

[Open Peer Review on Qeios](#)

MRONJ ONSET AFTER PRELIMINARY EVALUATION AND PREVENTIVE INTERVENTIONS - A SINGLE CENTER STUDY

KATIA RUPEL¹, GIULIA OTTAVIANI¹, Magdalena Theodora Bogdan Preda¹, AUGUSTO POROPAT, Daniele ANGERAME¹, matteo biasotto¹

¹ University of Trieste

Funding: The author(s) received no specific funding for this work.

Potential competing interests: The author(s) declared that no potential competing interests exist.

Abstract

Are preventive dental interventions potential triggers for MRONJ onset? The aim of the present study was to retrospectively analyze clinical charts of subjects candidate for medical therapies with ascertained risk of MRONJ observed at the Dental Unit of the Hospital of Gorizia from 2011 to 2019. Patients who underwent a preliminary dental evaluation and preventive interventions (n = 214) were assigned to a preventive protocol group basing on the therapies performed (Complete, Partial, Not necessary). Demographical and clinical data were recorded, alongside with the interventions performed and the possible onset of MRONJ and its treatment. The obtained data were then compared with the characteristics of patients who were evaluated and treated for MRONJ (n = 34), who didn't perform a preliminary oral and dental evaluation before. Our results indicate that strict preventive protocols including single or multiple dental extractions of non maintainable teeth may represent triggers for MRONJ onset.

Background

Medication-Related Osteonecrosis of the jaws (MRONJ) is an adverse drug reaction described as the progressive destruction and death of bone that affects the mandible and maxilla of patients exposed to the treatment with medications known to increase the risk of disease, in the absence of a previous radiation treatment^[1]. Considering that currently a therapeutic approach leading to a complete healing in the majority of patients is still lacking, major clinical research efforts are dedicated to the development of effective preventive measures. While it is undoubtable that the introduction of preventive dental evaluation prior to the initiation of the therapies, especially in oncological patients, is leading to an important decrease in MRONJ incidence^{[2][3]}, the recommendations and guidelines published so far are not aligned on all points^{[4][1][5]}. Open issues include among others the definition and diagnostic criteria, details regarding preventive dental treatments and waiting time from the last extraction or surgical treatment involving bone and the initiation of the therapy.

Methods

The aim of the present study was to retrospectively analyze clinical charts of subjects candidate for medical therapies with

ascertained risk of MRONJ observed at the Dental Unit of the Hospital of Gorizia from 2011 to 2019. Demographical and clinical data were recorded, alongside with the interventions performed and the possible onset of MRONJ. Patients who underwent a preliminary dental evaluation were assigned to a group basing on the therapies performed (Complete, Partial, and Not necessary prevention protocols). Results were then compared with the characteristics of 34 patients who were evaluated and treated for MRONJ, but did not undergo a preliminary oral and dental evaluation. Statistical analysis was performed using software Prism 6.0 (GraphPad Software, Inc., 7825 Fay Avenue, Suite 230, La Jolla, CA 92037 USA) and R 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria. <http://www.R-project.org/>). The Mann-Whitney U test was used to evaluate the significance of the differences in ordinal variables between groups. Chi-Squared and Fisher's exact test were employed to test the significance of the associations between categorical variables and MRONJ onset. For significantly associated variables, Odds Ratios (OR) and Confidence Intervals (95% CI) were obtained using a multiple logistic regression analysis. All statistical assessments were two-sided, and a p -value < 0.05 was used for the rejection of the null hypothesis.

Results

Our study included 214 subjects candidate for medical therapies with ascertained risk of MRONJ referred for a preliminary dental evaluation (group G1), and 34 patients with diagnosed MRONJ who did not perform a preliminary dental evaluation before the beginning of the therapy (group G2). In G1, mean age, gender, underlying disease, pharmacological therapy at risk, preventive dental extractions (single or multiple) and cause of extractions were not associated significantly to an increased risk of MRONJ. The type of preventive protocol performed ($p = 0,038$) and dental extractions during the therapy at risk were significantly associated to MRONJ onset. A healthy oral cavity at first evaluation (prevention protocol Not necessary) is the most important protective factor against MRONJ onset. A Complete prevention protocol (OR = 3,7), generally including multiple dental extractions, seems to be at higher risk of MRONJ onset with respect to a Partial prevention protocol (OR = 0,29). Dental extractions during a therapy with medications with ascertained risk of MRONJ represent the major risk factor for MRONJ onset (OR = 13,67). In early MRONJ cases (with onset time less than 1 year from the beginning of the therapy at risk; $p = 0,015$), and in patients who underwent a preliminary evaluation ($p = 0,00035$), preventive extractions were the most frequent triggers. A post-extraction waiting time of 6-8 weeks after the preliminary extraction seems to be protective for MRONJ onset.

Conclusions

Although the importance of maintaining oral health before and during pharmacological therapies at risk of MRONJ is not questionable, there is need for a better definition of indications for tooth maintenance or extraction in the preventive phase. Our results, indicating that strict preventive protocols including single or multiple dental extractions of non maintainable teeth may represent triggers for MRONJ onset, foster the continuation of the study in order to confirm the trend and may represent an interesting point of view for the implementation of present guidelines. The most important limitations of the present study are the limited number of subjects and a selection bias due to the absence of stratification of the included study population. Despite such limitations, retrospective clinical studies are crucial for the analysis of the efficacy of past and current management protocols for a continuous implementation.

References

1. ^{a, b}Giuseppina Campisi, Rodolfo Mauceri, Francesco Bertoldo, Giordana Bettini, et al. (2020). *Medication-Related Osteonecrosis of Jaws (MRONJ) Prevention and Diagnosis: Italian Consensus Update 2020*. *IJERPH*, vol. 17 (16), 5998. doi:10.3390/ijerph17165998.
2. [^]Vittorio Fusco, Claudia Galassi, Alfredo Berruti, Cinzia Ortega, et al. (2013). *Decreasing Frequency of Osteonecrosis of the Jaw in Cancer and Myeloma Patients Treated with Bisphosphonates: The Experience of the Oncology Network of Piedmont and Aosta Valley (North-Western Italy)*. *ISRN Oncology*, vol. 2013 , 1-8. doi:10.1155/2013/672027.
3. [^]Ie-Wen Sim et al.. (2015). *Declining incidence of Medication-Related Osteonecrosis of the Jaw in patients with cancer.. The Journal of Clinical Endocrinology and Metabolism*, vol. 100(10):3887-93 .
4. [^]Ruggiero SL et al.. (2014). *American Association of Oral and Maxillofacial Surgeons position paper on medication-related osteonecrosis of the jaw--2014 update*. *J Oral Maxillofac Surg.*, vol. 72(10):1938-56. .
5. [^]Yarom N et al.. (2019). *Medication-Related Osteonecrosis of the Jaw: MASCC/ISOO/ASCO Clinical Practice Guideline*. *Journal of Clinical Oncology*, vol. 37(25):2270-2290 .