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Journal of Interdisciplinary Medicine

ORIGINAL RESEARCH

PROSTHODONTICS // ORAL AND MAXILLOFACIAL SURGERY

Knowledge and Attitude of Dentists Regarding Patients Undergoing Bisphosphonate Treatment: a Comparative Questionnaire

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ARTICLE HISTORY

Received: June 12, 2018
Accepted: July 28, 2018

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ABSTRACT

Background: Osteonecrosis of the jaw is an uncommon but serious complication related to oral and intravenous bisphosphonate (BP) therapy. Its pathogenesis is not well understood, and there are no universal protocols accepted to treat it. The **aim** of our study was to use the same questionnaire as four years ago to evaluate the awareness of dentists in Tîrgu Mureș regarding the dental treatments that can be applied in patients on BP therapy, and to assess how their knowledge on the subject has evolved over these years. **Material and method:** We used the same questionnaire-based study as four years ago among dentists in Tîrgu Mureș, raising important issues such as: is the patient asked about current or previous treatments with BPs, do they perform surgical treatment in these patients, do they know under what conditions they can perform this treatment, or do they deem it necessary to contact the prescriber before surgical treatment. **Results:** One-hundred twenty questionnaires were returned. The majority of respondents (n = 113, 94.2%) included the question regarding the use of BPs in their medical records. Of all respondents, 48 (40%) perform dental or surgical treatments on patients undergoing BP therapy, 68 (56.7%) do not perform dental or surgical treatments on these patients, and four of the respondents (3.3%) did not know the answer. One hundred (83.3%) respondents always contact the prescriber prior to surgery in these patients, regardless of how BPs are administered. **Conclusions:** According to the findings of the present study, many of the respondent doctors have heard about BPs and their complications, but they are not aware of the fundamental concepts of bisphosphonate-related osteonecrosis of the jaw prevention and treatment protocols. In the absence of appropriate protocols, the quality of life of these patients is compromised.

Keywords: osteonecrosis, jaw, bisphosphonates, surgery, quality of life

INTRODUCTION

Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is an uncommon but serious complication, reported for the first time by Marx in 2003.[1] BRONJ is defined as necrotic bone exposed in the maxillofacial region for at least eight weeks with no signs of healing in patients treated with bisphosphonates (BPs) and without head and neck radiation therapy in the present or the past.[2] BPs are used in the treatment of Paget's disease, multiple myeloma, as well as osteolytic lesions associated with bony metastases and is the most prescribed therapy against osteoporotic pathology.

Due to the fact that BPs are not metabolized and accumulate in the bone, the osteoclastic activity is interrupted by other inhibitors, such as denosumab and bevacizumab, and under conditions of bone trauma, the osteonecrosis of the jaw is likely to be triggered. The uncontrolled therapeutic effect of monoclonal antibodies and BPs in reducing osteoclast function may lead to osteonecrosis when a critical limit of at least 50% of the total cell mass is reached.[3]

Various studies attempted to elucidate why BP treatment complications, such as inhibition of angiogenesis and apoptosis of osteoclasts, inhibition of bone remodeling and bone turnover, inflammation, infection, or the vast variety of microorganisms in the oral flora, occur only at the level of the oral cavity.[4–10]

The actual incidence of BRONJ is uncertain; it depends on treatment indication, sample size, and the studied population, and varies from 0.028% to 18.6%.[11,12]

Administering BPs via the intravenous route has a higher risk of developing BRONJ, although oral treatment longer than three years may also increase this risk.[2]

A frequent trigger factor is represented by dentoalveolar procedures in patients undergoing intravenous BP treatment. They are at least seven times more likely to develop osteonecrosis of the jaw than those who underwent intravenous BP treatment but are not subject to dentoalveolar surgery.[13]

Our study is focused on BRONJ, although other medications (denosumab, bevacizumab, cabozantinib, sunitinib) have also been associated with jaw osteonecrosis in 2014 by the special committee of American Association of Oral and Maxillofacial Surgeons (AAOMS), who called this condition medication-related osteonecrosis of the jaw (MRONJ).[14]

In 2014, we carried out a questionnaire-based study among dentists in Tîrgu Mureș.[15] At present, in June 2018, we intended to use the same questionnaire and assess how the dentists' knowledge regarding dental treatments in patients with current or previous BP therapy has evolved over these four years.

MATERIAL AND METHOD

In June 2018, we carried out a questionnaire-based study among dentists in Tîrgu Mureș. The questionnaire consisted of the same 13 questions included in the previous study, conducted in 2014.

