



## Medication-related osteonecrosis of the jaw treatment modalities: A review

Amir Ali Asadi

Department of Oral & Maxillofacial Surgery, Craniofacial Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran.

### ARTICLE INFO

Article Type:  
Review Article

Received: 23 Sep. 2019

Revised: 28 Nov. 2019

Accepted: 15 Dec. 2019

\*Corresponding author:

Amir Ali Asadi

Department of Oral & Maxillofacial Surgery,  
Craniofacial Research Center, Shariati  
Hospital, Tehran University of Medical Sciences,  
Tehran, Iran.

Tel: +98-21-84902473

Fax: +98-21-84902473

Email: Amiral\_i\_a\_2003@Yahoo.com

### ABSTRACT

**Introduction:** Medication-related osteonecrosis of the jaw (MRONJ) is a serious adverse reaction of antiresorptive and antiangiogenic agents. Management of MRONJ has remained a controversial topic within the oral and maxillofacial surgery community.

**Materials and Methods:** Articles from 2010 to 2020 were selected. We determined that all review studies evaluated the effectiveness of various MRONJ therapies to resolve the condition were eligible for this study. We determined that all review studies evaluated the effectiveness of various MRONJ therapies to resolve the condition were eligible for this study.

**Results:** Antibiotic therapy such as penicillin-based antibiotics plus  $\beta$ -lactamase inhibitor or metronidazole could decrease disease progression and may prevent super infection of the bone. Surgery should be considered in all stages of MRONJ as it confirms the histology. Fluorescence-guided surgery is helpful for MRONJ cases under Denosumab and it is recommended to use low level laser and PDT as adjuvant treatment of MRONJ.

**Conclusion:** It seems that conservative treatment, minimally traumatic extraction technique, removal of bone edges and mucosal wound closure may prevent the occurrence of MRONJ.

**Keywords:** Mronj; Bronj; Treatment; Prevention.

### Introduction

Medication-related osteonecrosis of the jaw (MRONJ) is a serious adverse reaction of antiresorptive and antiangiogenic agents; it is a potentially painful and debilitating condition that can considerably affect the quality of life of patients [1]. Depending on the drug, its dosage, and the duration of exposure, the occurrence of this adverse drug reaction may be rare (e.g. following the oral administration of bisphosphonate or denosumab treatments for osteoporosis, or antiangiogenic agent-targeted cancer treatment) or common

(e.g. following intravenous bisphosphonate for cancer treatment) [2].

The definition of medication-related osteonecrosis of the jaw (MRONJ) is:

- 1- Current or previous treatment with antiresorptive or antiangiogenic agents.
- 2- Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region

that has persisted for more than 8 weeks.

3- No history of radiation therapy to the jaw or obvious metastatic disease in the jaw [3]. Management of MRONJ has remained a controversial topic within the oral and maxillofacial surgery community. Therapeutic management has focused largely on symptomatic treatment, divided into the categories of surgical therapy and nonsurgical therapy. Examples of nonsurgical therapies include, but are not limited to, long-term use of local antimicrobials, systemic antimicrobials, or both; cessation of antiresorptive or antiangiogenic therapy; hyperbaric oxygen therapy; low intensity laser therapy; teriparatide; ozone; pentoxifylline; and tocopherol. Similarly, surgical treatment options for the management of MRONJ range from conservative to aggressive, such as curettage, sequestrectomy, and resection as a final resort [4].

The exact mechanisms underlying MRONJ remain unknown. Interestingly, MRONJ is primarily limited to the maxillofacial region. In contrast to other skeletal bones, jaw bones (the alveolar process and periodontium) have relatively high vascularity, bone turnover, and remodeling because of continuous mechanical stress, which may make them vulnerable to the adverse effects of drugs. Proposed hypotheses that attempt to explain the localisation of MRONJ exclusively to the jaws include altered boneremodeling, angiogenesis inhibition, constant microtrauma, suppression of innate or acquired immunity, and possible effects of inflammation or infection [2]. Aim of this study is to review all treatment modalities of Medication-Related Osteonecrosis of the jaw and to evaluate the effectiveness of the various treatment modalities used.

