INPLASY PROTOCOL

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Conflicts of interest:
The authors declared no potential conflicts of interest.

Use of drugs to control pain, edema and trismus after mandibular third molar surgery: systematic review and network meta-analysis

Drugos, LS[1]; Soares, BN[2]; Canellas, JV[3] ; Medeiros, PJA[4].

Review question / Objective: **Which medication or medication protocol are most effective in controlling pain, edema and trismus after mandibular third molar surgery.**
Condition being studied: **Facial edema, difficulty opening mouth and postoperative pain after mandibular third molar surgery.**
Information sources: **Literature search strategies will be developed using text words related to third molars and oral surgery. We will search the following electronic bibliographic databases: EMBASE, PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), LILACS data base, Scopus database na Web of Science database. There will be no language or year restrictions. We will use the PICOS strategy for 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 clarify any doubts.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 June 2020 and was last updated on 17 June 2020 (registration number INPLASY202060065).

INTRODUCTION

Review question / Objective: **Which medication or medication protocol are most effective in controlling pain, edema and trismus after mandibular third molar surgery?**

Rationale: **Discomfort in the post-operative period after mandibular third molar surgery is known as a major challenge to be controlled. Many medications are used for the purpose of controlling, reducing or even avoiding this discomfort, the study**

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aims to analyze the medications used and which ones would be more effective.

Condition being studied: Facial edema, difficulty opening mouth and postoperative pain after mandibular third molar surgery.

METHODS

Search strategy: The search strategy will be published with the final paper (supplementary materials).

Participant or population: This study will include health humans who had been submitted to mandibular third molar surgery. No restrictions regarding gener, ethnicity or age are applied.

Intervention: The use of systemic medications to control pain, edema and trismus after mandibular third molar surgery.

Comparator: Placebo or diferente types of medications used to control pain, edema and trismus in the postoperative period of third molar surgeries.

Study designs to be included: We will include only randomized controlled trials (RCTs).

Eligibility criteria: Studies will be select according to the PICOS criteria. Patients included in the primary studies must be ASAI or ASAII.

Information sources: Literature search strategies will be developed using text words related to third molars and oral surgery. We will search the following electronic bibliographic databases: EMBASE, PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), LILACS data base, Scopus database na Web of Science database. There will be no language or year restrictions. We will use the PICOS strategy for 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 clarify any doubts.

Main outcome(s): Pain and edema after mandibular third molar surgery.

Additional outcome(s): Trismus after third molar surgery.

Data management: The references will be imported into EndNote X9 software (Thompson Reuters, Philadelphia, PA, USA) where duplicates will 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", "emeta", "pcnetmeta" will be used. These packages are available from the Comprehensive R Archieve Network (CRAN).

Quality assessment / Risk of bias analysis: Two review authors will independently access 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 na 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 assessor – describe all measures used , if any, to blind study participants and personnel from knowledge of which intervention a participant received.

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

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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 χ2 test and the I2 statistic. We will consider an I2 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: There are no language restrictions.

Country(ies) involved: Brazil.

Other relevant information: None.

Keywords: Pain, edema, trismus, third molar, systematic review, network meta-analysis.

Dissemination plans: The results will be disseminated through peer reviewed journals.

Contributions of each author:
Author 1 - Luciana Drugos - The Author will draft the protocol and the manuscript. She will be the responsable of the methodology and the selection criteria. The author will select included studies and accomplish the risk of bias analysis.
Author 2 - Brunna Soares - The author will select included studies and accomplish the risk of bias assessment strategy.
Author 3 - Joao Canellas - The author contributed to the development of the selection criteria, and to the development of the present protocol. The referred author developed the search strategy and provided statistical expertise. The author will read, supervised, provided feedback and approved the final manuscript.
Author 4 - Paulo Medeiros - The author will read, supervised, provided feedback and approved the final manuscript.

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