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Original Research Article

Knowledge and attitude of dentists on bisphosphonates use in the UAE: a descriptive cross-sectional study

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ABSTRACT

Background: The aim of this study was to assess the level of awareness and attitude of dentists practicing in the UAE about bisphosphonate intake and its dental implications.
Methods: A descriptive cross-sectional study using a 15 close-ended and fixed choice questions was performed on a representative sample of 502 dentists practicing in the UAE.
Results: The majority of the practitioners did not report treating patients on a bisphosphonate. Most of the participants were not familiar with the route of administration of the drug or the spectrum of side effects except for BRONJ which was regarded as the most common adverse effect. Furthermore, only a minority were aware of the standard treatment for patients on Bps.
Conclusions: The responses received not only highlight the lack of knowledge among practicing dentists regarding dental management of such cases but also urges the need for dissemination of guidelines for best practice in this field.

Keywords: Cross-sectional studies, Dentists, Disphosphonate, Drug-related side effects and adverse reactions

INTRODUCTION

Bisphosphonates (Bps) were first synthesized in 1868 in the industry. In the late 1960's Bps were shown to prevent the dissolution of hydroxyapatite of bone, the principal mineral component of bone, which made them a promising tool in the fight against bone metabolism disorders.[1] By the 1990's their actual mechanism of action was demonstrated with the launch of Fosamax® (Alendronate) by Merk.[1] On 2003, there were 17 million prescriptions for an alendronate worldwide making it among the top twenty most commonly prescribed drug worldwide.[2,3] The popularity of the drug has risen over the last decade to become the treatment of choice for a number of serious disorders including; osteoporosis, cancer metastases to bone, hypercalcemia of malignancy, and multiple myeloma. The Bps inhibit osteoclastic bone resorption through attachment to hydroxyapatite binding sites on bony surfaces, especially surfaces undergoing active resorption. The drug also reduces osteoclasts by decreasing their progenitor cell development and recruitment and also by promoting osteoclast apoptosis.[2]

However, the side-effect of Bps-related osteo-necrosis of the Jaw, BRONJ has emerged as an alarming consequence of drug use; between 2001-2007 with more than 2,400 confirmed cases reported in the USA alone.[2,4] The BRONJ may represent the second epidemic of the phossy jaw which was reported between 1858 and 1906 with the similar clinical course of the current disease.[8]

To accommodate the growing number of osteonecrosis cases involving the maxilla and mandible associated with other antiresorptive (denosumab) and antiangiogenic

therapies, in addition to Bps, the Special Committee of American association of oral and maxillofacial surgeons has recommended that the nomenclature of BRONJ of the jaw be replaced with the term medication-related osteonecrosis of the jaw (MRONJ).[6,7]

The dental and oral surgical intervention on the patient on various types of Bps therapy are susceptible to a higher rate of post-operative complications as compared to those not taking the medicine.[3,4] Furthermore, patients on Bps therapy may seek dental care because of dental or jaw pain without any obvious signs of the complications of the therapy. If their symptoms do not resolve with routine dental and periodontal treatment, BRONJ must be considered as a differential diagnosis, even in the absence of exposed bone.[5]

The role of general dental practitioners (GDP) in prevention and early detection of BRONJ cases cannot be overemphasized. This study sought to assess the level of awareness and perceptions of practicing dentists in relation to bisphophonates and their associated risks, and how their knowledge influences the planning the management of patient taking such medications.

METHODS

This study was a descriptive cross sectional and involved a questionnaire which initially validated through multiple phases including experts review of the questions followed by a pilot study where 70 participants from Ajman, Sharjah and Dubai answered the questionnaire. The responses were revised for consistency of answers the negatively phrased questions. Finally, the principal component analysis was carried out to remove questions that measure the same variable. The revised questionnaire composed of 22 closed ended with fixed-choice questions. The proposal of the study was revised and approved by the research ethical committee at Ajman University. Then the questionnaire was distributed to a sample of 502 practicing dental practitioners. The questionnaire formed of the following components; 1) The frequency of patients on Bps seen by dental practitioners at regular basis, 2) The perception of practitioners of serious side effects of the drug, 3) The recognition of dental interventions that might be influenced by Bps therapy and 4) The knowledge of the optimal dental management of patients seek dental treatment during or after drug therapy.

