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Anticaries effect of low-fluoride dentifrices with phosphates in children: A randomized, controlled trial

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ABSTRACT

Low-fluoride dentifrices (LFD) have been recommended for young children aiming to minimize excessive fluoride intake during tooth brushing. Given the uncertainties surrounding the clinical efficacy of such formulations, alternatives to increase their anticaries effect have been investigated.

Objectives: This double-blind, randomized controlled trial assessed the clinical efficacy of LFDs supplemented with Calcium Glycerophosphate (CaGP) or Sodium Trimetaphosphate (TMP) on the progression of dental caries in the deciduous dentition.

Methods: Children (average age 48 months old) from two Brazilian cities (Araçatuba and Fernandópolis) were randomly assigned into 3 groups, according to the dentifrice to be used: 500 ppm F plus 1% TMP ("500TMP", n = 206), 500 ppm F plus 0.25% CaGP ("500CaGP, n = 201) and 1100 ppm F ('1100F', n = 193). Clinical exams (dmfs) were performed at baseline and 18 months after dentifrices started to be used, and the increment in the number of carious lesions (final dmfs – initial dmfs) was calculated. Data were analyzed by multivariate linear regression analysis to verify the influence of city, gender, previous caries experience and type of dentifrice on dmfs increment ($p < 0.05$).

Results: Mean caries increment observed for 500TMP (0.26) was significantly lower when compared with 1100F (0.74), while values found for 500CaGP (0.54) were not significantly different from 1100F. Caries increment was significantly higher in children from Araçatuba and in those with previous caries experience.

Conclusion: The results indicate that clinical efficacy of LFDs supplemented with TMP is superior to that observed for a conventional formulation (1100F), while the addition of CaGP leads to similar efficacy when compared to 1100F.

Clinical Significance: Children brushing with 500 ppm F toothpastes containing phosphate salts developed fewer caries lesions when compared with those using a 1100 ppm F dentifrice. The tested toothpastes can be regarded as a safe alternative to conventional formulations for children under 6 years of age, based on risk-benefit considerations.

1. Introduction

The decrease in caries incidence and prevalence observed around the world has been mainly attributed to the consumption of fluoridated water and to the regular use of fluoridated dentifrices [1,2]. The widespread use of dentifrices, however, has been associated to the increase in the prevalence of dental fluorosis, especially when products containing 1000 ppm F or above are used by children under 5–6 years of age [3].

Alternatives for reducing the amount of fluoride ingested include the reduction of the amount of dentifrice loaded on the toothbrush, as well as the supervision of children during toothbrushing regarding the amount of toothpaste used and the need to expectorate after brushing. Given that these measures depend primarily on patient's and caregivers' compliance, the impact of such strategies on fluoride intake is uncertain, so that the use of low-fluoride dentifrices (LFDs) by children under 6 years of age has been proposed [4,5]. Nevertheless, considering the lack of scientific consensus regarding the anticaries efficacy of these formulations when compared to conventional dentifrices

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(1000–1100 ppm F), alternatives as the reduction of the pH [6–8] or the addition of polyphosphate salts [9,10] to LFDs have been investigated.

The addition of sodium trimetaphosphate (TMP) to a LFD (500 ppm F) was shown to significantly reduce enamel mineral loss when compared to a conventional dentifrice *in vitro* [9,11] and *in situ* [12]. Similarly, the addition of calcium glycerophosphate (CaGP) to a LDF promoted similar anticaries effect to that attained after using a conventional dentifrice, according to *in vitro* [10] and *in situ* [13,14] studies. Despite the promising results reported for TMP- and CaGP-containing toothpastes, no clinical evidence is still available to attest the anticaries effects of LFDs supplemented with phosphate salts on the progression of caries lesions.

Therefore, the aim of the present study was to assess the anticaries efficacy of LFDs supplemented with TMP or CaGP on the primary dentition, in a randomized, controlled trial. Based on the above-mentioned *in vitro* and *in situ* data, the study's hypothesis was that the clinical efficacy of the LFDs containing phosphates would be similar or superior to that obtained after using a conventional formulation. The American Dental Association criteria for determination of efficacy in product evaluation were adopted [15].

2. Material and methods

2.1. Study design

This randomized clinical trial was approved by the IRB of Araçatuba Dental School (Protocol 2006-014112). The study population comprised children between 18 and 60 months old, attending public kindergartens of 2 cities of the State of São Paulo, Brazil. The aims were detailed explained to parents/caregivers and signed informed consent was obtained prior to the beginning of the study. Children were randomly assigned into 3 treatment groups, according to the dentifrice to be used, following a double-blind protocol. Parents/caregivers and children were instructed on oral hygiene procedures, brushing frequency and amount of dentifrice to be used. Caries status (dmfs) was determined at the beginning of the study and 18 months after using the dentifrices.