A total of 26 questionnaires were handed personally to clinicians within the Faculty of Dentistry of Tîrgu Mureș, and the others were sent to dental practitioners using social networks. The respondents were dentists, residents, and specialists, who were asked to choose one of the answers for every question. We asked whether the respondents were residents or medical specialists in a branch of dentistry. We also asked whether they had knowledge about BPs and whether they deem it necessary to ask their patients about current or previous BP treatments.

We considered it important to ask whether the respondents knew that they performed dental treatments/dentoalveolar surgery in patients who are/were treated with BPs and whether they know under what conditions they can perform tooth extractions or other dentoalveolar surgical treatments in patients treated with BPs.

An important aspect of the questionnaire was whether the respondents contacted the prescriber before performing a tooth extraction or dentoalveolar surgical treatment on a patient.

Statistical analysis was not carried out, as it was considered that it would not be helpful due to the large number of variants.

RESULTS

The questionnaires were completed and returned by 120 respondent clinicians. The results are presented and compared with those from the 2014 study in Table 1.

DISCUSSIONS

In the last years, the number of BRONJ cases reported in the literature has increased.[16–19] As far as we know, no study has been conducted in Romania yet to investigate the degree of dentists' knowledge about BRONJ.

The present study was developed in order to evaluate the awareness of dentists in Tîrgu Mureș using the same questionnaire we used four years ago, and to determine whether their knowledge regarding BRONJ has improved in these four years.

TABLE 1. Comparison between questionnaire response distribution in 2018 vs. 2014

No.	Question	Answers	Responses from 2014, 70 respondents	Responses from 2018, 120 respondents
1.	For how long have you been practicing dentistry?	a) less than three years b) three-six years c) more than six years	a) 27.14% b) 32.86% c) 40%	a) 35% b) 26.66% c) 38.34%
2.	Are you a resident doctor in a branch of dentistry?	a) no b) resident in dentoalveolar surgery/maxillofacial surgery c) other branches, please specify	a) 77.14% b) 7.14% c) 15.72%	a) 90% b) 4.17% c) 5.83%
3.	Do you have a specialty in a branch of dentistry?	a) no b) specialty in dentoalveolar surgery/maxillofacial surgery c) other branches, please specify	a) 47.37% b) 15.79% c) 36.84%	a) 69.17% b) 13.33% c) 17.5%
4.	Have you heard about bisphosphonate treatment?	a) no b) yes	a) 17.14% b) 82.86%	a) 3.33% b) 96.67%
5.	Do you know in which pathology/pathologies is this treatment recommended?	a) no b) yes, please specify	a) 25.71% b) 74.29%	a) 5.83% b) 94.17%
6.	Do you ask about treatments with bisphosphonates while completing the patient's medical history?	a) no b) yes c) not relevant in dentistry practice	a) 38.57% b) 60% c) 1.43%	a) 5.83% b) 94.17% c) 0%
7.	Have you performed dental treatments/ dentoalveolar surgery on a patient who was under/ has received bisphosphonate treatment?	a) no b) yes c) I do not know	a) 42.85% b) 34.29% c) 22.86%	a) 56.67% b) 40% c) 3.33%
8.	Do you know whether complications of bisphosphonate treatment occur only in the oral cavity or in other parts of the body as well?	a) no b) yes	a) 41.43% b) 58.57%	a) 20.83% b) 79.17%
9.	Do you know what kind of manifestations occur in the oral cavity after treatment with bisphosphonates?	a) no b) yes	a) 25.71% b) 74.29%	a) 15.83% b) 84.17%
10.	Do you know under what conditions you can perform tooth extractions or other dentoalveolar surgical treatments on patients treated with bisphosphonates?	a) no b) yes c) not relevant in dentistry practice	a) 48.57% b) 50% c) 1.43%	a) 11.67% b) 85% c) 3.33%
11.	Do you contact the prescriber before surgery in a patient that needs a tooth extraction or other dentoalveolar surgery and is under bisphosphonate treatment?	a) no b) yes c) not relevant in dentistry practice	a) 12.86% b) 85.71% c) 1.43%	a) 10% b) 86.67% c) 3.33%
12.	Do you think there are differences between the complications that occur after treatment with bisphosphonates administered intravenously or orally?	a) no b) yes	a) 40% b) 60%	a) 34.17% b) 65.83%
13.	Do you contact the prescriber before surgery in a patient who needs a tooth extraction or other dentoalveolar surgery and is under bisphosphonate treatment administered intravenously or orally?	a) I do not contact the prescriber b) I contact the prescriber only in case of oral administration c) I contact the prescriber only in case of intravenous administration d) I always contact the prescriber	a) 12.86% b) 0% c) 4.28% d) 82.86%	a) 11.67% b) 0% c) 5% d) 83.33%

