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Review; Efficacy of remineralization agents in arresting and reversing early carious lesions

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ABSTRACT
Dental caries is the most widespread chronic illness among children and adults globally, continuing to be the primary concern in dentistry. Dental caries is a complex, non-communicable illness characterized by biofilm mediation and dietary influence, leading to the net mineral loss of dental hard tissues. The contemporary understanding of caries development is founded on the repeated cycles of demineralization and remineralization, triggered by acidogenic bacteria inside the oral microenvironment. Dental remineralization is the process of depositing calcium and phosphate ions into the crystal gaps of demineralized enamel, resulting in a net mineral gain and inhibiting the advancement of early enamel diseases. The objective of the review was to qualitatively and quantitatively assess the remineralizing efficacy of various current treatments on simulated enamel defectsarresting and reversing early carious lesions.

Keywords: oral, microenvironment, phosphate, simulated.

INTRODUCTION

Notwithstanding advancements in dental care over recent decades, dental caries remains a pervasive global health issue impacting numerous children. The US Centers for Disease Control and Prevention indicates that 28% of all US toddlers and preschoolers are afflicted by caries, with over half of US children experiencing caries prior to entering kindergarten. Dental caries is the predominant chronic disease among US children aged 5-17, occurring at a rate five times greater than that of those afflicted with asthma [2]. Children from socially disadvantaged backgrounds, including those from impoverished homes and those with parents possessing low educational attainment, are disproportionately impacted. The incidence of dental caries is markedly elevated among children from lower socioeconomic backgrounds, rendering traditional dental care either inaccessible or prohibitively expensive. Furthermore, the deficiency of dental personnel and the advanced dental apparatus necessary render traditional restorative care an inadequate solution to the issue of caries. Consequently, alternative interventions for pediatric dental caries in underprivileged areas are essential, and professionally administered fluoride therapy has been suggested for the treatment of dental caries [4].
The modern philosophy of caries care has shifted from a conventional surgical approach to a medical model, with fluoride therapy employed not only for prevention but also for the arrest of caries. Professionally administered fluoride therapy is a cost-effective and straightforward treatment that has been utilized to halt active tooth cavities. Fluoride impedes enamel demineralization. Calcium fluoride produced on a tooth surface during fluoride therapy is not easily soluble and can serve as a fluoride reservoir [5]. This fluoride can also reduce the critical pH value for the breakdown of hydroxyapatite crystals, or the pH at which demineralization occurs, from around 5.5 to 4.5 in the oral cavity. Fluoride can be gradually integrated into fluorapatite crystals

on the tooth surface, enhancing its resistance to acid disintegration. Fluoride not only prevents demineralisation but also accelerates enamel remineralisation, augmenting both the rate of the remineralisation process and the mineral content of incipient carious lesions. The addition of fluoride renders the deposited mineral less soluble in acid. While the precise method by which fluoride prevents caries remains unclear, it is well acknowledged that topically applied fluorides influence tooth surfaces. Fluoride impedes plaque metabolism, modifies plaque composition, influences plaque formation, and diminishes the capacity of plaque bacteria to generate substantial acid from carbohydrates [6].

Timely and precise identification of caries and evaluation of lesion advancement are crucial to avert additional harm to the tooth structure. Recent investigations have concentrated on remineralizing early carious lesions with particular drugs, therefore regulating the degree of demineralization [7]. Demineralization is the process by which minerals are lost from tooth structure. Remineralization involves the incorporation of hydroxyapatite crystals into the dental structure. Artificial agents facilitate remineralization by forming a supersaturated layer over an incipient lesion. This inhibits the leaching of minerals and compels calcium and phosphate ions into the vacancies. These compounds typically comprise calcium phosphate, with or without fluoride. The remineralization process halts or reverses the chemical degradation of enamel without employing restorative materials. In children, demineralization occurs more significantly at low oral pH, whereas remineralization at normal oral pH is less pronounced compared to adults [7].