2.2. Study areas

The study was conducted in two cities of the State of São Paulo (Southeast macro region of Brazil): (1) Araçatuba, latitude 21°12′32" south and longitude 50°25′58" west, mean annual temperature 27.0 °C, Human Development Index 0.848 and mean fluoride concentration in the public water supply of 0.7 mg/L; (2) Fernandópolis, latitude 20°17′02″ south and longitude 50°14′47″ west, mean annual temperature 25.5 °C, Human Development Index 0.823 and mean fluoride concentration in the public water supply of 0.7 mg/L.

2.3. Sample size determination and selection of volunteers

Based on a pilot study assessing dmfs scores in 50 children from 18 to 60 months old (mean = 0.1, SD = 0.48), a sample size of 125 children for each treatment group was determined ($\alpha = 0.05$ e $\beta = 0.2$), considering a dropout rate of 20% at the end of the clinical trial.

The inclusion criteria were: (1) being a resident of Araçatuba or Fernandópolis; (2) age between 18 and 60 months old; (3) parents should sign the informed consent document; (4) children should present good general health status and not taking medicines likely to interfere with salivary flow and/or biofilm formation; and (5) not having participated in another clinical trial at least 3 months prior to the beginning of the study. The exclusion criteria were: (1) voluntary withdrawal; (2) use of mouthrinses or dentifrices different to those provided by the researchers; and (3) not following up the experimental protocol (assessed by periodic visits to kindergartens). Children were selected from public kindergartens from urban areas of the 2 above-mentioned cities, totaling 747 children from 15 kindergartens which were randomly selected from a list provided by the Education Department of each city. Among those, informed consent was obtained from 600 children who fulfilled the inclusion criteria. For random allocation to the groups, classrooms were considered as units of draw (conglomerate sampling), by simple drawing using the Microsoft Excel software, so that only 1 type of dentifrice was distributed in each classroom. Allocation was done by one investigator not involved in the clinical examinations (ACBD). This planning facilitated the controlled delivery and collection of the dentifrices by the classroom's teacher, as well as daily supervised toothbrushing at school. The flowchart with the distribution of children at the beginning and at the end of the study is presented in Fig. 1.

2.4. Dentifrice formulation

Experimental dentifrices contained the following components: titanium dioxide, carboxymethylcellulose, methyl-*p*-hydroxybenzoate, sodium saccharin, Tutti-frutti flavoring, glycerol, hydrated silica, sodium lauryl sulfate, and water. Sodium fluoride (NaF, Merck®, Darmstadt, Germany) was added to the formulations at 500 μg F/g (test dentifrices) and 1100 μg F/g (positive control). Sodium trimetaphosphate (TMP, Sigma™–Aldrich Co., USA) or Calcium glycerophosphate (CaGP, Sigma™–Aldrich Co., USA, dl, 50% α- and 50% β-isomer) were added to the 500 μg F/g formulations at concentrations of 1% and 0.25%, respectively. Prior to the beginning of the study, dentifrices were submitted to laboratory tests regarding their composition, pH, density, foaming ability, abrasiveness, consistency, rheological properties, concentration of fluoride, calcium and phosphate, as well as toxicological and microbiological tests, performed by the Brazilian Dental Association (Associação Brasileira de Odontologia – ABO) and by BITUFO Dental Products (Industry and commerce, Itupeva, SP, Brazil). All dentifrices were identical regarding their color, taste and appearance of the tube, and were coded by one author not involved in the clinical examinations (ACBD) so that the protocol was double-blind (children and examiners).

2.5. Study protocol

At the beginning of the study, school directors, teachers, and children's parents were instructed about the study protocol. Parents were asked to brush their children's teeth for 1 min at least twice a day at home (in the morning and before going to bed), with no restrictions regarding rinsing procedures. The amount of dentifrice to be used was standardized as the size of a rice grain ("smear"). For standardization of brushing procedures and the amount of dentifrice to be used, parents/caregivers were also instructed during a lecture.

Kits for oral hygiene contained 1 children's toothbrush, 4 dentifrice tubes (50 g each) and 1 leaflet about oral hygiene care and compliance need, which were replaced every three months. Compliance was facilitated by supplying the dentifrices to all family members, in order to guarantee that children would use the experimental dentifrice. Moreover, extra kits were available at the schools if families needed them to be replaced prior to the regular quarterly supplying periods. Besides the kits for home use, toothbrushes and dentifrices were also available for use at kindergartens, for toothbrushing once/day after the main meal.