The majority of respondents (38.34%) had a dental practice for more than six years, and most of them (96.67%) heard about BP therapy, representing a 13.81% increase compared to the responses received in 2014. Regarding the pathologies recommended to be treated with BPs, most of the respondents (15.7%) mentioned osteoporosis, 5.8% bone tumors, 4.1% bone metastases, and 1.65% mentioned chemotherapy. None of the respondents were aware of the use of BPs in the treatment of Paget's disease. In the 2014 study, 5.81% knew about Paget's disease and multiple myeloma, and they recognized osteoporosis as the main pathology to benefit from these drugs in a higher

percentage (55.82%). None of the dentists who responded to the questionnaire in 2014 and 2018 knew about the usage of BPs in the treatment of malignant hypercalcemia and osteogenesis imperfecta. Dentists should know the mechanism of action of BPs due to their adverse effects: bone turnover is reduced, and the function of osteoclasts is inhibited, which leads to the reduction of bone remodeling.[2,20] The consequent necrosis of bone cells appears due to the inhibition of angiogenesis, another mechanism of action of BPs.[2,5,14] The dentists' knowledge will influence the attention given to the patient, the way they draw up the patients' medical file, whether they ask about or recognize the medication. The majority of the respondents (94.17%) ask about a possible treatment with BPs while completing the patients' medical history. This is a step forward for the early identification of possible complications, especially as there is a significant increase from the 2014 questionnaire, where only 60% of the respondents had this question in their anamnesis.

In question number seven, a small percentage (3.33%) of respondents did not know if they performed surgical or dental treatments in patients who are/were treated with BPs. This percentage decreased compared to 22.86% obtained in the 2014 questionnaire.

A percentage of 20.83% said they do not know if BP treatment complications occur only in the mouth. Dentists should be aware of the manifestations of BRONJ and their preferred area of occurence. BRONJ is more common in the posterior mandible than the maxilla, in a ratio of 2 : 1.[2]

It is critical for dentists to be prepared to treat these patients appropriately. Dentoalveolar surgeries represent the main local risk factors for BRONJ, especially tooth extraction acts as a trigger point in the development of BRONJ. Periodontal diseases and denture use are also considered potential risk factors.[2,14]

Our study revealed that 11.67% of the respondents do not know under what conditions they can perform tooth extractions or other dentoalveolar surgical treatments on patients treated with BPs, and 3.33% considered the subject is not relevant for dentistry practice.

Besides dental procedures, BRONJ is related to trauma to the mouth caused by incorrectly adjusted prostheses, oral infection, poor oral hygiene, diabetes, and smoking.[9,21–24]

The percentage of respondents who contact the prescribing physician before carrying out a tooth extraction or other dentoalveolar surgery in a patient with BP treatment was similar in 2014 and 2018, 85.71% and 86.67% respectively.

About one-third of the respondents, 34.17%, said there is no difference between the oral or intravenous administration of BPs, but according to studies, the route of administration affects the skeleton differently. Oral BPs are poorly absorbed and present less than one percent of bioavailability, whereas BPs administered intravenously have maximum bioavailability.[25]

A large part of respondents, 100 from a total of 120 (83.33%), answered that they always contact the prescriber before dentoalveolar surgery in patients treated with BPs. The result is similar to the one from the 2014 questionnaire (82.86%). The percentage of those who never contact the prescriber before dental surgery has decreased only slightly, from 12.86% in 2014 to 11.67% in 2018, and due to these unsupervised procedures, the patients' quality of life is compromised.

CONCLUSIONS

According to the findings of the present study, many of the respondent dentists have heard about BPs and related complications, but they are not aware of the fundamental concepts of BRONJ prevention and treatment protocols. Despite the limited size of the studied sample, the data are enough to affirm that the dentists' knowledge about BRONJ and the treatment of patients undergoing BP therapy improved over four years, but there are still many unknowns. The literature reveals many unknowns in the pathogenesis of the disease, and universal protocols are not established. Without appropriate protocols for prevention and treatment, the patients' quality of life is affected. Dentists should be more prepared regarding the treatment of these patients and they should be aware that conservative attitudes are the most suitable for patients with a history of BP treatment. A complete medical history of the patient must be recorded carefully, and the treatment should be analyzed after contacting the prescriber. Therefore, practical initiatives, such as lectures and workshops at conferences, or even flyers, should be taken seriously, to help strengthen knowledge in this domain. Preventing or minimizing the occurrence of BRONJ must be known among doctors who prescribe BPs, such as oncologists, endocrinologists, hematologists (referring patients to the dentist before starting a BP treatment), but to the same extent by maxillofacial surgeons or dentists whom the patient are addressing.

CONFLICT OF INTEREST

The authors declare no conflict of interests.

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