

INPLASY PROTOCOL

To cite: Halai et al. Risk reduction strategies for patients at risk of medication-related osteonecrosis of the jaws undergoing dental extractions: a systematic review. *Inplasy protocol* 202160064. doi: 10.37766/inplasy2021.6.0064

Received: 19 June 2021

Published: 19 June 2021

Corresponding author:
Roberto Sacco

roberto.sacco@manchester.ac.uk

Author Affiliation:
Eastman Dental Institute -
University College London.

Support: No Financial Support.

Review Stage at time of this submission: Data extraction.

Conflicts of interest:
None declared.

Risk reduction strategies for patients at risk of medication-related osteonecrosis of the jaws undergoing dental extractions: a systematic review

Halai, T¹; Sacco, R²; Mercadante, V³; Eyeson, J⁴; Fedele, S⁵.

Review question / Objective: The focused question for this review was: “in individuals exposed to anti-resorptive and/or anti-angiogenic medications undergoing dental extractions, can any risk-reduction strategy lessen the risk of developing MRONJ?”.

Condition being studied: Medication-related osteonecrosis of the jaw (MRONJ) is an irreversible adverse effect of antiresorptive medications (e.g. bisphosphonates and receptor activator of nuclear factor Kappa-B ligand inhibitors) and angiogenesis inhibitors. Affected patients typically present with necrotic exposed bone often associated with pain, swelling, pus discharge, tooth mobility and in some cases, pathological fracture. Approximately 25%, can present with a range of the above symptoms but without frank bone exposure, also known as non-exposed MRONJ. The prevalence of MRONJ in cancer patients using intravenous BP and/or Denosumab is reported to be as high as 15.5%. Dental extractions in particular have been consistently identified as one of the main independent risk factors associated with MRONJ development. We performed a systematic review of the literature to assess the effects of interventions aimed at reducing the risk of MRONJ development in individuals exposed to antiresorptive and/or antiangiogenic drugs and undergoing dental extractions.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 June 2021 and was last updated on 19 June 2021 (registration number INPLASY202160064).

INTRODUCTION

Review question / Objective: The focused question for this review was: “in individuals exposed to anti-resorptive and/or anti-

angiogenic medications undergoing dental extractions, can any risk-reduction strategy lessen the risk of developing MRONJ?”.

Condition being studied: Medication-related osteonecrosis of the jaw (MRONJ) is an irreversible adverse effect of antiresorptive medications (e.g. bisphosphonates and receptor activator of nuclear factor Kappa-B ligand inhibitors) and angiogenesis inhibitors. Affected patients typically present with necrotic exposed bone often associated with pain, swelling, pus discharge, tooth mobility and in some cases, pathological fracture. Approximately 25%, can present with a range of the above symptoms but without frank bone exposure, also known as non-exposed MRONJ. The prevalence of MRONJ in cancer patients using intravenous BP and/or Denosumab is reported to be as high as 15.5%. Dental extractions in particular have been consistently identified as one of the main independent risk factors associated with MRONJ development. We performed a systematic review of the literature to assess the effects of interventions aimed at reducing the risk of MRONJ development in individuals exposed to antiresorptive and/or antiangiogenic drugs and undergoing dental extractions.

METHODS

Participant or population: Patient previously exposed to or actively receiving treatment with MRONJ-associated medications.

Intervention: Interventions included any type of risk-reduction strategy.

Comparator: Standard of care.

Study designs to be included: Randomised control trials (RCTs) and Case-control studies (CCS).

Eligibility criteria: We included studies (RCTs or CCs) reporting on patients undergoing dental extractions with any previous or ongoing use of MRONJ-associated medications (antiresorptive and/or antiangiogenic drugs) and any duration of therapy before surgery. We considered any intervention aimed at

reducing the risk of MRONJ in individuals undergoing dental extractions.

Information sources: An electronic search of the literature will be performed using the following databases: PubMed, MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL).

Main outcome(s): The primary objective of this review is to assess the effects of risk-reduction interventions in lessening the risk of MRONJ development in individuals exposed to anti-resorptive and/or anti-angiogenic medications undergoing dental extractions.

Additional outcome(s): Further data, where available, will be collected on safety of and adverse effects of the proposed interventions.

Quality assessment / Risk of bias analysis: Authors independently will assess the risk of bias in the included RCTs and case-control studies as per the “Cochrane Handbook for Systematic Reviews of Interventions” guidelines and “Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I)” respectively.

Strategy of data synthesis: Following a comprehensive screening to determine eligible studies, all selected papers will be carefully read to identify study and patient characteristics. To assess primary and secondary outcomes, data will be extracted from each study and analysed. Where pooling of results is inappropriate, the results will be reported as narrative descriptions using a detailed commentary.

Subgroup analysis: All participants will be included in the final analysis.

Sensitivity analysis: If sufficient data are extracted, a sensitivity analysis will be conducted to check the stability of the outcome results by excluding low methodological quality or high risk of bias studies.

Language: No language restrictions will be applied.

Country(ies) involved: United Kingdom.

Keywords: Osteonecrosis, medication-related osteonecrosis of the jaw, preventive strategies, dento-alveolar, extraction, oral surgery.

Contributions of each author:

Author 1 - Tina Halai.

Author 2 - Roberto Sacco.

Author 3 - Valeria Mercadante.

Author 4 - Josiah Eyeson.

Author 5 - Stefano Fedele.