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Fluoride kinetics in saliva after the use of a fluoride-containing chewing gum

Cinética de flúor na saliva após o uso de uma goma de mascar fluoretada

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ABSTRACT: There is a relationship between the use of fluoride, the reduction of dental caries and the increase of dental fluorosis. The purpose of this study was to analyze the fluoride kinetics in saliva after using the Happydent™ chewing gum, which contains 3.38 mg of fluoride as monofluorophosphate. Fifteen 7-9-year-old volunteers were instructed to chew the gum Trident™ (control) and Happydent™ on different days. Total saliva was collected for 3 minutes, at 0, 3, 6, 9, 15, 30 and 45 minutes after starting chewing. Salivary fluoride was analyzed with a fluoride-specific electrode (Orion 96-09) after acid hydrolysis. The data were analyzed by two-way analysis of variance and by Tukey's *post hoc* test ($p < 0.05$). The mean amounts ± sd (mg) of fluoride released in saliva were 0.276 ± 0.126 and 0.024 ± 0.014 for Happydent™ and Trident™ respectively. The fluoride amount in the saliva samples after the use of Happydent was significantly higher than after the use of Trident™ in all experimental periods, except after 30 and 45 minutes. The high fluoride presence in saliva after the use of Happydent may be significant to prevent dental caries and this should be evaluated in clinical researches. On the other hand, children at an age of risk for dental fluorosis should avoid the use of Happydent™.

DESCRIPTORS: Chewing gum; Dental caries; Fluorides; Fluorosis, dental.

RESUMO: Há uma relação entre o uso de fluoretos, a redução na cárie e o aumento da fluorose dentária. O objetivo deste estudo foi analisar a cinética do flúor na saliva após o uso da goma de mascar Happydent®, que contém 3,38 mg de flúor como monofluorfosfato. A saliva foi coletada de 15 voluntários entre 7 e 9 anos de idade, durante 3 minutos nos intervalos de 0, 3, 6, 9, 15, 30 e 45 minutos. Inicialmente, a coleta foi realizada com o Trident® (controle) e, após 24 h, a coleta foi repetida com a goma de mascar Happydent®. O flúor foi analisado com um eletrodo íon-específico (Orion 96-09) após a realização da hidrólise ácida. Os dados foram analisados através da análise de variância a dois critérios e pelo teste de Tukey ($p < 0,05$). A quantidade média ± dp (mg) de flúor liberado na saliva foi 0,276 ± 0,126 e 0,024 ± 0,014 para o Happydent® e o Trident®, respectivamente. A quantidade de flúor nas amostras de saliva após o uso do Happydent® foi significativamente maior do que após o uso do Trident® em todos os tempos experimentais, com exceção dos períodos de 30 e 45 minutos. A alta quantidade de flúor na saliva após o uso do Happydent® poderia ser eficiente na prevenção da cárie dentária, o que deveria ser avaliado clinicamente. Por outro lado, essa goma de mascar deveria ser evitada por crianças na idade de risco para a fluorose dentária.

DESCRITORES: Goma de mascar; Cárie dentária; Fluoretos; Fluorose dentária.

INTRODUCTION

Dental caries is a multifactor disease and one of the main public health problems. As a result of several studies carried out to understand the dental caries process as well as its risk factors, dental treatment emphasis has been moved from corrective to preventive methods. Fluoride is an extensively proven effective agent for the control of dental caries. Its cariostatic effect is related to its presence in the aqueous phase of the apatite crystals[8,20,24], which inhibits demineralization and activates remineralization[1].

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There are many studies supporting the frequent and repetitive use of low concentration and self-applied fluoride agents[4,7], stimulating the search for alternative devices to apply it in the mouth, such as professional products, at high fluoride concentrations (solutions, gels, pastes and varnishes) or through home care products, like toothpastes, mouth washes and, more recently, chewing gums[14,20].

The use of chewing gum increases the salivary flow, which helps to clean the oral cavity[11]. Chewing gums have been also introduced as useful vehicles for fluoride, calcium, phosphate and chlorhexidine delivery[23]. Fluoride-containing chewing gums increase salivary and dental plaque pH, calcium and phosphate concentration and also act on enamel remineralization[12].

