy
D) smoking
E) kidney insufficiency
F) long-term bisphosphonate therapy
D) i'm not sure

Q14 which dental procedures would you postpone on patients who have received or are currently on biphosphonate therapy without prior consultation with specialists? (More answers)
A) endodontic treatment
B) teeth extraction
C) endodontic surgery (apicoectomy)
D) production of prosthetic substitute
E) installation of dental implant
F) supragingival removal of hard dental deposits
G) subgingival removal of hard dental deposits
H) i'm not sure

Q15 is there a need to stop biphosphonate therapy before an invasive dental procedure? (More answers)
A) no need
B) yes, it depends on the duration of the same therapy
C) yes, it depends on the method of application of biphosphonate
D) i'm not sure

Q 16 do you know which factors affect complication reduction in patients on bisphosphonate therapy? (More correct answers)
A) use of antibiotics
B) topical rinsing with antiseptic liquids
C) enhanced oral hygiene
D) additional use of vitamin
E) type of dental procedure
F) i'm not sure

Q 17 do you think you can evaluate when to perform a procedure on a patient and when to contact a specialist?
A) yes
B) no

Q18 how many complications have you encountered related to bisphosphonate therapy, what are your experiences?
A) i comply with complications to a specialist
B) i successfully treat complications
C) i partially successfully treat complications
D) i am successfully treating complications

Q19 how many complications have you encountered since (number of patients)? _____

Q 20 have you participated in a course 5 years ago in which the topic was the side effects of biphosphonate (antiresoptive) therapy?
A) yes
B) no, such a course was not organized
C) no, i think i know enough about this topic
D) no, i am not interested in this topic

Q21 would you like to know more about the therapy and side effects of biphosphonate (antiresoptive) therapy?
A) yes
B) no

Dodatak
Anonimni anketni upitnik o nuspojavama BF/AR terapije u usnoj šupljini
BISFOSFONATNA (ANTIRESORPTIVNA) TERAPIJA U DENTALNOJ MEDICINI

1. Spol m. Ž.
2. Godina rođenja:__
3. Godina stjecanja diplome:____
4. Imate li specijalizaciju?
A) ne
B) da, koje grane dentalne medicine?_____
5. Jeste li bili na poslijediplomskom studiju?
A) nisam
B) specijalistički poslijediplomski studij (magisterij)
C) doktorski poslijediplomski studij
6. U kojoj županiji obavljate posao doktora dentalne medicine?

7. U kojoj ustanovi obavljate posao doktora dentalne medicine?
A) vlastita praksa
B) dom zdravlja
C) poliklinika
D) bolnica
E) fakultet

8. Jeste li tijekom obrazovanja stekli znanje o primjeni bifosfonatne/ antiresorptivne terapije?
A) da
B) ne
9. Znate li koje su glavne komplikacije pri primjeni bifosfonata u oralnoj šupljini?
A) subperiostalni i centralni osteom čeljusti
B) generalizirani parodontitis i gingivitis
C) osteonekroza čeljusti
D) sindrom suhih ili pekućih usta
E) ne znam
10. Jeste li se tijekom rada susretali s komplikacijama bifosfonatne/ antiresorptivne terapije?
A) da
B) ne
C) nisam siguran
11. Zaokružite vama poznate indikacije za primjenu bifosfonata (više odgovora):
A) osteoartritis
B) osteoporoza
C) metastatski karcinom prostate
D) sistemski eritemski lupus
E) multipli mijelom
F) diabetes mellitus
G) anemija
H) metastatski karcinom dojke
I) multipla skleroza
J) addisonova bolest
K) nisam upoznat s ovom problematikom
12. Veći rizik za nastanak komplikacija u usnoj šupljini uzrokuje:
A) peroralna primjena bifosfonata
B) intravenska primjena bifosfonata
C) podjednako (neovisno o načinu primjene)
D) nisam siguran
13. Koji čimbenici utječu na pojavu komplikacija prouzročenih bifosfontnim/antiresorptivnim lijekovima? (Više odgovora)
A) dob od 60 i više godina
B) umjetni srčani zalisci
C) kortikosteroidna terapija
D) pušenje
E) insuficijencija bubrega
F) dugotrajna bisfosfonatna terapija
G) nisam siguran
14. Koje stomatološke zahvate ne biste obavili bez konzultacije sa specijalistima ako je pacijent primao ili je trenutačno na bifosfonatnoj terapiji?
(Više odgovora)
A) endodontsko liječenje
B) ekstrakcija zuba
C) endodontski kirurški zahvat (apikotomija)
D) izrada protetičkoga nadomjestka
E) ugradnja dentalnoga implantata
F) supragingivno uklanjanje tvrdih zubnih naslaga
G) nisam siguran
15. Treba li prekinuti terapiju s bifosfonatima prije obavljanja nekoga invazivnog stomatološkog zahvata?
(Više odgovora)
A) nema potrebe
B) ima, ovisi o trajanju terapije
C) ima, ovisi o načinu primjene bifosfonata
D) nisam siguran
16. Znate li koji čimbenici utječu na smanjenje komplikacija ako je pacijent na bifosfonatnoj/ antiresorptivnoj terapiji? (Više točnih odgovora)
A) upotreba antibiotika
B) topikalno ispiranje antiseptičnim tekućinama
C) pojačana oralna higijena
D) dodatna upotreba vitamina D
E) vrsta stomatološkog zahvata
F) nisam siguran
17. Mislite li da ste sposobni procijeniti kada na pacijentu trebate obaviti zahvat, a kada je bolje obratiti se specijalistu?
A) da
B) ne
18. Ako ste se susretali s komplikacijama bifosfonatne/ antiresorptivne terapije, kakva su vaša iskustva?
A) komplikacije upućujem specijalistu
B) uspješno liječim komplikacije
C) djelomično uspješno liječim komplikacije
D) bezuspješno liječim komplikacije
19. S koliko ste se do sada komplikacija susreli (broj pacijenata)?
_____
20. Jeste li unatrag 5 godina sudjelovali na nekom tečaju u sklopu kojega je bilo govora o nuspojavama bifosfonatne/ antiresorptivne terapije?
A) da
B) ne, takav tečaj nije bio organiziran
C) ne, smatram da znam dovoljno o toj temi
D) ne, ne zanima me ta tema
21. Biste li željeli doznati više o terapiji i nuspojavama bifosfonatne/ antiresorptivne terapije?
A) da
B) ne

DDMs with more than 20 years of work experience, which is consistent with many publications (24-27,29).

