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Bisphosphonate induced necrosis of jaws-the emerging challenging epidemic

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Abstract

Background: The bisphosphonates are widely prescribed drugs to prevent bone resorption, however, are associated with the potential risk of osteonecrosis of jaws in patients receiving dental treatment.

Methods: The study was designed to evaluate the chances of osteonecrosis in patients referred for management in whom dental treatment was carried out of negligence or lack of knowledge.

Results: Out of 74 patients studied, 16 patients had developed osteonecrosis, particularly after dental extraction, and out of 16 patients, 12 patients were having underlying malignancy.

Conclusion: Medication-induced necrosis of jaws is more in patients with underlying malignancy or other comorbidities compared to patients who are not suffering from malignancy, and dental treatment particularly extraction is a trigger in such patients for developing the debilitating condition.

Keywords: Bisphosphonates, MRONJ, osteonecrosis.

Introduction

Ever since Marx and Stern described BRONG in 2004, an increasing number of cases are getting reported and recognized.[1] Due to increasing size of population with improvement of lifespan and unfortunate increased incidence of malignancies and other chronic bone wasting disease, the use of bisphosphonates and other antiresorptive drugs has increased to counter bone loss. BRONJ is defined as a condition wherein there is exposure of bone for 8 or more than 8 weeks in mandible or maxilla in a patient who has been or is currently on bisphosphonates and has not received any radiation therapy. Bisphosphonates are currently exploited for the treatment of metastatic bone disease, hypercalcemia of pregnancy, Paget's disease, and other osteoporotic conditions. Very recently the literature suggests their role in osteonecrosis of jaws particularly after any sort of surgical or dental intervention particularly extractions of teeth in jaws.[2-5] The American Association of Oral and Maxillofacial Surgeons changed the term BRONG to MRONG meaning medication-related osteonecrosis of jaws in 2014 as other drugs like denosumab a RANKL ligand inhibitor and other antiangiogenic drugs were also found to be incriminated in the osteonecrosis of jaws.[6] MRONG is most commonly found in the mandible with incidence rate of 68% compared to the maxilla where it is 28% and it has

around 4% incidence together.[7] Robert Marx in his study on patients of intravenous bisphosphonates observed about 75% of Brong was post-trauma due to some invasive dental procedure and 25% of times it was spontaneous development, particularly in patients with compromised oral hygiene.[7]

Materials and Methods

The study was conducted in the Department of Oral and Maxillofacial Surgery on patients on antiresorptive drugs for different underlying medical conditions who were referred for management of oral conditions after receiving dental treatments for their decayed or diseased teeth from 2021 to 2023. The study was approved by the Institutional Ethical Committee with no OMFS 2021/47, and only such patients who were on injectable therapy for more than a year were included and followed, some of them had already developed osteonecrosis of jaws due to negligent dental treatement like extraction or curettage by their earlier dentist [Figures 1-3], and were referred for further treatement in our department. In this way, we studied 74 patients who were on antiresorptive therapy. The study excluded patients who had received radiation or steroid therapy. The MRONG was diagnosed by clinical, radiological, and histopathological examination to rule out any malignancy or recurrence. The patients were treated according to the protocol of stage of disease and were put on Vitamin E 500 mg twice a day and pentoxyphyline 400 mg twice a day after cardiac clearance and according to the stage. Debridement, prf therapy, or resection of diseased part was carried out wherever needed. In seven patients, a platelet rich fibrin membrane was used after surgery as dressing and wound cover. The data were entered into SPS software and Chi-square test was applied for compilation.