The chewing gum Happydent™ was recently introduced in the Brazilian marketplace as an additional agent to prevent dental caries. Each piece of the product contains 3.38 mg of fluoride as monofluorophosphate. Despite the possibility of helping to prevent dental caries, a concern arises about its contribution as an additional source of fluoride intake when consumed by children in the age of risk for dental fluorosis. Thus, the aim of the present study was to analyze the amount of fluoride released in saliva after chewing the gum Happydent™.

MATERIAL AND METHODS

Experimental design

The study was carried out with fifteen 7-9 year-old children, living in Bauru, state of São Paulo, Brazil, a city which is supplied with optimally fluoridated water. All of them had good oral and general health, and normal salivary flow. The protocol was reviewed by the Institutional Review Board of the Bauru Dental School, University of São Paulo, and the parents signed an informed consent.

Prior to the beginning of the experiment, the children used a non-fluoridated toothpaste for seven days (washout period).

This blind study was accomplished on two separate days, with a 24 hour interval. In the first day, the control chewing gum (Trident™, Adams, Bauru, Brazil), containing no fluoride, was used, and in the second day the children chewed the fluoridated gum (Happydent™, Perfetti Van Melle, Vinhedo, Brazil), containing 3.38 mg of fluoride as monofluorophosphate. Both the control and the experimental chewing gums were purchased in Bauru, São Paulo, Brazil.

In both days, the whole stimulated saliva was collected in cooled plastic containers for 3 min at 0, 3, 6, 9, 15, 30, and 45 min after starting chewing. During this period, the volunteers remained seated and were not allowed to have any food or drink. The samples obtained were stored at –18°C until fluoride analysis.

Fluoride analysis

Acid hydrolysis

The acid hydrolysis of fluoride was done because Happydent™ contains fluoride as monofluorophosphate. The method used was adapted from the method proposed by Cury[6] (1987) modified by Orth *et al.*[16] (2001) for the analysis of monofluorophosphate in saliva after using a dentifrice containing monofluorophosphate. To 0.25 ml of each saliva sample, 0.25 ml of 2 mol L^{-1} hydrochloric acid (Merck, Darmstadt, Germany) was added, and the samples were kept for 1 hour at 45°C under agitation. Then, neutralization was accomplished with 0.5 ml of 1 mol L^{-1} sodium hydroxide (Merck, Darmstadt, Germany), and the samples were buffered with 1 ml of TISAB (total ionic strength adjustment buffer).

Fluoride measurement

Fluoride was analyzed by the direct method, using a fluoride specific electrode (Orion 96-09, Orion Research Inc., Beverly, USA) and an ion analyzer (Procyon™, model SA 720, Orion Research Inc., Beverly, USA). Prior to the samples analysis, a set of standards (ranging between 0.025-3.2 ppm F) was prepared in triplicate, using serial dilution from a 100 ppm NaF stock solution (Orion#940907, Orion Research Inc., Beverly, USA). The millivoltage potentials were converted to μg F using a standard curve with a correlation coefficient of $r \geq 0.99$. The mean repeatability of the fluoride readings, based on the duplicate samples, was 94%.

Calculation of the salivary flow rate

The expectorated saliva was collected in preweighed plastic vessels (± 0.01 mg) and after that, vessels were re-weighed. Assuming the specific density of saliva as 1 mg mL^{-1}, the volumes were calculated by subtracting the initial from the final weight. Then, the salivary flow (mL min^{-1}) was cal-

culated dividing the salivary volume obtained by the time of collection.

Furthermore, salivary flow was used to obtain the total amount of fluoride released in saliva (mg of fluoride).

