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RESEARCH ARTICLE

Bisphosphonate-Related Osteonecrosis of the Jaws: a real Challenge for Dentists

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Background: Osteonecrosis of the jaw is a serious complication associated with oral and intravenous bisphosphonate therapy. Its pathogenesis is not well understood and its management is difficult.The aim of ourstudy was to evaluate the awareness of dentists in Târgu Mureș on the possibilities of treating patients who are treated with bisphosphonate in dental offices. **Material and method**: We carried out a questionnaire-based study among dentists in Târgu Mureș reaching important issues such as: if the patient is asked if medical history follows / followed treatment with bisphosphonates, if they made surgical treatment in these patients, if they know under what conditions can they perform this treatment, if they deem it is necessary to contact the prescriber before surgical treatment. **Results**: Seventy questionnaires were returned. During the medical history most clinicians (60%) asked the patients whether they follow/followed treatment with bisphosphonates and most of them (42.85%) did not perform treatments in these patients. While 85.71% of respondents declared that they do contact the prescriber before performing surgical treatment, 48,57% were not aware under what conditions they could undergone the treatment. **Conclusions**: The dentists did not seem to be well informed about this pathological entity, known only since 2003. In the absence of appropriate protocols they could not provide a high quality treatment and in these circumstances they might do more harm than good.

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

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Introduction

Bisphosphonate-related osteonecrosis of the jaws (BRONJ) is a serious complication of antiresorptive agents including aminobisphosphonates and denosumab. Osteonecrosis of the jaws induced by the treatment with bisphosphonates is described as a pathological entity since 2003, when oromaxillofacial surgeons recognized and reported patients with denuded bone in the jaw and no signs of healing while being on bisphosphonates treatment (1,2). More definitions were formulated by American Association of Oral and Maxillofacial Surgeons (AAOMS) over the years, but the most recent, American Association of Oral and Maxillofacial Surgeons Position Paper on Medication-Related Osteonecrosis of the Jaw-2014 Update, describes it as it follows: current or previous treatment with antiresorbtive or antiangiogenic agent, exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region that has persisted for longer than eight weeks, and no history of radiation therapy to the jaws or obvious metastatic disease to the jaws (3). Bisphosphonates (BPs) are the most popular antiresorptive drugs for the management of bone disorders, with a high affinity for bone tissue. BPs therapy is indicated in a number of diseases associated with metabolic bone disorders such as malignant hypercalcemia, Paget's disease, osteoporosis, multiple myeloma, osteolytic bone metastases, osteogenesis imperfecta (4-10). In recent years (2001-2014), there is an increase in the incidence of jaw osteonecrosis induced by BP treatment. Although the pathogenesis of BRONJ is not fully elucidated, it is a known fact that BPs alters angiogenesis and bone microarchitecture (3,4,11-13). Different hypotheses attempt to explain the unique location of this jaw-only complications, such as: inhibition of bone remodeling and bone turnover (14-16), inhibition of angiogenesis and apoptosis of osteoclasts (2,17), inflammation and infection (18,19), variety of microorganisms in the oral flora (20-22), or a combination of the above.

The main purpose of our study was to observe the dentists awareness regarding treatments that may apply in dental offices on patients who are/were treated with bisphosphonates.

Material and method

We carried out a questionnaire-based study among dentists in Târgu Mureș during the months of October and November 2014. A total of 40 questionnaires were personally handed to clinicians at local meetings and courses within the Faculty of Dentistry Târgu Mureș and other questionnaires were sent by email and social networks. The questionnaire, which included a total number of 13 closed-ended questions, is presented in Annex 1.

The clinicians who were asked to complete the questionnaires, included dentists, residents, specialists.They were asked to choose one or more of the option given.We were interested in the respondents' practice period, whether they are residents or medical specialists on a branch of dentistry, if they had knowledge about BP treatment andin

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which pathology it isrecommended to use this treatement.

Other important points in the questionnaire were: whether or not they knew if they made dental treatments / dentoalveolar surgery in patients who are / were treated with BP, if they knew under what conditions they can perform tooth extractions or other dentoalveolar surgical treatments on patients treated with BP, and a final important aspect is whether they 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 in view of the large number of variants.

Results

The questionnaires were returned by 70 respondentclinicians, including 19 doctors practicing dentistry for less than 3 years (27.14%), 23 clinicians with a practice between three and six years (32.86%), and most of the respondents, 28 clinicians (40%), practiced dentistry for more than six years.

Most of them (n=54) were not residents (77.14%), five were dentoalveolar surgery residents or oral and maxillofacial surgery residents (7.14%) and 11 were residents in other dental branch as follows: five endodontics, three orthodontics, two periodontics and one dental prosthetics.