The sample size was determined using the ministry of health records of the dentists currently practicing in the UAE. The number of target participants was calculated at 95% confidence interval with error margin less than 4%. The representative sample size was 499 dentists (Table 1). A random selection of dentists was invited to take part in the survey. The inclusion criteria were practice in the UAE and willingness to participate with no specific exclusion criteria.

Table 1: Sample stratification of the participants.

Stratification procedure		
Emirates	**Stratification (ideal sample size)**	**No. of participants**
Abu-Dhabi	$(\frac{950}{2921})\times500 = 162$	160
Dubai	$(\frac{1137}{2921})\times500 = 194$	190
Sharjah	$(\frac{522}{2921})\times500 = 89$	83
Ajman	$(\frac{124}{2921})\times500 = 21$	21
Umm Al-quwain	$(\frac{15}{2921})\times500 = 5$	10
RAK	$(\frac{108}{2921})\times500 = 18$	25
Al-Fujairah	$(\frac{65}{2921})\times500 = 11$	13
Total	**500**	**502**

The data collected were entered and analyzed using software IBM SPSS Statistics version 20. Descriptive statistics were produced to classify the participants in relation to their specialties, working places and years of experience. The responses were compared in relationship to the participant data Chi square test. The statistical significance (p-value) was set at below 0.05 at 95 confidence rate.

RESULTS

The participants were divided according to their working place as following: 248 (49.4%) practice in private clinics, 105 (20.9%) in private hospitals, followed by 92 (18.3%) employed by public hospitals and 57 (11.4%) by public dental centers. More than two-thirds of the respondents 343 (n=343) had more than 5 years of experiences. The majority of the participants were general dental practitioners (302), the remaining were a quiet homogenous mix of the main dental specialties.

Frequency of patients on Bps receiving dental treatment

Two thirds of all participants didn't report treating any patients on Bps therapy followed by 19.9% (n=100) they had seen at least one patient on the medicine over the last year. Only 10 (1.99%) of those who claimed treated patients on Bps therapy were able to recall the brands of the drugs like Zometa, Fosamax, and Risedronate.

Awareness of the route of administration

A good number of participants (n=67, 13.3%) were not aware of the route of administration of the drug. The orthodontists gave the highest rate of unsatisfactory answers throughout the study. On the other hand, oral surgeons scored very high as compared to other dental disciplines (Table 2).

Indications of Bp therapy

While the majority of participants in the study (68.4%) identified, the osteoporosis being the commonest indication for Bps treatment, only 5.9% reported that cancer as another major indication to take the medicine and only 1.6% mentioned other conditions like Paget's disease, multiple myeloma, fibrous dysplasia and osteogenesis imperfecta. The remaining a 15.7% of participants couldn't recall any indications for Bps prescription (Table 3).

Table 2: Knowledge on route of administration of the Bps.

Route of administration of Bps therapy							
			Administration				Total
			One satisfactory answer	>One satisfactory answer	Not satisfactory	Not aware	
Specialty	GDP	Count	146	20	42	94	302
		% within administration	60.1%	58.8%	62.7%	59.5%	60.2%
		% of Total	29.1%	4.0%	8.4%	18.7%	60.2%
	Oral surgeon	Count	20	8	3	9	40
		% within administration	8.2%	23.5%	4.5%	5.7%	8.0%
		% of Total	4.0%	1.6%	0.6%	1.8%	8.0%
	Endodontists	Count	21	1	6	13	41
		% within administration	8.6%	2.9%	9.0%	8.2%	8.2%
		% of Total	4.2%	0.2%	1.2%	2.6%	8.2%
	Prosthodontists	Count	22	3	5	11	41
		% within administration	9.1%	8.8%	7.5%	7.0%	8.2%
		% of Total	4.4%	0.6%	1.0%	2.2%	8.2%
	Orthodontists	Count	25	0	7	14	46
		% within administration	10.3%	0.0%	10.4%	8.9%	9.2%
		% of Total	5.0%	0.0%	1.4%	2.8%	9.2%
	Others	Count	9	2	4	17	32
		% within administration	3.7%	5.9%	6.0%	10.8%	6.4%
		% of Total	1.8%	0.4%	0.8%	3.4%	6.4%
Total		**Count**	**243**	**34**	**67**	**158**	**502**
		% within administration	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**
		% of total	**48.4%**	**6.8%**	**13.3%**	**31.5%**	**100.0%**

Table 3: The indication and potential side effects of the Bps treatment.

