Oncologists awareness about bisphosphonate related osteonecrosis of the jaws

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Abstract

Objective: To evaluate the oncologists thoughts about the positive and adverse effects of bisphosphonates, drug holiday and the awareness about BRONJ.

Methods: A written questionnaire was sent to 7 hospitals, which have oncology facilities in Ankara, Turkey. Results were evaluated as percentages. Chi Square and Kruskal Wallis H test was used to analyze the data.

Results: A total of 53 oncologists replied to the questionnaire. BRONJ is the most seen complication (66%) due to bisphosphonates usage. Temporary suspension of the drug (52.8%) is the best treatment choice for this complication. Oncologists usually prefered dentist consultatation (39.6%).

Conclusion: A good cooperation of oncologists and dentists is very important to prevent BRONJ.

Keywords: Bisphosphonates related osteonecrosis of the jaw (BRONJ), oncologists, questionnaire. (JPMA 66: 880; 2016)

Introduction

Bisphosphonates are specific inhibitors of osteoclastic activity and they reduce pathological fractures, skeletal related events and pain, and improve the quality of life in patients with metastatic cancers and multiple myeloma.[1,2] Although usage of bisphosphonates is thought to be safe, in 2003, Marx and Stern reported the Bisphosphonate related osteonecrosis of the jaws (BRONJ).[3] Nomenclature of this phenomenon changed as medication related osteonecrosis of the jaws (MRONJ) in 2014. The change is justified to accommodate the growing number of osteonecrosis cases involving the maxilla and mandible associated with other antiresorptive (denosumab: Xgeva®,Prolia®) and antiangiogenic therapies.[4] Although exact etiology of BRONJ is still unknown, the pathway of it is very clear such as prescription of biphosphonates, long term usage of the drug and history of dental trauma or oral surgery. Regarding this pathway, it is very important to evaluate the patients dental situation and oral hygiene before and during the bisphosphonate therapy to prevent BRONJ.

In this study a questionnaire was filled up by oncologists so as to assess their thoughts about the positive and adverse effects of bisphosphonates, drug holiday and the awareness of the potential risks regarding the patients under bisphosphonates therapy.

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Methods and Result

A written questionnaire was sent to 7 hospitals, which have oncology facilities in Ankara Turkey between June 2010- February 2011. The questionnaire had the following questions:

- Years of experience as an oncologist
- What are your indications for biphosphonates
- Which bisphosphonates do you prescribe routinely
- Do you think bisphosphonates are effective for your patients
- Do you prefer to consult or do tests before prescribing bisphosphonates
- Have you ever faced complications related to bisphosphonates
- Have you ever faced BRONJ
- What was your choice of treatment when you faced with a complication
- Do you rely on the drug companies
- Do you follow literature especially for BRONJ and if yes from which journal?

Results were evaluated as percentages, relation between the complication rate and experience were evaluated

Table-1: Preferred bisphosphonates by the oncologists.

Bisphosphonate	Number of Oncologists	%
Zolendronate	52	98,1
Alendronate	13	24,5
Ibandronate	13	24,5
Pamidronate	10	18,9
Klondronate	8	15,1
Risendronate	6	11,3
Etidronate	3	5,7

Table-2: Preferred consultaions and test by the oncologists before bisphosphonate treatment. MRI: Magnetic Resonance Imaging CT: Computorized Tomography BSG Bone scintigraphy xray Convetional X-ray.

Preferred Consulatiton	Number of Onclogist - (%)	Preffered Tests	Number of Onclogist - (%)
Dentist	21 (39,6%)	Biochemical Tests	34 (64,1%)
Physiotherapist	2 (3,8%)	Renal Function Tests	21 (41,5%)
Rheumatologist	1 (1,9%)	Imagening (MRI/CT/BSG/XRay)	21 (39,6%)
Orthopaedic Surgeon	2 (3,8%)	Bone Mineral Density	6 (11,3%)
Nephrologist	1 (1,9%)		

Table-3: Oncologists choice of treatment in case of a complication.

Choice of Treatment in case of Complication	Number of Oncologists	%
Drug Holiday	28	52,8
Drug Holiday, if complication still exits rearrangement of the dose	8	15
Quitting the Drug Immediately	6	11,3
Dose Arrangement	4	7,5
Drug Holiday, if complication still exits rearrangement of the dose and if complications still exits quitting the drug	3	5,6
Drug holiday, if complications still exits quitting the drug	2	3,7
Changing the Agent	2	3,7
Continuing the Drug	0	-

with Kruskall Wallis H, drug company reliability vs oncologists literature followed were evaluated with Chi Square statistical test.

