INPLASY PROTOCOL

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Support: **None**

Review Stage at time of this submission: **The review has not yet started.**

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Conflicts of interest:
None declared.

What is the best biomaterial for alveolar ridge preservation after tooth extraction? A systematic review and network meta-analysis protocol

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Review question: **The objective of this systematic review is to analyze the effectiveness of different biomaterials used for alveolar ridge preservation after tooth extraction. To this end, the proposed study will answer the following question: What is the best biomaterial for alveolar ridge preservation after tooth extraction?**
Condition being studied: **The alveolar bone loss after tooth extraction.**
Information sources: **We will search the following electronic bibliographic databases: EMBASE, PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), LILACS database, Scopus database and Web of Science database. There will be no language restrictions and no year restriction. We will use the PICOS strategy for the research question construction and evidence search. The reference lists of the articles identified will be cross-checked. Furthermore, and studies from the 'grey literature' will be screened through the following trial registry platform: clinicaltrials.gov (http://www.clinicaltrials.gov). A manual search will be done in the relevant journals of Dentistry. We will contact study correspondent authors to solve any uncertainties.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 March 2020 and was last updated on 23 May 2020 (registration number INPLASY202030005).

INTRODUCTION

Objectives / Review question: **The objective of this systematic review is to analyze the effectiveness of different biomaterials used for alveolar ridge preservation after tooth extraction. To this end, the proposed study will answer the following question: What is the best biomaterial for alveolar ridge preservation after tooth extraction?**

Condition being studied: The alveolar bone loss after tooth extraction.

Rationale: It is well recognized that tooth extraction induces an alveolar bone remodeling process, which may compromise subsequent implant rehabilitation. Several biomaterials can be indicated to reduce the quantity of bone resorption. However, primary studies comparing more than three biomaterials are not feasible, and there is no systematic review comparing different types of biomaterials using a frequentist network approach. To date, several systematic reviews have investigated the comparative efficacy of biomaterials.

METHODS

Participant or population: We will include studies examining the healthy adult humans (18 years or older) undergoing tooth extraction for any reason. None restrictions about sex, gender, or ethnicity will be applied on the population of study.

Intervention: Socket filling with a bone grafting biomaterial after tooth extraction.

Comparator: Tooth extraction without any additional intervention (natural healing) or using a different grafting biomaterial.

Study designs to be included: Randomized clinical trials.

Eligibility criteria: Studies will be selected according to the PICOS criteria (Participant, intervention, comparator, outcomes, and study design) outlined in the referred sections. Additionally, we will exclude studies without the description of the method used to measure the alveolar bone. Similarly, studies comparing only membrane barriers will be excluded, as well as studies the used a barrier membrane in the placebo group (blood clot). When a multi-arm study uses the same biomaterial in two groups, with and without a barrier membrane, only the data come from the group that used a membrane will be included in the network meta-analysis. Studies without width measurement will be excluded.

Information sources: We will search the following electronic bibliographic databases: EMBASE, PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), LILACS database, Scopus database and Web of Science database. There will be no language restrictions and no year restriction. We will use the PICOS strategy for the research question construction and evidence search. The reference lists of the articles identified will be cross-checked. Furthermore, and studies from the 'grey literature' will be screened through the following trial registry platform: clinicaltrials.gov (http://www.clinicaltrials.gov). A manual search will be done in the relevant journals of Dentistry. We will contact study correspondent authors to solve any uncertainties.

Main outcome(s): The primary outcome will be: 1 - Horizontal bone resorption at coronal region in mm (+-1mm bellow the alveolar crest) measured between 3 and 6 months; 2 - Vertical bone resorption expressed in mm (vestibular wall) measured between 3 and 6 months.

Additional outcome(s): The secondary outcomes will be: 1 - Horizontal bone resorption at middle region in mm (+-3mm bellow the alveolar crest) measured between 3 and 6 months. 2 - Horizontal bone resorption at apical region in mm(+-5mm bellow the alveolar crest) measured between 3 and 6 months.

Data management: The studies will be imported into Endnote X9 software (Thompson Reuters, Philadelphia, PA, USA) where duplicates will be automatically removed. All analyses will be performed using the software R version 3.6.2 or updated Mac OS X computer system. The packages "meta", "metafor", "metasens", "dosresmeta", "netmeta", "rmeta", "pcnetmeta" will be used. These packages are available from the Comprehensive R Archive Network (CRAN).

Quality assessment / Risk of bias analysis: Two review authors will independently assess the risk of bias. We will use the Cochrane tool for assessing risk of bias. Sequence generation - Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups. Allocation concealment - Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrollment. Blinding of participants, personnel and outcome assessors - Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Incomplete outcome data - Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group, reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors. Were incomplete outcome data adequately addressed? Selective outcome reporting - State how the possibility of selective outcome reporting was examined by the review authors, and what was found. Other sources of bias - State any important concerns about bias not addressed in the other domains in the tool.

Strategy of data synthesis: A pairwise meta-analysis for direct evidence and a network meta-analysis for direct and indirect evidence of eligible comparisons will be accomplished. We will provide a quantitative and narrative synthesis. We will provide provide summaries of intervention effects for each study by calculating standardized mean differences or mean differences. We will pool the results using a fixed or random-effects meta-analysis. Heterogeneity will be assessed using both the χ^2 test and the I^2 statistic. We will consider an I^2 value greater than 50% indicative of substantial heterogeneity. In addition to the heterogeneity assessment using theI2 statistic, the assumption of transitivity and similarity based on clinical and methodological characteristics will be assessed. The inconsistency will be explored using the Net Heat Plot. We will also assess evidence of publication bias.

Subgroup analysis: None.

Sensibility analysis: None.

Language: No language restrictions.

Countries involved: Brazil and United States of America.

Other relevant information: This study will be performed by frequentist approach, which will enable us to estimate which intervention has the highest probability to be the best using net rank function.

Keywords: Alveolar ridge preservation; tooth extraction; systematic review; network meta-analysis; grafting materials.

Dissemination plans: The results of this systematic review will be disseminated through peer reviewed journal.

Update information: Three additional authors was included in the present study during the screening process (Soares, B; Vidigal, GM; and Vettore, MV).

Contributions of each author:
Author 1 - João Vitor Canellas - The author will draft the protocol and the manuscript. Contributed to the development of the selection criteria, the risk of bias assessment strategy, and data extraction criteria. The referred author developed the search strategy and provided statistical expertise. The risk of bias assessment and screening of search studies against eligibility
Author 2 - Brunna Soares - The author will draft the manuscript. The risk of bias assessment and screening of search studies against eligibility criteria. The author will read, provided feedback, and approved the final manuscript.

Author 3 - Fabio Gambôa Ritto - The author will read, perform the risk of bias assessment, supervise, provided feedback, and approved the final manuscript.
Author 4 - Ricardo Guimarães Fischer - The authors will read, supervise, provided feedback, and approved the final manuscript.
Author 5 - Guaracilei Maciel Vidigal Junior - The authors will read, supervise, provided feedback, and approved the final manuscript.
Author 6 - Mario Vianna Vettore - The authors will read, supervise, provided feedback, and approved the final manuscript.
Author 7 - Paulo Jose Medeiros - The authors will read, supervise, provided feedback, and approved the final manuscript.