## Methods and Materials

The authors conducted a comprehensive search of Pubmed, Embase, the Cochrane Library, and Scholar to identify the effectiveness of management strategies for the treatment of MRONJ and different modalities of treatment. We used key words “MRONJ”, “BRONJ”, “Prevention” and “Treatments”. Articles from 2010 to 2020 were selected.

Following criteria were used for inclusion criteria:

- 1- We determined that all review studies evaluated the effectiveness of various MRONJ therapies to resolve the condition were eligible for this study.
- 2- We included studies that involved patients older than 18 years who had a diagnosis of MRONJ.

## Discussion

Ristow et al. have found that conservative treatment may be able to slow down disease progression and alleviate superinfection of the exposed bone, surgical treatment protocols have returned superior results in particular regarding the complete mucosal healing. They confirmed surgical intervention should be considered in all MRONJ stages as it allows the histological confirmation of the diagnosis MRONJ and is instrumental in the prevention of disease progression. The fluorescence guided bone resection is an innovative and promising treatment modality for MRONJ [2].

Akashi et al. declared that the most common regime for perioperative antibiotic administration for MRONJ surgery is penicillin-based antibiotics plus  $\beta$ -lactamase inhibitor or metronidazole but the duration of administration is diverse [3]. Hayashida et al. results indicate that extensive surgery is superior to conservative surgery and nonsurgical therapy in the treatment of patients with MRONJ [5]. Hasegawa et al. have successfully demonstrated multivariate relationships among the various risk factors for MRONJ after tooth extraction in patients receiving oral Bisphosphonates. The performance of root amputation, the extraction of a single tooth, the presence of bone loss or severe tooth mobility, and an unclosed wound were all significantly associated with the development of MRONJ. So they recommended a minimally traumatic extraction technique, removal of bone edges and mucosal wound closure. The effectiveness of a short-term drug holiday was not confirmed as it has no significant impact on MRONJ incidence [6]. Otto et al. revealed that fluorescence-guided surgery is a safe and successful treatment option which can be considered for all stages of MRONJ. The technique seems also promising for MRONJ cases under denosumab [7].

findings of Ribeiro et al. study suggest that both Low Level Laser Therapy (LLLT) and Photo Dynamic Therapy (PDT) brought important benefits to patient, assisting in clinical management of the MRONJ. The proposed new therapeutic approach led to decreased stage of MRONJ lesion, acting as an adjuvant treatment within a set of clinical maneuvers, bringing beneficial effects to control the disease, and providing improved patient quality of life. Based on results it is recommended to use LLLT and PDT as adjuvant treatment of MRONJ. It is also suggested that further researches be conducted to obtain more relevant data to the action of these therapies in the management of MRONJ lesions [8]. Rugani et al. declared that Preservation of function

and minimization of morbidity are the most important issues in dealing with MRONJ. Therefore, prevention by pre-therapeutic establishment of optimal dental and oral health conditions and ongoing dental supervision after the start of antiresorptive therapy are crucial. They found that if MRONJ develops, the early initiation of therapeutic measures is essential because the condition is likely to be manageable with conservative or minimal invasive means. Therapy should aim at achieving a stable mucosal coverage. If conservative measures are not successful after 8 weeks, surgery is indicated.

Resection should be as limited as possible but should include all necrotic bone. In advanced cases of MRONJ, respective surgery is indicated, but only if improvement of patients' quality of life is conceivable [9]. Alves et al. mentioned in their article that surgical treatment was effective and exhibited a low complication rate. They also have found that posterior region of the mandible presented the worst healing response, and that the number of intravenous applications of bisphosphonates might influence the response to surgical treatment [10].

Tenore and colleagues recommended that in order to provide a comprehensive patient-centered oral care delivery; in particular all patients with past, current, or planned Bisphosphonates therapy, follow three possible care pathways, consisting in prevention, surgery and oral clinics. In the prevention path patients receive oral hygiene and personal oral hygiene instructions every 4 months [11].

