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MARIA CLARA FARIA POLI

Análise *in vitro* do potencial remineralizador de formulações dentifrícias contendo trimetafosfato de cálcio e sódio em lesões de cárie em dentina

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MARIA CLARA FARIA POLI

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Dissertação apresentada à Faculdade de Odontologia de Araçatuba da Universidade Estadual Paulista (UNESP), como parte dos requisitos para a obtenção do título de Mestra em Ciências na Área de Concentração de Saúde Bucal da Criança.

Orientador: Prof. Dr. Alberto Carlos Botazzo Delbem

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“Os seus cargos são temporários, os títulos que tem são provisórios, mas a maneira como você trata as pessoas sempre será lembrada.”

Autor desconhecido

RESUMO

Poli, MCF. **Análise *in vitro* do potencial remineralizador de formulações dentifrícias contendo trimetafosfato de cálcio e sódio em lesões de cárie em dentina**. 2024. Dissertação (Mestrado) – Faculdade de Odontologia, Universidade Estadual Paulista (UNESP), Araçatuba, 2024.

O objetivo do presente estudo foi avaliar a capacidade de dentifrícios contendo apenas diferentes concentrações de trimetafosfato de cálcio e sódio (CaNaTMP) em promover a remineralização de lesões de cárie artificais em dentina em um modelo *in vitro*. Para tanto, foi feito inicialmente a síntese e caracterização do CaNaTMP e 60 blocos de dentina radicular bovina foram preparados nas dimensões 4 mm x 4 mm x 2 mm e selecionados por dureza de superfície e lesões de cárie artificial foram induzidas em dois terços da superfície por meio de um protocolo de 7 dias. Assim, os blocos com cárie artificial foram divididos aleatoriamente em 5 grupos/dentifrícios experimentais (n = 12): 1) sem F/NaCaTMP (Placebo-controle negativo); 2) contendo 1100 ppm F (controle positivo); 3) contendo 0,25% de CaNaTMP; 4) contendo 0,5% de CaNaTMP; e 5) contendo 1% de CaNaTMP. Para o tratamento, os blocos de dentina foram submetidos a ciclagem de pH de 7 dias e ao tratamento com suspensão aquosa dos dentifrícios experimentais durante 1 minuto, 2 vezes ao dia. A concentração mineral ($g_{Hap} \times cm^{-3}$) foi determinada por microtomografia computadorizada de raios-X. Os dados obtidos foram submetidos à ANOVA seguida do teste de Student-Newman-Keuls ($p<0,05$). A incorporação de 0,5% e 1% de CaNaTMP em dentifrícios promoveu efeito remineralizador superior ao dentifrício convencional, dose-dependente, em cárie dentinária artificial. O tratamento com 1% CaNaTMP levou a menor perda mineral e reduziu a profundidade das lesões quando comparado ao dentifrício fluoretado ($p < 0,001$). Dessa forma, conclui-se que dentifrícios contendo 0,5% e 1% de CaNaTMP mostraram maior capacidade remineralizadora de lesões artificiais de cárie em dentina, sugerindo que podem ser uma alternativa terapêutica eficaz para melhorar a saúde bucal de todos os indivíduos, especialmente aqueles com alto risco e/ou atividade de cárie e crianças em idade precoce.

Palavras-chave: Cárie Dentária; Dentifrícios; Remineralização Dentária; Dentina.

ABSTRACT

Poli, MCF. ***In vitro* analysis of the remineralizing potential of dentifrice formulations containing calcium and sodium trimetaphosphate in dentin caries lesions.** 2024. Dissertação (Mestrado) – Faculdade de Odontologia, Universidade Estadual Paulista (UNESP), Araçatuba, 2024.