Indications of Bps and side effects of Bps therapy									
			Indications reported			Side effects of Bps			Total
			One indication	>One indications	Not aware	Satisfactory answer	Unsatisfactory answer	Not aware	
Specialty	GDP	Count	236	23	43	206	38	58	302
		% of Total	47.0%	4.6%	8.6%	41.0%	7.6%	11.6%	60.2%
	Oral surgeon	Count	26	11	3	28	3	9	40
		% of Total	5.2%	2.2%	0.6%	5.6%	0.6%	1.8%	8.0%
	Endodontists	Count	30	6	5	30	5	6	41
		% of Total	6.0%	1.2%	1.0%	6.0%	1.0%	1.2%	8.2%
	Prosthodontists	Count	30	4	7	23	9	9	41
		% of Total	6.0%	0.8%	1.4%	4.6%	1.8%	1.8%	8.2%
	Orthodontists	Count	33	2	11	17	14	15	46
		% of Total	6.6%	0.4%	2.2%	3.4%	2.8%	3.0%	9.2%
	Others	Count	19	3	10	22	0	10	32
		% of Total	3.8%	0.6%	2.0%	4.4%	0.0%	2.0%	6.4%
Total		**Count**	**374**	**49**	**79**	**326**	**69**	**107**	**502**
		% within indications	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**
		% of Total	**74.5%**	**9.8%**	**15.7%**	**64.9%**	**13.7%**	**21.3%**	**100.0%**

Common side effects of Bps therapy

About sixty percent of participants (n=314) regarded the BRONJ as the most serious side effect of the drug with a minority (n=12, 2.4%) added the oral ulcerations. Approximately one-fifth of dentists (n=107) were not familiar with any side effects of Bps at all. The least awareness level reported by orthodontists (37%) (Table 3).

Table 4: The dental treatments that may be influenced by the Bps intake.

			Dental Rx that may be affected by BP-therapy						
			One relevant answer	More than one relevant answer	Not relevant answer	Not aware	Not asked	Not satisfactory	Total
Specialty	GDP	Count	113	93	12	30	40	14	302
		% of Total	22.5%	18.5%	2.4%	6.0%	8.0%	2.8%	60.2%
	Oral surgeon	Count	6	23	1	1	6	3	40
		% of Total	1.2%	4.6%	0.2%	0.2%	1.2%	0.6%	8.0%
	Endodontists	Count	16	14	1	4	2	4	41
		% of Total	3.2%	2.8%	0.2%	0.8%	0.4%	0.8%	8.2%
	Prosthodontists	Count	11	13	5	3	9	0	41
		% of Total	2.2%	2.6%	1.0%	0.6%	1.8%	0.0%	8.2%
	Orthodontists	Count	19	11	4	5	6	1	46
		% of Total	3.8%	2.2%	0.8%	1.0%	1.2%	0.2%	9.2%
	Others	Count	4	13	1	6	7	1	32
		% of Total	0.8%	2.6%	0.2%	1.2%	1.4%	0.2%	6.4%
Total		**Count**	**169**	**167**	**24**	**49**	**70**	**23**	**502**
		% of Total	**33.7%**	**33.3%**	**4.8%**	**9.8%**	**13.9%**	**4.6%**	**100.0 %**

Table 5: The dental treatment of patients on Bps therapy.

Dental treatment of patients on Bps therapy						
			Dental treatments			Total
			Standard practice	Substandard practice	Not aware	
Specialty	GDP	Count	11	202	89	302
		% within treatments	64.7%	61.2%	57.4%	60.2%
		% of total	2.2%	40.2%	17.7%	60.2%
	Oral surgeon	count	2	30	8	40
		% within treatments	11.8%	9.1%	5.2%	8.0%
		% of total	0.4%	6.0%	1.6%	8.0%
	Endodontists	count	1	30	10	41
		% within treatments	5.9%	9.1%	6.5%	8.2%
		% of total	0.2%	6.0%	2.0%	8.2%
	Prosthodontists	count	2	27	12	41
		% within treatments	11.8%	8.2%	7.7%	8.2%
		% of total	0.4%	5.4%	2.4%	8.2%
	Orthodontists	count	1	25	20	46
		% within treatments	5.9%	7.6%	12.9%	9.2%
		% of total	0.2%	5.0%	4.0%	9.2%
	Others	count	0	16	16	32
		% within treatments	0.0%	4.8%	10.3%	6.4%
		% of total	0.0%	3.2%	3.2%	6.4%
Total		**count**	**17**	**330**	**155**	**502**
		% of total	**3.4%**	**65.7%**	**30.9%**	**100.0%**

Table 6: Dentist view on discontinuation of the Bps.