Review

Diverse types and formulations of fluoride compounds in varying concentrations are employed in dentistry. Numerous studies have demonstrated its efficacy in reducing dental cavities in children and adolescents [8].

The bacterial breakdown of fermentable carbohydrates generates acids that lead to the dissolution of mineral ions, including calcium and phosphate, which constitute enamel hydroxyapatite crystals [9]. Consequently, enamel demineralization might render the dentine susceptible to dentinal hypersensitivity associated with fluid migration in dentinal tubules and the initiation of caries disease. Nonetheless, the demineralized enamel prism may revert to its original state when subjected to oral conditions conducive to remineralization [9].

Furthermore, tooth decay is significantly avoidable and reversible in its first stages, and the cessation of enamel and dentin demineralization can be achieved through the prevention of biofilm development and the action of salivary protective factors. Recent advancements in caries research have concentrated on creating approaches for the non-invasive therapy of early carious lesions by remineralization to maintain tooth integrity [10]. Remineralization can occur naturally via the saliva buffering system or biologically through the application of remineralizing chemicals.

The scientific literature substantiates that demineralization can be mitigated or reversed by various remineralization agents in non-cavitated carious lesions [9,10]. Various types and quantities of remineralizing agents containing fluoride, calcium, and phosphate ions are available for commercial use. These agents emit active ions that securely attach to the crystalline enamel structures, resulting in the formation of new crystals and the repair of broken ones [11].

The age of preventive and minimally invasive dentistry necessitates the formulation of novel strategies to remineralize early enamel defects. Currently, numerous treatments containing bioavailable calcium, phosphate, and fluoride are extensively utilized to remineralize enamel and mitigate dentin hypersensitivity, available in the forms of toothpastes, mouth rinses, and gels [12].

Fluoride ions serve as the primary mechanism for inhibiting enamel demineralization by facilitating the synthesis of fluorapatite in enamel, in conjunction with calcium and phosphate ions released during demineralization caused by organic acids from plaque bacteria. Fluoride solutions are available in low concentrations for daily use, including toothpastes and mouthwashes, and in greater concentrations for professional application, such dental gels and varnishes. Additionally, various calcium and phosphate compounds, including casein phospho-peptide and amorphous calcium phosphate (CPP-ACP) as well as biomimetic hydroxyapatite, have demonstrated encouraging outcomes. CPP-ACP, a derivative of milk protein, was commercially launched due to its demonstrated anticariogenic properties [14]. CPP stabilizes elevated levels of calcium and phosphate ions in conjunction with fluoride ions at the tooth surface by adhering to the pellicle and plaque. ACP administers calcium ions (e.g., calcium sulfate) and phosphate ions (e.g., ammonium phosphate, occasionally alongside fluoride ions) individually to facilitate the formation of ACP or amorphous calcium fluoride phosphate (F-ACP) intra-orally. Research indicates that CPP-ACP application can inhibit demineralization and promote remineralization via calcium and phosphate ion interactions, thereby stabilizing ACP in dental plaque under neutral or alkaline pH conditions and preserving a state of supersaturation concerning enamel [15].

A significant source of mineral ions for remineralization is nano-hydroxyapatite (N-HA), characterized by crystals measuring between 50 and 1000 nm. N-HA exhibited characteristics akin to those of biological apatite. The N-HA has a distinctive bonding capacity due to the dimensions of nanoparticles, which significantly enhance the bonding surface area, facilitating the attachment of accessible calcium or phosphate ions to the

enamel surface and occluding the porosities of carious lesions. N-HA crystals infiltrate enamel pores and serve as a template throughout the precipitation process, enhancing crystal integrity and growth [15].