The objective of the present study was to evaluate the ability of dentifrices containing only different concentrations of calcium and sodium trimetaphosphate (CaNaTMP) to promote remineralization in artificial caries lesions in dentin in an *in vitro* model. To this end, the synthesis and characterization of CaNaTMP was initially carried out and 60 blocks of bovine root dentin were prepared in dimensions 4 mm x 4 mm x 2 mm and selected by surface hardness and artificial caries lesions were induced on two thirds of the surface by through a 7-day protocol. Thus, the blocks with artificial caries were randomly divided into 5 groups/experimental toothpastes (n = 12): 1) without F/NaCaTMP (Placebo-negative control); 2) containing 1100 ppm F (positive control); 3) containing 0.25% CaNaTMP; 4) containing 0.5% CaNaTMP; and 5) containing 1% CaNaTMP. For treatment, the dentin blocks were subjected to pH cycling for 7 days and treatment with an aqueous suspension of the experimental dentifrices for 1 minute, twice daily. Mineral concentration ($g_{Hap} \times cm^{-3}$) was determined by X-ray microcomputed tomography. Data were subjected to ANOVA followed by Student-Newman-Keuls test ($p < 0.05$). The incorporation of 0.5% and 1% of CaNaTMP in dentifrices promoted a remineralizing effect superior to conventional dentifrice, dose-dependently, in artificial dentin caries. Treatment with 1% CaNaTMP resulted in the lowest mineral loss and reduced lesion depth compared to fluoridated toothpaste ($p < 0.001$). Therefore, it is concluded that dentifrices containing 0.5% and 1% CaNaTMP showed greater remineralizing capacity for artificial caries lesions in dentin, suggesting that they can be an effective therapeutic alternative to improve the oral health of all individuals, especially those with high risk and/or caries activity and children at an early age.

Keywords: Dental Caries; Toothpastes; Dental Remineralization; Dentin.

Sumário

1. Introduction

Dental caries is one of the highly prevalent diseases worldwide, with an estimated 600 million children affected by it, considered by the American Academy of Pediatric Dentistry as the most common oral disease in childhood (Moraes et al., 2021; Pitts et al., 2019). The development of caries is influenced by various factors, mediated by biofilm and modulated by diet, and, in molecular terms, it occurs due to the loss of hydroxyapatite structure. Specifically, the metabolic action of dietary carbohydrates by bacteria present in the oral cavity causes an initial decrease in the pH of the oral environment and promotes an imbalance between remineralization and demineralization processes, favoring the demineralization of dental structure (Díaz et al., 2024; O'Hagan-Wong et al., 2021).

In the treatment of caries lesions, the use of fluoride (F) is a well-established strategy to prevent and inhibit demineralization, as well as to favor the remineralization process, with effective responses in dental enamel (Choi et al., 2023; Caravalho et al., 2024), with the use of fluoride being considered the main reason for the reduction in caries prevalence observed in recent decades. However, fluoride as the sole means of prevention and remineralization does not provide a complete solution, as fluorides are limited only to the superficial remineralization of carious lesions and by the availability of calcium and phosphate ions (Gonçalves et al., 2018; O'Hagan-Wong et al., 2021; Nunes et al., 2022). Additionally, in dentin tissue, the complexity of lesion arrest and remineralization process is expanded by the heterogeneity and dynamics of dentin, where organic components such as matrix metalloproteinases and cysteine-cathepsins (Dias et al., 2023; Nunes et al., 2022) play an important mechanical and biological role (Gonçalves et al., 2018).

It is already known that when caries affects dentin, mineral loss, and collagen breakdown are events that lead to substrate alteration, even impacting adhesive restorative procedures. Therefore, strategies adopted in dentin substrates must allow for the arrest of demineralization and not interfere with the restorative process; they must also preserve and stabilize the dentin collagen matrix, which is essential for the remineralization process, as it provides support for mineral deposition in the presence of non-collagenous proteins [Toledano et al., 2022; Tao et al., 2022]. Therefore, to enhance the preventive potential of fluoride, especially in dentin tissue, there has been a quest for strategies that minimize damage to dentin and are focused on preserving collagen fibrils and promoting structured remineralization.

Among biomimetic and remineralizing agents, sodium trimetaphosphate (NaTMP) is an inorganic cyclic polyphosphate that has been widely tested in fluoride vehicles, mainly in with high caries risk and/or activity.

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