Discontinuation of Bps therapy										
			Discontinuation				If Yes			
			No	Yes	I don't Know	Total	5-10 days	1 month	3 months	Total
Specialty	GDP	count	77	78	147	302	21	19	38	78
		% of total	15.3%	15.5%	29.3%	60.2%	14.5%	13.1%	26.2%	53.8%
	Oral surgeon	count	16	17	7	40	0	1	16	17
		% of total	3.2%	3.4%	1.4%	8.0%	0.0%	0.7%	11.0%	11.7%
	Endodontists	count	5	18	18	41	4	4	10	18
		% of total	1.0%	3.6%	3.6%	8.2%	2.8%	2.8%	6.9%	12.4%
	Prosthodontists	count	7	15	19	41	8	2	5	15
		% of total	1.4%	3.0%	3.8%	8.2%	5.5%	1.4%	3.4%	10.3%
	Orthodontists	count	7	10	29	46	4	2	4	10
		% of total	1.4%	2.0%	5.8%	9.2%	2.8%	1.4%	2.8%	6.9%
	Others	count	5	7	20	32	3	2	2	7
		% of total	1.0%	1.4%	4.0%	6.4%	2.1%	1.4%	1.4%	4.8%
Total		**count**	**117**	**145**	**240**	**502**	**40**	**30**	**75**	**145**
		% of total	**23.3%**	**28.9%**	**47.8%**	**100.0%**	**27.6%**	**20.7%**	**51.7%**	**100.0%**

Dental interventions affected by Bp therapy

When asked about the impact of Bp therapy on dental treatment, the responses obtained from various participant were not consistent with one quarter (n=124) believe the only extraction of teeth is adversely affected by the Bps intake. However, 15.9% of the participant expanded their responses to include periodontal treatment and insertion of implants and others (11.9) added the orthodontic treatment to the previous list. On the other hand, around one third of participants (n=166) were not aware of any relationship between the Bps therapy and dental treatment interventions.

Dental management of patients on Bps therapy

Thirty percent of respondents were not aware of the 'standard' dental treatments for a patient on Bps treatment. The majority (65.7%) of participants reported substandard treatment plans for such a patient, these include: planned surgical tooth extraction versus closed method (35.1%), routine extraction of teeth without any additional measures (10.8%), prescribing antibiotics and retain the tooth in situ (9.6%), or performing conventional endodontic treatment to affected tooth (6.6%). The answers of only 17 (3.4%) divulge a standard treatment for patients required dental extraction during their treatment with Bps (Table 5). The responses of nearly half of the participating dentists (47.8%) showed a lack of awareness of issues of discontinuation of Bps prior to dental and surgical intervention. However, about one third of dentists suggested to stop the drug for; 5 days (4%), 10days (4%), 1 month (4), or 3 months (14.9%) prior to the commencement of dental treatment. Around one quarter of participants (23.3%) do not consider stopping the drug pre-operatively. When asked about using alternative medications instead of Bps or altering the dose of such therapy, almost half of the participants (48.2%) were ready to adopt such an approach (Table 6).

International guidelines on dental management of patient on Bps therapy

Nearly two thirds of participants irrespective of their specialties (n=337) were not aware of any specific guidelines for dental management of patients taking Bps. Around one third (n=175) of participants would prescribe antibiotics to patients on Bps regardless the dental interventions as compared to 3.8% of who opposed antibiotics prescription in all the dental interventions. On the other hand, 40.6% who recommended the antibiotics when only surgical extraction is planned for such patients. Finally, most of the participants (89.2%, n=448) were keen to attend updated CME courses on the dental management of patients on Bps.

DISCUSSION

The Bps group of medications have proven effective in treating many conditions. They were introduced to the middle-east and Gulf region quiet recently. However, their prescription showed a significant spread due to the demand of local patients and the relative absence of tight authoritive restriction. The current study obviously has the limitations of the questionnaire-based survey and may not precisely reflect the real practice of the participants. The authors consider the possibility of response distortion as participants attempt to create a positive impression that is aware of all aspects of the issue. The tendency to respond positively and not revealing the weakness can adversely influence the outcome of this survey. However, the study of current practice usually starts with such surveys to understand the awareness and attitude of the dentists till it can be further verified by investigation of

patient records when a sufficient number of the later are available for review and study.

