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Fluoride concentration and pH of pediatric medicines regulary and long-term used by children

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Abstract
Objectives: Our aim in this study was to determine the fluoride concentration and pH of 71 pediatric medicines regularly and long-term used by children.
Study Design: The fluoride concentration was evaluated by selective electrode of fluoride (Orion). The pH was confronted using specific electrode (Orion) coupled to a potentiometer (Orion). The analyses were accomplished in duplicate. Pearson´s correlation and Kruskal-Wallis test were used. P-values below 5% were considered statistically significant.
Results: Medicine pH averages ± SD varied from 2.3 ±0.01 to up 10.6 ±0.02. Values below critical pH were observed in 42.25% (n=30) of presentations, with 25.35% (n=18) below 4.5 pH. Most medicines (84.5%) presented fluoride concentration below 0.05 mg/L.
Conclusions: Among the pediatric medicines evaluated, this study has showed that 2-4 times-a-day posology and syrup formulations presented lowest pH and fluoride concentration, resulting in factors that predict highest cariogenic and erosive potential.

Key words: *Fluoride, pH, medicines, dental erosion, dental caries.*

Introduction
The dental surface is constantly exposed to the liquid products from the diet, hygiene and therapeutic products. Many children need to ingest liquid medicines frequently for a long period of time (1). Epidemiologic studies emphasize the association between chronic use of liquid medicines and dental caries (2-4). Added to this studies, researches have regarded the erosive and cariogenic potential of liquid pediatric medicines although limited to a small number of medicines (5).
The frequent and prolonged ingestion of acid liquids is considered the etiologic factor of dental erosion (6). Among these liquids, the possible erosive effect presented by pediatric medicines with low pH is investigated (7). Researches reveal that there is high variation in the number of children that exhibit at least one tooth with dental erosion (8). The importance of this investigation is that this lesion might be a public health problem for children in the future.
The fluoride in the medicines would represent a pro-

tection factor (6). In addition, as preventive action for cavity and erosion, the use of topical fluorides has been widely described in the last few years (9-11). However, literature about the presence of fluoride in medicines is scarce.

The aim of this study was to determine the fluoride concentration and the pH of pediatric medicines regulary and long-term used by children to estimate the cariogenic and erosive potential.

Material and Methods

Products of the investigation

For selecting the chronic-use pediatric medicines, 19 doctors of the Lauro Wanderley/UFPB Hospital were interviewed. This hospital is the reference service in Paraíba state- Brazil.

Doctors have indicated 16 types of medicines resulting in 71 chronic-use presentations that were purchased in pharmacies of João Pessoa-Brazil.

Fluoride Determination

The ionized fluoride was measured using a fluoride-specific electrode (model 94-09, Orion Research Corp., Cambridge, Mass., USA) on the a potentiometer (model 290A+, Orion Research Corp., Cambridge, Mass., USA). Orion fluoride standard solutions 6.4-0.2 mg/L were used to calibrate the measuring instrument.

Two samples of 1 mL were taken from each drug and mixed using a magnetic mixing at the 8 speed (model MA-162, Marconi, Brazil), after the addition of an equal volume of buffer TISAB II to adjust pH to 5.5 and standardize the ionic power. Measurements were performed after electrode submersion at room temperature.

pH determination

The medicines pH determination was carried out using pH electrode (model 91-02 Orion Research Corp. Cambridge Mass, USA) in a potentiometer (model 290 A +, Orion Research Corp., Cambridge, Mass, USA). Five mL of the drugs were put in contact with electrode after agitation at the 8 speed (MA-162, Marconi, Brazil). Medicines in powder for suspension with "dilute with filtered water" indication were incorporated to deionized-distillated water. Standard solutions of 4.01, 7.00 and 10.01 were used for calibration (Slope> 95 %). All measurements were performed in triplicate and expressed as average ± standard error.

Very viscous syrups and suspensions could not be pipetted, and therefore, the density was obtained for weighting per milliliter using balance (Gehaka high precision analytical scale).

$$\text{Density} = \frac{\text{Weight (g)}}{\text{Volume (mL)}}$$

Statistical analysis

Results for pH and fluoride concentration were statistically analyzed (Pearson´s Correlation and Kruskal-Wallis test) by using the SPSS (Statistical Package for Social Science). P-values below 5% were considered statistically significant.