## Results & Conclusion

MRONJ is a significant complication for patients receiving Bisphosphonates. As discussed above it seems that conservative treatment, minimally traumatic extraction technique, removal of bone edges and mucosal wound closure may prevent the occurrence of MRONJ. Antibiotic therapy such as penicillin-based antibiotics plus  $\beta$ -lactamase inhibitor or metronidazole could decrease disease progression and may prevent superinfection of the bone. Surgery should be considered in all stages of MRONJ as it confirms the histology. Fluorescence-guided surgery is helpful for MRONJ cases under Denosumab and it is recommended to use LLLT and PDT as adjuvant treatment of MRONJ.

## Conflict of Interest

There is no conflict of interest to declare.

## References

- [1] Di Fede O, Panzarella V, Mauceri R, Fusco V, Bedogni A, Lo Muzio L, et al. The Dental Management of Patients at Risk of Medication-Related Osteonecrosis of the Jaw: New Paradigm of Primary Prevention. *BioMed research international*. 2018; 2018:2684924.
- [2] Beth-Tasdogan NH, Mayer B, Hussein H, Zolk O. Interventions for managing medication-related osteonecrosis of the jaw. *The Cochrane database of systematic reviews*. 2017; 10: Cd012432.
- [3] Akashi M, Kusumoto J, Takeda D, Shigeta T, Hasegawa T, Komori T. A literature review of perioperative antibiotic administration in surgery for medication-related osteonecrosis of the jaw. *Oral and maxillofacial surgery*. 2018; 22(4):369-78.
- [4] El-Rabbany M, Sgro A, Lam DK, Shah PS, Azarpazhooh A. Effectiveness of treatments for medication-related osteonecrosis of the jaw: A systematic review and meta-analysis. *Journal of the American Dental Association (1939)*. 2017; 148(8):584-94.e2.
- [5] Hayashida S, Soutome S, Yanamoto S, Fujita S, Hasegawa T, Komori T, et al. Evaluation of the treatment strategies for medication-related osteonecrosis of the jaws (MRONJ) and the factors affecting treatment outcome: a multicenter retrospective study with propensity score matching analysis. *Journal of Bone and Mineral Research*. 2017; 32(10):2022-9.
- [6] Hasegawa T, Kawakita A, Ueda N, Funahara R, Tachibana A, Kobayashi M, et al. A multicenter retrospective study of the risk factors associated with medication-related osteonecrosis of the jaw after tooth extraction in patients receiving oral bisphosphonate therapy: can primary wound closure and a drug holiday really prevent MRONJ? *Osteoporosis International*. 2017; 28(8):2465-73.
- [7] Otto S, Ristow O, Pache C, Troeltzsch M, Fliefel R, Ehrenfeld M, et al. Fluorescence-guided surgery for the treatment of medication-related osteonecrosis of the jaw: a prospective cohort study. *Journal of Cranio-Maxillofacial Surgery*. 2016; 44(8):1073-80.
- [8] Minamisako MC, Ribeiro GH, Lisboa ML, Mariela Rodríguez Cordeiro M, Grandó LJ. Medica-

tion-related osteonecrosis of jaws: a low-level laser therapy and antimicrobial photodynamic therapy case approach. *Case reports in dentistry*. 2016; 2016.

- [9] Rugani P, Acham S, Kirnbauer B, Truschnegg A, Obermayer-Pietsch B, Jakse N. Stage-related treatment concept of medication-related osteonecrosis of the jaw—a case series. *Clinical oral investigations*. 2015; 19(6):1329-38.
- [10] Lopes RN, Rabelo GD, Rocha AC, Carvalho PAG, Alves FA. Surgical therapy for bisphosphonate-related osteonecrosis of the jaw: six-year experience of a single institution. *Journal of Oral and Maxillofacial Surgery*. 2015; 73(7):1288-95.
- [11] Tenore G, Palaia G, Gaimari G, Brugnoletti O, Bove L, Giudice RL, et al. Medication-related osteonecrosis of the jaws (MRONJ): Etiological update. *Senses and Sciences*. 2014; 1(4).

*Please cite this paper as:*

Asadi A; Medication-related osteonecrosis of the jaw treatment modalities: A review. *J Craniomax Res* 2020; 7(1): 1-4