Despite the noticeable expansion of the drug prescription in the region, about two-thirds of participants did not report treating any patient using the medicine. This may, in part, indicate that Bps intake is not yet among the routine case history checklist of dental practice in this region. Furthermore, this reflects the lack of awareness of the drug's effects and side-effects, more importantly, the clinical indications for their use. This notion is supported by the failure of a good proportion of respondents to recall any indication for Bps use with nearly three quarters only identified the osteoporosis as a sole indication. However, this positive response from the majority of participants was not matched with their failure to report treating any patient using the drug considering the relatively high incidence of osteoporosis cases in this region and the increasing trend in prescribing Bps to treat the condition. Failure of respondents to report any additional indications for the drug use implies that dentist may not to anticipate that their dental patients might be using this medicine for various problems thus will not enquire about the intake of Bps in such cases. More than half of the dentists reported that they are aware of BRONJ of side effect of the drug which can be compared favourably to the number of healthcare professionals aware of BRONJ as a side-effect in North Wales.[9]

This study also showed that two-thirds of the practicing dentists are aware of the dental interventions that might be troubled by Bps therapy such as; oral surgery, periodontal therapy, and orthodontics. The awareness rate reported here was higher than that reported by dentists in South Korea (56.5%) [10, 11], in Canada (60%) [12-16] and physicians in Saudi Arabia (31%) [17,18]. Dentoalveolar surgery may cause or exacerbate an existing BRONJ in patients during or after Bps therapy. Although this is more prevalent in those taking intravenous Bps, it has also been reported in those taking these drugs orally over long periods of time. Concomitant risk factors include poorly controlled diabetes mellitus and other immuno-compromised states, concurrent use of corticosteroids, chemotherapeutic drugs, radiotherapy, advanced age, alcohol abuse and smoking.

It is estimated that the majority of BRONJ cases are preceded by dental surgical treatment, with twice as many occurring in mandible as in maxilla. It was suggested that Bp treatment should be postponed during active dental treatment is concluded to minimize the risk of BRONJ development.[2,3,9] Local risk factors include the presence of mandibular tori, periodontal disease, periapical disease and recent trauma.[11,19,20]

In a South Korean study, involving 226 dentists, around half of the respondents were aware of BRONJ, with the practitioners with fewer than 5 years' experience were reported to be significantly more aware of the condition than those qualified for more than 5 years.[11] This reflects that younger dentists know more about the medicine as compared to senior counterparts and this was also supported by the current study. Unfortunately, only minority of participants were familiar with the standard treatment of patients on Bps require tooth extraction procedure. Moreover, the highest level of substandard practice was mainly reported by oral surgeons who are expected to manage the oral complications seen on the patient on Bps. A referral of patients for comprehensive oral evaluation before commencing Bps treatment should be considered by the prescribing physicians.[21] Once patient started the Bps treatment, a great emphasis on oral hygiene measured should be exercised to minimise risk factors for infection. Regular prophylactic chlorhexidine rinse and modified treatments such as coronal amputation and endodontic treatment of retained roots are advised for non-restorable teeth. If surgery is unavoidable, focus on minimally invasive procedures with proper sterile technique and effective empirical antibiotic therapy.[22-24]

This study also raises the issue of drug holiday preoperatively, most of the respondents did not show any updated or evidence based knowledge on this option. Many researchers questioned the value of stopping Bps pre-operatively as the drug tend to remain bound to the bone for years after the administration. On the contrary, others suggested considering interrupting Bps treatment for three months prior to surgery and restarting after bone healing. This suggestion has not been supported by the ADA.[11] According to the latter, no evidence to date has confirmed that drug holidays are effective in preventing BRONJ without increasing the skeletally-related risks of low bone mass during treatment.[21]

The current study analysis reveals that most of the participants were not familiar with any dental guidelines for treating patients with Bps therapy that highlight the importance of CME courses and establishing local authoritive guidance in this area.

CONCLUSION

An increasing number of dental patients are currently undergoing a form of Bps therapy and according to this descriptive survey, the dentists do not seem to be aware of this. It is also apparent that those dentists who are aware of their patients' drug regimens are not always aware of all potential side effects of these medications and the impact of poorly planned dental treatment. The responses received not only highlight the lack of knowledge among dentists regarding Bps and their dental implications but also reinforce the value of dissemination of guidelines for best practice in this field.

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