We were interested in whether or not they had a dental specialty. The questionnaires showed that 36 of them (47.37%) did not havea dental specialty, 15.79% (n=12) were specialists in dental alveolar surgery or oral and maxillofacial surgery, and 22 had other specialty such as orthodontics (n=8), periodontics (n=7), general dentistry (n=7), endodontics (n=3) and three dental prosthetics. Most of them (n=58, 82.86%) heard about the treatment with BP, however when we asked in which pathology BP treatment is recommended only 52 of respondents were aware (74.29%) and 25.71% did not know (Figure 1).

Most of them (n=42, 60%) included in their patient's medical history the question regarding the use of BPs, 27 respondents did not use this question (38,57%) and one of them (1.43%) considered that the question has no relevance in the practice of dentistry.

From our total questioned doctors, 42.85% (n=30) did not perform dental or surgical treatment onpatients undergoing BP therapy, 24 of them did perform (34.29%) and 16 did not know (22.86%). The majority of the respondents (n=41, 58.57%) knew if BP treatment complications occur only in the oral cavity or in other areas of the body, and 52 of them (74.29%) recognizedin whichform the manifestations occur in the oral cavity.

Thirty five of the respondents (50%) knew under what conditions they can perform tooth extractions or other dentoalveolar surgical treatments on patients treated with BP, 34 of them did not know (48.57%) and one respondent said it is not meaningful. A percentage of 85.71% from the total respondent clinicians (n=60) contacted the prescriber before dentoalveolar surgery on a patient, while 42 of them (60%) believe that there is a difference in complications following treatment with intravenous or oral BP.

At the last question in Figure 2, it is shown that 82.86% of the respondents checked that they always contact the prescriber while 12.86% of them never do.

Discussions

The questionnaire used in the present study was developed in order to observe the level of knowledge among dentists about the relationship between BP treatment and the limitations regarding surgical dental interventions, applicablein dental offices.

Most of them had a dental practice for more than six years and the majority heard about the BP treatment. Among the diseases known to be treated using BP,none of the respondents were aware about the usage of BP in the treatment of malignant hypercalcemia and osteogenesisimperfecta.

Hypotheses attempting to explain the specificity of BRONJ, include increased turnover of the jaws, the variety of microorganisms in oral cavity, inhibition of neo-

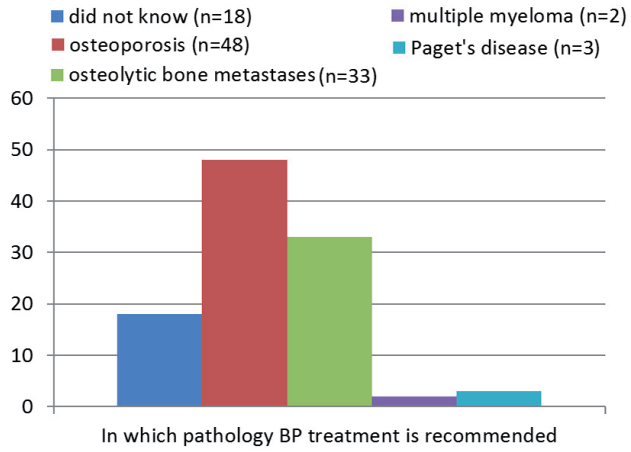

Fig. 1. Questionnaire answers regarding BP treatment recommendation

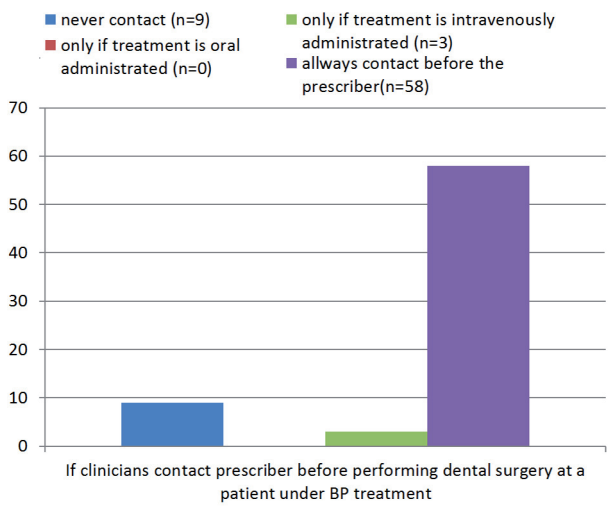

Fig. 2. Questionnaire answers regarding prescriber contact

angiogenesisby BP and apoptosis of osteoclasts, or a combination of these factors (23-25). Orofacial complex is a complicated system composed of teeth, oral mucosa, periodontal tissue, alveolar bone, tongue, muscle and salivary glands, which interact to perform a number of unique functions of the body, fromthe processes of chewing and speaking to deglutition and tasting. Maxilla and mandible bones are covered by the mucosa only near the external environment, where bacterial infections often occur, leading to cavities and periodontal disease (26).