Since the discovery of fluoride's cariostatic actions, caries prevention has predominantly depended on fluoride ions' capacity to impede enamel disintegration and promote the remineralization of incipient lesions. Gao et al. demonstrated that a 5% SF varnish can remineralize incipient carious lesions, rendering this approach a significant method for preventing enamel demineralization [16]. G3, coated with a varnish containing 5% SF, exhibited minor remineralization; however, the Ca/P ratio (1.88 ± 0.06) is marginally elevated compared to G6 (1.74 ± 0.04) and demonstrates a statistically significant difference from all other groups. Our analysis demonstrated that after seven days of treatment, 5% SF is less effective than the other tested remineralizing products [16].

Casein phosphopeptide-amorphous calcium phosphate serves as a non-invasive approach to inhibit demineralization and facilitate the remineralization of initial enamel lesions. The tailored toothpaste can prevent demineralization and promote remineralization, therefore halting carious lesions in their initial phase. Additional in vivo investigations are necessary to evaluate the effectiveness of tailored dentifrice on the remineralization of incipient carious lesions. Should the study results prove favorable, the tailored dentifrice may serve as an alternative to conventional dentifrices. A cost-effective remineralizing agent can be created. Results may be contributed to the scientific literature [16].

A meta-analysis would yield more credible and less biased results due to the incorporation of numerous research [17]. It yields more trustworthy estimates by synthesizing data from multiple independent research and doing a statistical analysis of diverse outcomes. Meta-analysis, while extensively utilized for aggregating data from several clinical studies, necessitates that the trials employ comparable outcome measurements and maintain consistency in result presentation. Certain clinical trials cannot be chosen due to discrepancies in outcome assessments. Furthermore, standardizing all published clinical trials is challenging, and the impact of variability among trials remains ambiguous [17].

Despite the systematic review being conducted using four prominent databases, the quantity of clinical trials incorporated was limited. Furthermore, the methodologies and outcome measurements differed among the research, complicating comparisons. Consequently, not all chosen studies could be incorporated into the meta-analysis. The baseline prevalence of caries varied among the studies. Consequently, the quantity of apprehended caries was excluded from analysis in this evaluation. This study utilized the ratio of remineralized early enamel caries and halted dentine caries for meta-analysis. The risk of bias for each study was assessed using six criteria as outlined in the Cochrane Handbook of Systematic Reviews of Interventions [18]. In certain trials, blinding of outcome assessment and allocation concealment were either not implemented or not reported by the researchers. Some studies had a limited sample size, and others failed to provide the statistical methodology for sample size computation or to justify the sample size employed. Furthermore, clinical trials yielding positive results typically have a greater likelihood of publication compared to those with inconsequential outcomes. This publishing bias may cause reviewers to reach a favorable judgment. In this review, two independent reviewers (SSG and SZ) conducted a literature screening independently, employing well stated inclusion criteria to mitigate selection bias.

CONCLUSION

Caries is the most widespread chronic noncommunicable disease. Strategies to prevent start and early therapies to halt the advancement of first lesions have been emphasized in recent decades to avoid or postpone the restorative cycle of the tooth. An increasing number of persons are preserving their natural teeth into advanced age, thus requiring continuous restorative dental care for their upkeep. The initial surface of enamel demineralization can be addressed using topical remineralizing agents, resulting in nearly full remineralization and restructuring of the enamel's prismatic structure. Carious lesions result from oral bacteria metabolizing eaten carbohydrates, producing organic acids and enzymes that promote demineralization of tooth structures, ultimately leading to cavitation or additional deterioration of the damaged teeth.

REFERENCES

1. Dye BA, Tan S, Smith V, Lewis B, Barker L, Thornton-Evans G, et al. Trends in oral health status: United States, 1988-1994 and 1999-2004. Vital and health statistics. Series 11, Data from the national health survey, 2007(248):1-92.
2. Bagramian RA, Garcia-Godoy F, Volpe AR. The global increase in dental caries. A pending public health crisis. Am J Dent. 2009;22(1):3–8.
3. Chu C-H, Ho P-L, Lo EC. Oral health status and behaviours of preschool children in Hong Kong. BMC Public Health. 2012;12(1):767. doi: 10.1186/1471-2458-12-767.
4. Chu C, Lo E. Promoting caries arrest in children with silver diamine fluoride: a review. Oral Health Prev Dent. 2008;6(4):315–321.