Written questionnaires were sent to 60 oncologists. 53 oncologists responded to our questionnaire while 7 oncologists refused to answer. Average experience was found 8,5 years. 51 oncologists (96,2%) believe that bisphosphonates are effective drugs.

Most preferred bisphosphonate by oncologists was zolendronate (98%), followed by alendronate and ibandronate (Table-1).

In all 33 oncologists (62,3%) preferred a consultations before prescribing bisphosphonates while 3 (5,7%) did not prefer consultation and 17 (32,1%) consulted when they needed to. The most preferred consultation was with the dentists, however it was practiced by only 21 (39,6%) oncologists. Preferred consultations and tests by the oncologists before bisphosphonates treatment are shown at Table-2.

The choice of treatment for complications is shown in Table-3. Most of the oncologists preferred temporary suspension of the drug as the best treatment until the complications resolved.

Discussion

Nitrogen containing bisphosphonates have proved to be very effective drugs for various malignancies and multiple myeloma.[5,6] Although there are some different types of bisphosphonates, zolendronate appears to be superior to others.[2] In our study oncologists opined that these drugs were extremely effective in the above reported diseases, especially when they are used in intravenous (I.V) form. Zolendronate was their first choice for bisphosphonate therapy. These resutls are similar to others in literature.

Suppression of bone turnover, soft tissue toxicity, infection as a result of cellular response, ischaemia due to antiangiogenic effect of bisphosphonates are the theories of BRONJ pathophysiology. These theories are well known but have faced controversies also. When newly formed BRONJ were described, called as MRONJ, 2014 by American Association of Oral and Maxillofacial Surgery (AAOMS), constant microtrauma, supression of acquired immunity, and vitamin D deficiency were added to controversial mechanisms.[4]

Although the first MRONJ case was reported over a decade ago, the pathophysiology of the disease has not been fully elucidated. To date many hypothesis exist that disease may be multifactorial. But none of them (in isolation or combination) are able to explain the exact reason.[4,7,8]

The exact pathway of BRONJ is very clear. Starting or previously using the Bisphosphonate therapy is the main characteristic of BRONJ. If this condition is supported with exposed bone and fistula, longer than 8 weeks, in the maxillofacial region and no history of radiation therapy to

the jaws, it is defined as BRONJ.[4,8]

Regarding the duration, a longer duration appears to be associated with increased risk.[8] Studies on duration showed that the basis of duration is 12 months. However BRONJ risk increases, if duration takes longer such as 2,3 or 4 years.[4]

Operative treatment especially tooth extraction is considered a major risk for BRONJ. Several studies reported that tooth extraction is a common predisposing event in MRONJ cases with the high rate like 52-61%.[4,9-11] In a cohort study cancer patients recieving IV bisphosphonates (zoledronate) and undergoing dentoalveolar surgery(tooth extraction) are associated with a 33 fold increased risk for BRONJ than patients who are not undergoing dentoalveolar surgery.[4,9] For other dentoalveolar operations such as dental implant placement and endodontic or periodontal procedures, the definition of ONJ risk is not fully elucidated.[4]

Being aware of this pathway oncologists and dentists would play an important role in decreasing the risk and controlling BRONJ. On the other hand also drug companies being more instructive could be effective in supporting this mission for MRONJ.

Our findings showed that, majority of the oncologists preferred a drug holiday until the complications resolved. Temporary interruption of the drug, so called "drug holiday" is shown to be beneficial and suggested to be the first choice of treatment modality for BRONJ.[12,13] However temporary interruption of bisphosphonate therapy offers no short-term benefits, while long-term discontinuation may be beneficial in stabilizing sites of BRONJ and reducing symptoms with the risk of the progression of metastases or increase in related skeletal events in patients with cancer.[14-16]

As stated in literature, prevention remains the most important aspect of the management.[8,17] This proves that the risk of BRONJ would be minimized when dental consultation is preferred by oncologists. In the literature it was recommended that prior to bisphosphonate therapy, patients should have an oral health assessment and should be educated about the risks of BRONJ.[12] Also patients who are planned for or still under bisphosphonate therapy should be instructed about oral hygiene and clinical signs and symptoms of BRONJ.[14] Screening of the patient and routine dental assessment every 3 months must continue for the remainder of the patient's life because of the long lasting effect of these drugs on bone.[8] Thus, prior to and during the bisphosphonate therapy, dentists must be the part of the management. As mentioned previously assessing and eliminating the dental problems and potential risk factors is very important in the prevention of BRONJ.

The results of this study reveal that oncologists and dentists should jointly manage such cases. It has been observed that this mutual collaboration is not common so it is important to increase the awareness of oncologists on BRONJ. BRONJ needs multidisciplinary approach for successful treatment.

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Conflict of Interest: None.

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