In question number six we see a high percentage of clinicians that do not ask about a possible treatment with BP while doing the patient medical history, and in question number seven a large percentage do not know if they performed surgical dental treatments to patients who are / were treated with BP.A fairly large number, 34 respondent clinicians, do not know under what conditions they can perform tooth extractions or other dental surgical treatments in patients treated with BP.Studies have shown that dentoalveolarsurgery is considered a major risk factor, namely tooth extraction which acts as a trigger point in the development of BRONJ (27-29). Besides dental extractions, other dentoalveolar surgical procedures were incriminated, such as periapical and periodontal surgical procedures and implant insertion (30-32).

A large percentage (41.43%) doesnot know if BP treatment complications occur only in the mouth. BRONJ is more common in the posterior mandible than the maxilla, in a ratio of 2: 1 (33) and it is related to dental extraction (20,34), trauma to the mouth caused by incorrectly adjusted prostheses (35), oral infection (36), poor oral hygiene (37),dentoalveolar procedures on the bone (38), diabetes and smoking (20,39).

In our questionnaire 40% of the questioned doctors said that there is no difference between oral or intravenously administration of BP, but according to studies, it is estimated that the incidence of BRONJin intravenous therapy varies from 0.8% to 12% (1,11,21,30,31,33,40-52) while during oral administration, it varies from 0.01% to 0.04% (53).

Aquite encouraging number of respondents, 53 from a total of 70, noted that they always contact the prescriber before dentoalveolar surgery in patients treated with BP. Nine of the respondents never contact the prescriber and because of such unsupervised procedures, the patients' quality of life is compromised. The risk of developing osteonecrosis of the jaws is seven times higher among patient which develop inflammatory dental disease, dental and periodontal abscesses during BP therapy (31).

Conclusions

1. BRONJ is a new clinical entity, insufficiently known. Data collected from the literature reveals many unknowns in pathogenesis of the disease and universal protocols are not established in the prevention and treatment of this complication.
2. In the absence of appropriate protocols patients may not receive quality treatment, therefore dentists with or without specialty, should be informed about the conduct surgical treatments performed in dental offices. Conservative attitudes are most appropriate in patients with a history of treatment with BP.
3. We believe that disease management must be known among prescribers (oncologists, endocrinologists, haematologists), maxillofacial surgeons or dentists to whom the patients are going to be addressed.

Annex 1

Questionnaire addressed to dentists, residents and specialists

1. For how long do you practice dentistry?
   a) less than three years
   b) three-six years
   c) more than six years
2. Are you a resident doctor on a branch of dentistry?
   a) no
   b) dentoalveolar surgery/ maxillofacial surgery resident
   c) other branch, please specify……
3. Do you have a speciality on a branch of dentistry?
   a) no
   b) dentoalveolar surgery/ maxillofacial surgery specialty
   c) other branch, please specify……
4. Have you heard about bisphosphonate treatment?
   a) no
   b) yes
5. Do you know in which patology/ pathologies is recommended this treatment?
   a) no
   b) yes, please specify……
6.Do you ask about a possible treatment with BP while doing the patient medical history?
   a) no
   b) yes
   c) is no relevant in dentistry practice
7. Have you performed dental treatments/ dentoalveolar surgery on a patient which is under/ has received bisphosphonate treatment?
   a) no
   b) yes
   c) I do not know
8. Do you know if complications of bisphosphonate treatment occur only in the oral cavity or in other parts of the body as well?
   a) no
   b) yes
9. Do you know in what form manifestations occur in the oral cavity after treatment with bisphosphonates?
   a) no
   b) yes

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) is no relevant in dentistry practice
11. Do you contact the prescriber before surgery on a patient who needs a tooth extraction or other dentoalveolar surgery which is under bisphosphonate treatment?
    a) no
    b) yes
    c) is no relevant in dentistry practice
12. Do you think is there a difference in complications that occur after treatment with bisphosphonate administered intravenously or orally?
    a) no
    b) yes
13. Do you contact the prescriber before surgery on a patient who needs a tooth extraction or other dentoalveolar surgery which is under bisphosphonate treatment administered intravenously or orally?
    a) I do not contact the prescriber
    b) I contact only in orally administration
    c) I contact only in intravenously administration
    d) I always contact the prescriber before.

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