INPLASY PROTOCOL

To cite: Brito et al. Strategies for enamel remineralization. Overview about methodological quality. Inplasy protocol 2021100001. doi: 10.37766/inplasy2021.10.0001

Received: 01 October 2021

Published: 01 October 2021

Corresponding author: Ma. Auxiliadora Becerra

auxibecerra@hotmail.com

Author Affiliation: Universidad de Cuenca

Support: Self-financed.

Review Stage at time of this submission: Formal screening of search results against eligibility criteria.

Conflicts of interest: None declared.

Strategies for enamel remineralization. Overview about methodological quality

Brito, C1; Becerra, M2; Delgado, B3; Astudillo, D4; Wilson, B5.

Review question / Objective: P: Early enamel lesions; E: Enamel remineralization treatment; 0: Enamel remineralization What do we know so far about the clinical performance of effectiveness in the remineralization of incipient enamel lesions, using different therapeutic alternatives, as well as what is the general confidence of the systematic reviews evaluating this issue?

Condition being studied: Caries lesions manifest as white spots (LMB) on the enamel surface, which are a type of non-cavitated lesion, with an opaque and whitish appearance; These are located in fissures, pits or free surfaces of the teeth; and as the demineralization process progresses, the tooth surface cavitates; which generates aesthetic and functional problems. The early treatment of LMB is of great importance to maintain the integrity of the tooth, therefore, alternatives have been developed for remineralization, which consists of providing minerals from the surrounding environment to structures that are partially demineralized.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 October 2021 and was last updated on 01 October 2021 (registration number INPLASY2021100001).

INTRODUCTION

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alternatives, as well as what is the general confidence of the systematic reviews evaluating this issue?

Rationale: In recent years, several systematic reviews have been carried out evaluating the effectiveness of the different treatments for the remineralization of incipient enamel lesions, with promising

results compared to fluoride. However, there is no concordance of the results between the individual studies, which makes it difficult to integrate knowledge on the subject, generating a gap between research and decision-making. This research is a synthesis of knowledge that will facilitate the delivery of pertinent information, accessible to the clinician in a single document, facilitating the reading, understanding of the subject and the interpretation of the studies within a global context.

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METHODS

Search strategy: PUBMED P: "dental enamel"[MeSH Terms] OR Enamel Organ [Title/Abstract] OR Tooth demineralization [Title/Abstract] OR Enamel [Title/Abstract] OR "Enamel caries"[Title/Abstract] OR "Enamel demineralization"[Title/Abstract] OR white spot lesión [Title/Abstract] OR Incipient caries lesion [Title/Abstract] E: "toothpastes"[MeSH Terms] OR "phosphates"[MeSH Terms] OR "Arginine"[MeSH Terms] OR Casein phosphopeptide-amorphous calcium phosphate [Title/Abstract] OR Non-fluoride remineralization [Title/Abstract] OR tooth mousse [Title/Abstract] OR "GC tooth mousse"[Title/Abstract] "Recaldent"[Title/Abstract] OR "Remineralizing agents"[Title/Abstract] OR "Remineralization techniques"[Title/ Abstract] OR CPP-ACP [Title/Abstract] OR Self-assembling peptide P11-4 [Title/ Abstract] OR Nano-hydroxyapatite [Title/ Abstract] OR bioactive glasses [Title/ Abstract] OR Fluoride booster [Title/ Abstract] OR "fluorides"[MeSH Terms] OR "topical fluorides"[Title/Abstract] O: "fluorescence"[MeSH Terms] OR "remineralization"[Title/Abstract] OR remineralizing potential [Title/Abstract] OR "remineralization effect" [Title/Abstract] OR effectiveness remineralizing [Title/Abstract] OR enamel remineralization [Title/Abstract] OR "Surface roughness" [Title/Abstract] OR "Vickers microhardness"[Title/Abstract] OR "Knoop microhardness"[Title/Abstract] OR "Photographs"[Title/Abstract] OR "ICDAS"[Title/Abstract] OR effectiveness [Title/Abstract] OR efficacy [Title/Abstract] SCOPUS P: (TITLE-ABS-KEY ("dental enamel" OR "enamel organ" OR "tooth demineralization" OR "enamel" OR "enamel caries" OR "enamel demineralization" OR "white spot lesión" OR "incipient caries lesion")) AND E: (TITLE-ABS-KEY ("toothpastes" OR "phosphates" OR "Arginine" OR casein AND phosphopeptide AND amorphous AND calcium AND phosphate OR non-fluoride AND remineralization OR tooth AND mousse OR "GC tooth mousse" OR "Recaldent" OR "Remineralizing agents" OR "Remineralization techniques" OR "CPP-ACP" OR "Self-assembling peptide P11-4" OR "Nanohydroxyapatite" OR "bioactive glasses" OR "Fluoride booster" OR "fluorides" OR "topical fluorides")) AND O:: AND (TITLE-ABS-KEY ("fluorescence" OR "remineralization" OR "remineralizing potential" OR "remineralization effect" OR "effectiveness remineralizing" OR "enamel remineralization" OR "Surface roughness" OR "Vickers microhardness" OR "Knoop microhardness" OR "Photographs" OR "ICDAS" OR "effectiveness" OR "efficacy")) AND (TITLE-ABS-KEY ("Systematic Review")) WEB OF SCIENCE P: TEMA: (dental enamel) OR TEMA: (Enamel Organ) OR TEMA: (Tooth demineralization) OR TEMA: (Enamel caries) OR TEMA: (Enamel demineralization) OR TEMA: (white spot lesion) OR TEMA: (Incipient caries lesión) OR TEMA: (enamel) OR TEMA: (systematic review) E: TEMA: (dental enamel) OR TEMA: (remineralization) OR TEMA: (Casein