5. Chu C, Mei ML, Lo E. Use of fluorides in dental caries management. Gen Dent. 2009, 58(1):37-43; quiz 44-35, 79-80.
6. Mei ML, Chu CH, Low KH, Che CM, Lo EC. Caries arresting effect of silver diamine fluoride on dentine carious lesion with S. mutans and L. acidophilus dual-species cariogenic biofilm. Med Oral Patol Oral Cir Bucal. 2013;18(6):e824. doi: 10.4317/medoral.18831.
7. Balakrishnan A, Jonathan R, Benin P, et al. Evaluation to determine the caries remineralization potential of three dentifrices: an in vitro study. J Conserv Dent. 2013;16(4):375–379. doi: 10.4103/0972-0707.114347.
8. Marinho V.C.C., Chong L.Y., Worthington H.V., Walsh T. Fluoride Mouthrinses for Preventing Dental Caries in Children and Adolescents. Cochrane Database Syst. Rev. 2016;7:CD002284. doi: 10.1002/14651858.CD002284.pub2.
9. Abou Neel E.A., Aljabo A., Strange A., Ibrahim S., Coathup M., Young A.M., Bozec L., Mudera V. Demineralization-Remineralization Dynamics in Teeth and Bone. Int. J. Nanomed. 2016;11:4743–4763. doi: 10.2147/IJN.S107624.
10. Kim M.-J., Lee M.-J., Kim K.-M., Yang S.-Y., Seo J.-Y., Choi S.-H., Kwon J.-S. Enamel Demineralization Resistance and Remineralization by Various Fluoride-Releasing Dental Restorative Materials. Materials. 2021;14:4554. doi: 10.3390/ma14164554.
11. Selwitz R.H., Ismail A.I., Pitts N.B. Dental Caries. Lancet. 2007;369:51–59. doi: 10.1016/S0140-6736(07)60031-2.
12. Roles of physicians, and nurses in the management approve of systemic lupus erythematosus; Review
13. Nakagiri A., Imamura K., Yanagisawa K., Onda A. The Role of the Surface Acid-Base Nature of Nanocrystalline Hydroxyapatite Catalysts in the 1,6-Hexanediol Conversion. Nanomaterials. 2021;11:659. doi: 10.3390/nano11030659.
14. Orilisi G., Tosco V., Monterubbianesi R., Notarstefano V., Özcan M., Putignano A., Orsini G. ATR-FTIR, EDS and SEM Evaluations of Enamel Structure after Treatment with Hydrogen Peroxide Bleaching Agents Loaded with Nano-Hydroxyapatite Particles. PeerJ. 2021;9:e10606. doi: 10.7717/peerj.10606.
15. Thimmaiah C., Shetty P., Shetty S.B., Natarajan S., Thomas N.-A. Comparative Analysis of the Remineralization Potential of CPP-ACP with Fluoride, Tri-Calcium Phosphate and Nano Hydroxyapatite Using SEM/EDX-An in Vitro Study. J. Clin. Exp. Dent. 2019;11:e1120–e1126. doi: 10.4317/jced.55941.
16. Gao S.S., Zhang S., Mei M.L., Lo E.C.-M., Chu C.-H. Caries Remineralisation and Arresting Effect in Children by Professionally Applied Fluoride Treatment-A Systematic Review. BMC Oral Health. 2016;16:12. doi: 10.1186/s12903-016-0171-6.
17. Wong AW, Zhang C, Chu C-h. A systematic review of nonsurgical single-visit versus multiple-visit endodontic treatment. Clin Cosmet Investig Dent. 2014;6:45. doi: 10.2147/CCIDE.S61487.
18. Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions, vol. 5: Wiley Online Library; 2008.