The prevention and treatment of MRONJ require the cooperation of physicians and DDMs (34-36). The worrying results from this study demonstrate that additional education is needed for all physicians considering the prevention and early detection of this disease. It is a promising fact that during the survey 93.89% of respondents expressed a desire to be educated about the issue. All participant DDMs received a brochure as part of the national disease prevention program, so we expect better results and understanding on this topic in the future.

Conclusion

Osteonecrosis reduces the quality of life and requires long-term and complex treatment. Due to the increased incidence of osteonecrosis over the past few years, it is important to establish DDM`s knowledge on the same issue. Prevention and early diagnosis are most important in reducing its incidence. This is evidenced by the national program of Information and prevention of side effects of antiresorptive therapy, which was also the impetus for this study. It is recommended that lifelong learning about this issue preferably with multidisciplinary collaboration is necessary to prevent and treat this disease.

Author's contribution: **S. B.** - designed the study in collaboration with the co-authors and wrote the Discussion; **L. Š.** - participated in designing the questionnaire and wrote the Introduction; **A. B.** - participated in collecting data and wrote the Conclusions; **L. B.** - has reviewed recent literature and wrote the Abstract; **D. V.** - has done data processing and wrote Materials and Methods; **M. G.** - designed the study, interpreted and analyzed the data and wrote the Introduction, Discussion and Results.

tijekom studija, a najmanje točnih odgovora dali su oni s više od 20 godina radnog iskustva, što je u skladu s mnogim publikacijama (24 – 27, 29).

Za uspješniju prevenciju i liječenje MRONJ-a potrebna je kvalitetna suradnja svih liječnika i doktora dentalne medicine (34 – 36).

Rezultati ovog istraživanja zabrinjavaju jer pokazuju da je za prevenciju i rano otkrivanje te bolesti potrebna dodatna izobrazba svih liječnika. Obećava činjenica da je tijekom istraživanja 93,89 % ispitanika izrazilo želju da se educira o toj temi. Svi sudionici dobili su brošuru u sklopu nacionalnog programa prevencije bolesti, tako da u budućnosti očekujemo bolje rezultate i razumijevanje te teme.

Zaključak

Osteonekroza smanjuje kvalitetu života i zahtijeva dugotrajno i kompliciranо liječenje. Zbog njezine povećane incidencije u posljednjih nekoliko godina važno je bilo utvrditi znanje doktora dentalne medicine o toj temi. Prevencija i rana dijagnoza najvažniji su čimbenici za smanjenje incidencije osteonekroze. O tome svjedoči i nacionalni program informiranja i prevencije nuspojava BF/AR terapije koji je i bio poticaj ovom istraživanju. Preporučuje se cjeloživotno učenje o tom problemu, ako je moguće uz multidisciplinarnu suradnju.

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Sažetak

Antiresorptivni lijekovi (AR) koriste se godinama u liječenju različitih koštanih stanja kao što su osteoporoza, osteopenija i Pagetova bolest te u liječenju zloćudnih bolesti (mijelom koštane metatstatske bolesti, maligna hiperkalcemija). Nuspojava AR terapije, medikamentna osteonekoza čeljusti (MRONJ) koja češće zahvaća donju čeljust nego gornju, negativno utječe na zdravlje i kvalitetu života bolesnika. Incidencija osteonekroze čeljusti značajno je porasla u posljednjih nekoliko godina. Jedna od glavnih metoda prevencije te bolesti jest edukacija liječnika, posebice doktora dentalne medicine (DDM), i samog pacijenta. O tome svjedoči i nacionalni program informiranja i prevencije nuspojava antiresorptivne terapije koji je bio i poticaj za ovo istraživanje. **Svrha rada:** Cilj ovog rada jest na temelju anonimnoga anketnog upitnika provjeriti znanje doktora dentalne medicine o AR lijekovima, posebice o bisfosfonatima (BF) i osteonekozi te čimbenike rizika same bolesti. **Materijal i postupci:** U anketi je sudjelovalo 458 doktora dentalne medicine iz Republike Hrvatske koji su u anonimnom upitniku odgovorili na pitanja o poznavanju AR/BF-a i o riziku od MRONJ-a. **Rezultati:** Rezultati su pokazali da 36,68 % doktora dentalne medicine ne zna da je MRONJ glavna komplikacija AR/BF terapije. Rezultati se značajno razlikuju s obzirom na akademski stupanj, specijalizaciju, radno mjesto i radno iskustvo. Tako 60,26 % ispitanika ne zna koje su glavne indikacije za primjenu AR/BF-a, 53,26 % ne zna glavne čimbenike koji utječu na nastanak bolesti, a 42,58 % ne zna koja se terapija ne preporučuje bolesnicima na AR/BF terapiji. Želju za edukacijom o toj temi izrazilo je 93,89 % ispitanika. **Zaključak:** Istraživanje pokazuje da je daljnja edukacija doktora dentalne medicine o toj temi prijeko potrebna zbog prevencije ili početka ranog liječenja MRONJ-a.

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