INPLASY PROTOCOL

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None declared.

Efficacy of hemostatic agents in endodontic surgery: A protocol of systematic review and network meta-analysis

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Review question / Objective: **What is the most efficient hemostatic agent used to control bleeding during endodontic surgery?**
Condition being studied: **Bleeding during endodontic surgery.**
Information sources: **PubMed, Scopus, Embase, Web of Science, the Cochrane Library, and the grey literature in ProQuest/ EBSCOhost will be searched. We will also conduct hand manual searches for the reference lists of studies retrieved for full-text screening and prospective hand-searching of those journals (Journal of Endodontics, International Endodontic Journal, and Australian Endodontic Journal) identified as having the highest yield of eligible studies. We will use the Medical Subject Headings (MeSH) feature or equivalent synonyms.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 February 2021 and was last updated on 10 February 2021 (registration number INPLASY202120038).

INTRODUCTION

Review question / Objective: **What is the most efficient hemostatic agent used to control bleeding during endodontic surgery?**

Rationale: **Endodontic surgery is a procedure aimed to treat endodontic lesions when conventional nonsurgical endodontic therapy has failed. Bleeding control during endodontic surgery is essential to accurately visualize the root-end surface and facilitate placement and**

setting of the root-end filling. As such, the reduction of blood loss during the surgery, facilitating the operation, and minimizing the time of surgery could consequently increase the surgery's success rate and reduce the postoperative complications. Therefore, this systematic review and network meta-analysis aims to identify the most efficient hemostatic agent used to control bleeding during endodontic surgery.

Condition being studied: Bleeding during endodontic surgery.

METHODS

Search strategy: PubMed: ((("Hemostatics"[Mesh] OR "Hemostatics" [Pharmacological Action]) AND ("Periapical Diseases/drug effects"[Mesh] OR "Periapical Diseases/drug therapy"[Mesh] OR "Periapical Diseases/surgery"[Mesh] OR "Periapical Diseases/therapy"[Mesh])) OR ("Periapical Tissue/drug effects"[Mesh] OR "Periapical Tissue/surgery"[Mesh])) OR ("Dental Pulp Diseases/drug effects"[Mesh] OR "Dental Pulp Diseases/drug therapy"[Mesh] OR "Dental Pulp Diseases/surgery"[Mesh]).

Participant or population: Patients undergoing endodontic surgery.

Intervention: Hemostatic agents (e.g., Epinephrine, Aluminum chloride, PTFE strips + epinephrine, Electrocauterization, and Ferric sulfate).

Comparator: The most widely used hemostatic agent in RCTs.

Study designs to be included: Parallel-design Randomized clinical trial (RCT).

Eligibility criteria: We will include randomized controlled trials that evaluate the effectiveness of hemostatic agents used in endodontic surgery.

Information sources: PubMed, Scopus, Embase, Web of Science, the Cochrane Library, and the grey literature in ProQuest/EBSCOhost will be searched. We will also conduct hand manual searches for the reference lists of studies retrieved for full-text screening and prospective hand-searching of those journals (Journal of Endodontics, International Endodontic Journal, and Australian Endodontic Journal) identified as having the highest yield of eligible studies. We will use the Medical Subject Headings (MeSH) feature or equivalent synonyms.

Main outcome(s): Control bleeding during endodontic surgery (Adequate hemostasis).

Additional outcome(s): If the following information is available, we will include them for further analysis: 1. Postoperative pain and complications; 2. Impact of the hemostatic agent on healing and prognosis.

Data management: Two authors will independently extract the data (name of the first author, year of publication, country, study environment, age of participants, sample size, male to female ratio, intervention, comparator, number of each group, results of hemostatic efficacy, and funding source) from the included the study.

Quality assessment / Risk of bias analysis: Two authors will independently evaluate the quality of included studies using the Cochrane risk of bias tool for randomized trials (RoB 2.0).

Strategy of data synthesis: We will provide a qualitative and quantitative synthesis of the evidence as follow: First: Pair-wise meta-analysis will be conducted to compare all direct comparisons using random-effects meta-analysis of our outcome (adequate hemostasis, entered as events per total) via the Review Manager Software version 5.3 (RevMan, Cochrane Collaboration). Second: Network meta-analysis will be conducted to compare all direct and indirect comparisons using the frequentist approach via the statistical package "netmeta" in the R program (version 4.0.2). We will pool the results as the odds ratio (OR) with a 95% confidence interval (CI). We will use the I2 statistics to assess the statistical heterogeneity that

reflects the variability of the total outcome based on the variability between studies, as I2<50% reflects low heterogeneity and I2≥50% significant heterogeneity. Also, the node splitting method will be used to calculate the inconsistency of the model. Finally, we will evaluate the certainty of cumulative evidence by the Confidence in Network Meta-Analysis (CINeMA) approach. The quality of evidence will be rated as high, moderate, low, or very low based on the following domains: study limitations, publication bias, indirectness, imprecision, heterogeneity, and incoherence.

Subgroup analysis: None.

Sensitivity analysis: If needed, sensitivity analysis will be done.

Language: English.

Country(ies) involved: Egypt, Canada, Italy.

Keywords: Bleeding, Endodontic surgery, Evidence-based dentistry, Hemostasis, Hemostatic agent, Systematic review, Network meta-analysis.

Dissemination plans: We will disseminate the findings of this review in a peer-reviewed journal.

Contributions of each author:

Author 1 - Ahmad G. A. Khater - The author has drafted the protocol and will work on study conceptualization, design, data collection, data analysis, draft the initial manuscript, and approve the final manuscript.
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Author 2 - Faez Saleh Al-hamed - The author has drafted the protocol and will work on study conceptualization, design, draft the initial manuscript, critically review the manuscript, and approve the final manuscript.
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