phosphopeptide-amorphous calcium phosphate) OR TEMA: (non-fluoride remineralization) OR TEMA: (tooth mousse) OR TEMA: (Recaldent) OR TEMA: (Remineralizing agents) OR TEMA: (Remineralization techniques) OR TEMA: (Nano-hydroxyapatite) OR TEMA: (Fluoride booster) OR TEMA: (fluorides) OR TEMA: (topical fluorides) OR TEMA: (systematic review) OR TEMA: (bioactive glasses) O: TEMA: (fluorescence) OR TEMA: (remineralization) OR TEMA: (remineralizing potential) OR TEMA: (remineralization effect) OR TEMA: (effectiveness remineralizing) OR TEMA: (enamel remineralization) OR TEMA: (surface roughness) OR TEMA: (Vickers microhardness) OR TEMA: (tooth demineralization) GOOGLE SCHOLAR P: In title:("enamel caries" OR "incipient caries lesion") E: AND("casein" "phosphopeptide" OR"CPP-ACP" OR "peptide P11-4" OR"fluorides") O: AND("remineralization" OR"effectiveness" OR"efficacy") AND("Systematic review").

Participant or population: Incipient enamel lesions in human permanent teeth.

Intervention: Use of fluorinated and non-fluorinated remineralizing compounds.

Comparator: Does not apply.

Study designs to be included: Systematic reviews of RCTs and in vitro studies.

Eligibility criteria: 1. Clearly established objectives with predefined eligibility criteria for the studies.2. A systematic search that attempts to identify all studies that meet the eligibility criteria.3. An explicit and reproducible methodology, 4. An assessment of the validity of the findings of the included studies, for example, through assessment of risk of bias.5. A systematic presentation and synthesis of the characteristics and findings of the included studies. There were no time or language restrictions. The exclusion criteria included:1.Studies with methodological designs other than systematic reviews (narrative reviews, rapid reviews, intervention studies, observational studies,

preclinical and basic research, summaries, comments, case reports, protocols, personal opinions, letters and posters).2. Studies evaluating the remineralization of enamel defects such as: hypomineralization and fluorosis.3. Studies evaluating the prevention of carious lesions not established.4. Studies evaluating restoration techniques on incipient lesions. 5. Studies that did not meet the minimum criteria for systematic reviews proposed by the Cochrane Handbook for Systematic Reviews.

Information sources: An electronic search was conducted on December 5, 2020 in four digital databases (Cochrane, PubMed, Scopus, Web of Science). Gray literature was also consulted through Google Scholar.

Main outcome(s): - Visual examination. - Light induced quantitative fluorescence. - Visual inspection (Gorelick criteria) of digital and quantitative photographs induced by fluorescence light. - Computerized image analysis. - Diagnodent transillumination. - International Caries Detection and Evaluation System II (ICDAS). - Average surface roughness (Vickers microhardness). - Surface microhardness (Knoop hardness).

Additional outcome(s): Does not apply.

Data management: The selection of the studies was carried out in two phases. In phase 1, the studies were independently selected by two reviewers by reading the title and abstract. Thereafter, phase 2 was carried out, which consisted of reading the full text, carried out independently by the two reviewers. A third reviewer was consulted in case of disagreements.

Quality assessment / Risk of bias analysis: The assessment of the methodological quality of the included systematic reviews (SR) was independently assessed in duplicate by two reviewers using the AMSTAR 2 checklist (AMeaSurement Tool for assessing systematic reviews). The AMSTAR 2 assesses the methodological

quality of the SR through 16 questions that can be answered with three possible answers: "yes", "no" or "partially yes.

Strategy of data synthesis: - Narrative synthesis. - Illustrative graphics. - Synthesis of data in tables. - Combination of data in color tables.

Subgroup analysis: Does not apply.

Sensitivity analysis: Does not apply.

Language: No limitation.

Country(ies) involved: Ecuador.

Keywords: Dental Enamel; Enamel Organ; Tooth Remineralization; Toothpastes; Casein phosphopeptide-amorphous calcium phosphate nanocomplex; Fluorides; Phosphates; Arginine; Fluorides Topical; White spot lesión.

Dissemination plans: Publication in scientific journal.

Contributions of each author:

Author 1 - Brito Christian - Data collection, data management, data analysis, protocol writing or review; provide financing.

Email: od_christiandavidbrito@outlook.com Author 2 - Becerra Ma. Auxiliadora - Data collection, data management, data analysis, protocol writing or review, providing funding.

Email: auxibecerra@hotmail.com

Author 3 - Delgado Bolivar - Conception of the review, design of the review, interpretation of data.

Email: andydg86@gmail.com

Author 4 - Astudillo Daniela - Conception of the review, interpretation of data.

Email: daniela.astudillor@ucuenca.edu.ec Author 5 - Bravo Wilson - Design of the data review, coordination of the data interpretation review.

Email: wilson.bravo@ucuenca.edu.ec