

# INPLASY PROTOCOL

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None declared.

## Comparative efficacy of different topical anesthetics to reduce the perception of pain during intraoral anesthesia: A systematic review and network meta-analysis

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**Review question / Objective:** This systematic review aims to investigate which is the best topical anesthesia marketed and used by dentists in an attempt to reduce pain (oral punctures and injections) in the maxillary and mandibular region, by applying a frequentist network meta-analysis approach. To achieve the proposed objective, the following question was used: " What topical anesthesia is more effective in reducing perceived pain (punctures and needle injections) when performing dental anesthetic techniques?

**Condition being studied:** Evaluate what is the best topical anesthetic used in infant, young adult and adult patients to reduce pain during puncture and anesthetic injection.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 December 2022 and was last updated on 08 December 2022 (registration number INPLASY2022120034).

### INTRODUCTION

**Review question / Objective:** This systematic review aims to investigate which is the best topical anesthesia marketed and used by dentists in an attempt to reduce pain (oral punctures and

injections) in the maxillary and mandibular region, by applying a frequentist network meta-analysis approach. To achieve the proposed objective, the following question was used: " What topical anesthesia is more effective in reducing perceived pain

(punctures and needle injections) when performing dental anesthetic techniques?

**Rationale:** Several topical anesthetics are currently marketed in order to reduce pain (puncture and needle injection) when performing intraoral anesthetic techniques. Numerous clinical trials have been conducted to investigate which is the best topical solution that can reduce pain (puncture and needle injections) during dental anesthetic technique; however, due to the high heterogeneity of clinical studies, it is difficult to indicate which topical anesthetic is the best for clinical management. Moreover, most patients do not perform elective dental procedures for fear of the pain that will be produced by their chosen anesthetic technique. Thus, this review will provide us with significant advances on what is known by the academic community and what Stiller needs to be clarified, since this subject is extremely relevant to clinical practice. Evaluate what is the best topical anesthetic used in infant, young adult and adult patients to reduce pain during puncture and anesthetic injection.

**Condition being studied:** Evaluate what is the best topical anesthetic used in infant, young adult and adult patients to reduce pain during puncture and anesthetic injection.

## METHODS

**Search strategy:** 1- MEDLINE via PubMed: #1 (((("Anesthesia,Dental"[MeSH Terms]) OR (Anesthetics,Dental[Title/Abstract])) OR ("Anesthetic,Dental"[Title/Abstract]) OR ("Infiltration,Dental"[Title/Abstract]) OR ("Anesthesia, Local"[MeSH Terms]) OR (Anesthetics, Local[Title/Abstract]) AND #2 (((((((((Topic[MeSH Terms]) OR (Topical[MeSH Terms])) OR ("Topical Anesthetic"[Title/Abstract]) OR ("Topical anaesthesia"[Title/Abstract])) OR (EMLA[Title/Abstract]) OR (Xylocaine[Title/Abstract]) OR (Lignocaine[Title/Abstract]) OR (Carticaine[MeSH Terms]) OR (Lidocaine[MeSH Terms]) OR (Benzocaine[MeSH Terms]) AND #3 (("Pain Measurement"[MeSH Terms]) OR ("Pain

Measurements"[MeSH Terms])) OR ("Pain"[MeSH Terms]) AND #4 (Dentistry [MeSH Terms])

2- EMBASE and Cochrane Library: #1 (Anesthesia,Dental) OR (Anesthetics,Dental) OR (Anesthetic,Dental) OR (Infiltration,Dental) OR (Anesthesia, Local) OR (Anesthetics, Local) AND #2 (Topical) OR (Topic) OR (Topical Anaesthetics) OR (Topical anaesthesia) OR (Carticaine) OR (EMLA) OR (Lidocaine) OR (Benzocaine) OR (Xylocaine) OR (Lignocaine) AND #3 (Pain Measurement) OR (Pain Measurements) OR (Pain) AND #4 (Dentistry).

**Participant or population:** Studies with patients who underwent dental treatment requiring the use of topical anesthetics for pain reduction during puncture and intraoral anesthetic injection will be included. We will not apply filters regarding the age range of the population, gender, ethnicity, and dental procedure reported in the studies.

**Intervention:** The use of different types of topical anesthetics marketed and used in clinical practice for pain reduction.