Results

Out of 74 patients studied 58 patients had not developed osteonecrosis after dental treatment even after extraction in mandible/maxilla but all such patients were receiving bisphosphonates for

Figure 1: Orthopantomogram depicting lytic none changes in a pt on bp

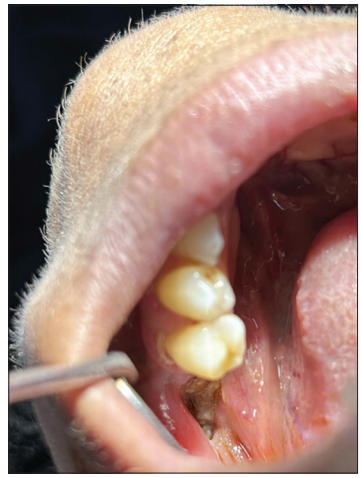

Figure 2: Intra-oral mucosal dehiscence and sequestration

Figure 3: Extra-oral scar of healed fistula

Table 1: The patients developing MRONG after treatement antiresorptive drugs with underlying conditions

n=74	MRONG present	Mrong absent
Malignancy patients	12	0 (P<0.01)
Other than malignancy	4	58 (P>0.1)

osteoporosis. About 12 patients who had developed osteonecrosis were having underlying malignancies such as breast, prostrate, or multiple myeloma [Table 1]. The other four patients who were having MRONG were receiving bisphosphonates for osteoporosis. Of the 16 patients with MRONG, mandible was involved as many as in 12 cases. In our series, a total of 6.25% cases were found to have osteonecrosis and most of them were due to negligence and lack of information or knowledge by the earlier dentists or quacks.

Discussion

MRONG is a new age epidemic due to an increase in malignancy and other bone-wasting diseases and negligence and lack of information in certain professionals. Although MRONG can develop spontaneously however about 80% develop post-dental treatment, particularly extractions. The literature reports an incidence of 2.9% of MRONJ after tooth extraction in cancer patients and 0.15% in patients being treated for osteoporosis.[8] The other studies instead show that the incidence can be 18.6% in relation to the dose and time of administration of bisphosphonates in cancer patients.[9,10] A review of 114 cases of bisphosphonates-associated osteonecrosis of jaws in Australia showed that 73% of the cases occurred after dental extractions. The frequency of osteonecrosis of jaws in bisphosphonates-treated osteoporotic patients was 0.01–0.04% and if dental extraction occurred 0.09–0.34%. In patients on bisphosphonates for bone malignancies, the incidence was 0.33–1.15%, and after dental extractions 6.7–9.1%.[11] A holistic and multidisciplinary team approach for evaluation and management of the conditions is recommended including a dentist, an oral-maxillofacial surgeon, and an oncologist and information about its usage should be given to masses and patients should be encouraged to inform about these drugs to their dentists before receiving the treatement of their ailments. In early stages, surgical debridement and coverage have been successful.[12] Osteotomies or resection are recommended only for severe cases,[13-16] due to relatively high levels of morbidity and impaired quality of life for the patients prevention is a cornerstone to reduce the incidence of osteonecrosis of jaws and before starting bisphosphonate therapy, the patient should be referred for thorough dental evaluation to identify and treat any potential source of infection. Start of bisphosphonates therapy should be delayed by 4–6 weeks to allow appropriate bone healing.[17] In our study, we carried resection for one case for mandible; in other 17 cases, conservative measures such as local debridement, curettage, and prf therapy were done for the relief of symptoms and personal hygiene instructions. In our study, a greater propensity was seen for progression to osteonecrosis of jaws in patients with underlying malignancy with $P < 0.01$ [Table 1]. The treatment of bisphosphonate-related osteonecrosis of the jaw needs comprehensive and holistic approach but it is better to launch a campaign about its information in the general public and concerned professionals.[17] The fellow medical colleagues should educated about dental clearance before the start of therapy to eradicate potential trigger for osteonecrosis of jaws in the form decayed, diseased teeth or poor oral condition.

Conclusion

Based on experimental and clinical original papers as well as previous reviews, it can be inferred that osteonecrosis of the jaw in antiresorptive medication patients is more often trigged by dental trauma or dental treatment, particularly in patients with underlying malignancy and hence strict guidelines should be followed before the start of therapy in such patients and dental professionals also need to be educated about the effect of

such medication The patients with underlying malignancy have more propensity of going in osteonecrosis of jaws and hence proper dental referral should be encouraged before the start of such medication from oncologists, orthopedicians and gynecologists.

Conflicts of Interest

None.

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Nill.

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