Statistical analysis

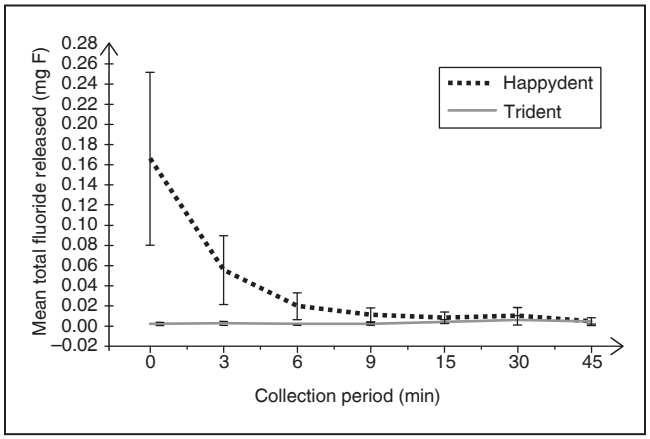
The data were analyzed by repeated measures two-way analysis of variance and by Tukey's *post hoc* test. The criteria used were: type of chewing gum (Happydent™ or Trident™) and time (0, 3, 6, 9, 15, 30 or 45 min). The comparison between the total amount of fluoride released after using the different gums was made by the paired Student's *t* test. A significance level of 5% was selected *a priori*.

RESULTS

Graph 1 shows the mean total fluoride released (mg) with time. The two-way ANOVA showed a statistically significant difference between the gums ($F = 287.6$, $p < 0.0001$), as well as among the different times ($F = 215.93$, $p < 0.0001$), and for the interaction of both ($F = 219.65$, $p < 0.0001$). Tukey's test for individual comparisons showed that the chewing gum Happydent™ released significantly higher amounts of fluoride when compared to Trident™, up to the 15 min collection time. The amount released decreased with time, and after 30 min the amount released was similar to that of Trident™ ($p > 0.05$).

Table 1 represents the total amount of fluoride released by subject (mg), during the whole experiment, for the two gums. Despite the variation among the volunteers (from 0.118 to 0.547 mg of fluoride for Happydent™ and from 0.007 to 0.050 mg of fluoride for Trident™), a significantly higher amount of fluoride was released when Happydent was chewed (0.276 ± 0.126 mg of fluoride) when compared to Trident (0.024 ± 0.014 mg of fluoride), as shown by the paired Student's *t* test ($t = 8.332$, $p < 0.001$).

Table 2 shows the contribution, as a percentage, of one piece of each chewing gum to the maxi-



GRAPH 1 - Mean total fluoride released (mg) in saliva (n = 15) with time (min) after chewing the gums Happydent™ or Trident™. Bars indicate standard deviation.

TABLE 1 - Total fluoride released (mg) by subjects during the whole experiment.

Subject	Happydent™	Trident™
1	0.547	0.041
2	0.181	0.013
3	0.198	0.014
4	0.259	0.020
5	0.368	0.050
6	0.286	0.025
7	0.481	0.026
8	0.345	0.028
9	0.378	0.035
10	0.229	0.045
11	0.241	0.014
12	0.118	0.008
13	0.211	0.007
14	0.149	0.026
15	0.146	0.007
Mean ± sd	0.276 ± 0.126*	0.024 ± 0.014*

*Significantly different ($p < 0.001$). SD: standard deviation.

TABLE 2 - Contribution of one tablet of each chewing gum to the maximum (max.) recommended daily fluoride intake (as a percentage), for 1-7 year-old children, to avoid dental fluorosis.

Age (years)	Mean weight* (kg)	Max. ingestion (mg F^- /day)	Happydent™ (%)	Trident™ (%)
1	10	0.70	39.4	3.4
2	12	0.84	32.8	2.9
3	15	1.05	26.3	2.3
4	18	1.26	21.9	1.9
5	20	1.40	19.7	1.7
6	22	1.54	17.9	1.6
7	24	1.68	16.4	1.4

*According to Silva[21] (2002).

mum daily recommended fluoride intake (0.07 mg of fluoride/kg of body weight[3]) for 1 to 7-year-old children. A single tablet of Happydent represents 39.4% and 16.4% of the maximum daily fluoride ingestion recommended for children aged 1 and 7 years old, respectively.

DISCUSSION

It is known that the frequent and repeated use of low fluoride concentration products, which promote low and constant salivary fluoride levels, is the most efficient way to prevent dental caries[12,15,23]. Levels between 1 and 10 ppm of fluoride reduce the enamel solubility and increase the remineralization rate, facilitating the precipitation of minerals on the enamel surface[12,15].