**Comparator:** In this frequentist network meta-analysis each anesthetic topic will be compared to each other and the placebo will be the reference. We will include only randomized controlled trials (RCTs).

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

**Eligibility criteria:** Studies will be selected according to the PICO criteria (Participant, intervention, comparator and outcomes) outlined in the aforementioned sections. The following will be included: articles that described the use of topical anesthetics before puncture and/or needle injection in intraoral anesthetic techniques, articles that described pain assessment by means of scales and no chronological restrictions will be applied to the studies included. Publications in conference proceedings, book chapters, clinical case reports, literature reviews, letters to the editor, and

brief communications were excluded. Research that evaluated the use of experimental or non-marketable topical anesthetics. Articles that were not available to be read in full.

**Information sources:** Electronic searches will be conducted in the databases of Web of EMBASE, MEDLINE via PubMed, e Cochrane library for publications up to November, 2022. Relevant articles will be selected by English language descriptors indexed in Medical Subject Headings (MeSH) and relevant non-indexed acronyms. Terms will be separated by the Boolean controllers "AND" and "OR". A comprehensive hand-search was performed by one author through a manual, page-by-page examination of the entire contents of the following relevant journals: Journal of Oral and Maxillofacial Anesthesia; Journal of Dental Anesthesia and Pain Medicine; International Journal of Oral and Maxillofacial Surgery; Journal of Oral and Maxillofacial Surgery; Journal of Cranio-Maxillofacial Surgery; British Journal of Oral and Maxillofacial Surgery; Oral Surgery Oral Medicine Oral Pathology Oral Radiology; Journal of Dental Research, Journal of Clinical Oral Investigation. We will contact study correspondent authors to clarify any doubts. Finally, the reference lists of the included studies will be checked to identify additional potential primary studies.

**Main outcome(s):** For the analysis we will evaluate 1) Anatomical region used in the anesthetic technique; 2) Type of anesthetic solution; 3) Type of topical anesthetic and its concentration; 4) Needle size; 5) Type of scale used to evaluate the patients' pain with its respective means and standard deviation.

**Additional outcome(s):** None.

**Data management:** The literature search in all databases will be exported to the Rayyan platform to eliminate duplicate references. Two researchers will perform the initial search for titles and abstracts independently. The full text of articles judged relevant based on title and abstract

will be read and evaluated independently based on the established selection criteria. Any discrepancies will be resolved through discussion with a third reviewer. After selecting the studies, the researchers will extract the qualitative information using a standardized table in Microsoft Excel. The frequentist network meta-analysis will be performed using R software version 3.6.2 or if available a later version. Network Meta-analysis will be performed using Frequentist Methods (netmeta package) for the Mac OS X computer system.

**Quality assessment / Risk of bias analysis:** Two authors will assessed the quality of the included studies separately. Any disagreement will be discussed with a third reviewer. Randomized clinical studies will be evaluated using the Cochrane collaboration 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. The effect size measure for continuous outcomes will be the standardized mean difference (SMD). We will pool the results using a random-effects meta-analysis. Heterogeneity will be assessed using both the  $\chi^2$  test and the I<sup>2</sup> statistic. We will consider an I<sup>2</sup> value greater than 50% indicative of substantial heterogeneity. We will investigate the assumption of transitivity and similarity based on clinical and methodological characteristics. Inconsistency will be assessed by comparing direct and indirect evidence. The net heat plot will be used to show the contribution of each design to the network estimate and the extent of inconsistency due to each design. We will also assess evidence of publication bias. Intention-To-treat (ITT) data will be used whenever available. To rank the various corticosteroids interventions for each outcome, we will use the P-scores which are equivalent to SUCRA values. Finally, we will compare the efficacy of different routes of corticosteroid administration by applying the same frequentist network meta-analysis approach used in this study to compare different topical anesthetics.

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**Subgroup analysis:** None planned.

**Sensitivity analysis:** None planned.

**Language restriction:** No language restriction will be imposed.

**Country(ies) involved:** Brazil and USA.

**Other relevant information:** None.

**Keywords:** Anesthesia,Dental; Topical; Pain Measurement; Review.

**Contributions of each author:**

**Author 1 - Rodrigo Alvitos - Formal screening of search results against eligibility criteria, data extraction, risk of bias assessment, drafting of manuscript.**

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