Sjögren *et al.*[23] (1997) found the greatest fluoride values in saliva between 5 and 10 minutes after the use of a fluoridated chewing gum. In the subsequent periods, the fluoride concentration in saliva decreased gradually. In this study, the fluoride release was significantly higher at 0, 3, 6, 9 and 15 min compared to 30 and 45 min when the fluoridated gum was chewed. Although Sjögren *et al.*[23] (1997) also suggest that the salivary flow stimulation may have a negative effect on the fluoride retention in the mouth, Bruun *et al.*[2] (1982) demonstrated that a single chewing gum tablet with 0.5 mg of fluoride can maintain high fluoride levels in saliva for at least 60 min.

Lamb *et al.*[12] (1993) sustained in their study that chewing a fluoridated gum with only 0.1 mg of fluoride five times a day favors the remineralization of initial dental caries lesions, and that this frequency could maintain high fluoride levels in saliva during most part of the day.

Silva *et al.*[22] (2003) evaluated the effect of two commercially available chewing gums with fluoride on the cariogenic microbiota of saliva and dental plaque. The gum Fluorette showed a faster pH recovery and a F release to saliva after up to 30 minutes.

The potential anticariogenic effect of chewing gums containing fluoride has been proposed by Lamb *et al.*[12] (1993) and Sjögren *et al.*[23] (1997). However, there are no data regarding the fluorosis risk that this type of product may promote. It has been suggested that the incidence and severity of dental fluorosis have become greater in the last decade in both optimally fluoridated and non-fluoridated areas in many countries, as well as in Brazil[5,9,13,17,19]. This has been attributed to an increase in the fluoride level of foods and beverages through processing with fluoridated water, inadvertent ingestion of fluoride toothpaste, and the inappropriate use of dietary supplements[14].

Considering that the highest risk factor for the development of dental fluorosis is the total amount of fluoride ingested, and that nowadays there are several available sources, the chewing gum Happydent™ can cause concern for children at the age of risk for dental fluorosis, which comprises 11 months to 7 years of age. Studies conducted with Brazilian children have shown that most of the 2-3[18], and one-third of the 4-7, year-old children[17] are usually exposed to a combined dose of fluoride (diet + dentifrice) above the risk threshold for dental fluorosis. According to table 2, in which the mean weights for each age are presented, a single tablet of Happydent™ represents 39.4% and 16.4% of the maximum daily fluoride ingestion recommended for children aged 1 and 7 years old, respectively. Considering 2-3-year-old children that are at risk for the development of dental fluorosis in the upper permanent incisors, which causes the major esthetic concern, one tablet of Happydent™ could represent 26-32% of the maximum daily fluoride ingestion. This maximum daily ingestion was calculated, based on the literature, as being 0.07 mg of fluoride/kg of body weight[3] and considering the use of a single tablet. Unfortunately, there is no data available on the consumption of chewing gum by children. However, it is possible that children use more than one tablet per day, which increases the risk of dental fluorosis development.

Hattab *et al.*[10] (1989) demonstrated a mild increase of fluoride plasma levels after the use of a fluoridated chewing gum and concluded that this product offers a minimal risk of adverse effects. However, this study was carried out in fluoride deficient areas and with adult subjects, using a chewing gum with smaller amounts of fluoride (0.113 mg) when compared to that used by the present study (approximately 0.4 mg, according to the manufacturer). Therefore, other studies with children living in optimally fluoridated areas are necessary to observe the effect of Happydent™ on the plasma fluoride levels.

CONCLUSIONS

This study indicated that:

1. The fluoride concentration in saliva samples after the use of Happydent™ was significantly higher than that observed after the use of Trident™ in all the experimental times, except for 30 and 45 minutes;

2. The mean fluoride release during the experiment was 0.276 mg for Happydent™ and 0.024 mg for Trident™;
3. The high fluoride concentration in saliva after the use of Happydent™ may be important on dental caries prevention in children or adults, especially for individuals with compromised salivary flow or the ones who live in deficient fluoride areas. However, further clinical research is necessary to clarify this issue;
4. The use of Happydent™ should be avoided by children at the age of risk for dental fluorosis because the fluoride release varied from 39 to 16% of the maximum recommended daily intake for children aged 1 and 7 years old, respectively.

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