Results

Of the 71 formulations tested, only 5 (7.04%) were generic preparations, being the others proprietary or brand-name preparations. Overall, eighteen (25.3 %) presented pH below 4.5. The pH values of pediatric medicines varied from 2.3, in an iron sulfate syrup, to 10.6 in an azitromicine suspension. Considering the main substance, iron sulfate medicines (Nutrition and blood of Therapeutic group) had the lowest endogenous mean pH and fluoride, with values from 2.3 to 3.6 and 0.005 and 0.02 mg/L.

The distribution of the 71 formulations according to therapeutic group was as follows: 17 (23.9%) respiratory; 34 (47.9%) anti-infectives; 12 (16.9%) nutrition and blood; 2 (2.8%) cardiovascular system and 6 (8.5%) endocrine.

Mean (± SD) values of fluoride concentration were higher than normal salivary values of 0,01 mg/L. The highest value (mg/L) was observed for anti-infective drugs with 0.34 ± 1.57. However, all the other observations for respiratory, nutrition and blood, cardiovascular system and endocrine medications were below mean values of 0.08 mg/L which indicate that these medicines are not a significant source of fluoride for the oral environment.

When pH and concentration fluoride were analyzed according to the daily dose indicated for 7 to 12 year-old children: 13 formulations (18.31%) were once a day posology; 22 (30.99%), twice-a-day and 30 (42.25%) three and four times a day (Table 1).

The mean fluoride concentrations were converted to logarithmic scale. Positive statistically significant correlation between pH and fluoride concentration was observed (r= 0.292; p=0.01).

Medicines with lower pH ± SD (5.48 ± 1.17) were indicated to be consumed three and four times per day, while those consumed once a day had high pH (8.48 ± 2.72). This difference was statistically significant (H= 16.38; d.f.= 2; p= 0.002). Twenty-four formulations were indicated to be consumed three times a day (pH ± DP of 5.53 ± 1.19). While six medicines were indicated to be consumed four times a day (pH ± SD of 5.28 ± 1.15).

In terms of fluoride concentration, the highest mean pH ± SD was observed in medicines to be consume three and four times a day (0.33 ± 1.66) with no statistically significant differences being observed (p>0.05).

Twenty three formulations (32.40%) were syrup with mean pH ± SD of 5.11 ± 1.34; while 48 (67.60%) were suspension, solution or elixir form, with mean pH ±

Table 1. Endogenous pH mean and fluoride concentration of 71 pediatric medicines regularly and long-term used by children according to the daily posology and formulation.

Pediatric Medicines					
		pH		Fluoride (mg/ L)	
Posology (daily)[1]	n	Mean±SD	CI	Mean±SD	CI
Once	13	8.48 ± 2.72[a]	6.83-10.13	0.13 ± 0.34[a]	-0.07-0.34
Twice	22	5.49 ± 1.22[b]	4.94-6.03	0.06 ± 0.12[a]	0.002-0.11
Three/ four times	30	5.48 ± 1.17[b]	5.04-5.92	0.33 ± 1.66[a]	-0.28-0.96
Total	71	5.89 ± 2.02	5.41-6.37	0.18 ± 1.09	0.07-0.44
Formulation[1]	n	Mean±SD	CI	Mean±SD	CI
Syrup	23	5.11 ± 1.34[a]	4.53-5.69	0.02 ± 0.02[a]	0.01-0.03
Suspension, liquid, solution and elixir	48	6.27 ± 2.19[b]	5.63-6.91	0.26 ± 1.32[a]	-0.12-0.64
Total	71	5.89 ± 2.02	5.4-6.37	0.18 ± 1.09	0.07-0.44

Groups whose means/average are followed by distinct letters are statistically different (p values obtained by Kruskal-Wallis test) 1p< 0.001.

SD of 6.27 ± 2.19. This difference was statistically significant (p= 0.04). Syrups presented the lowest fluoride concentration (0.02 ± 0.02) with no statistically significant differences observed (p= 0.07).

Discussion

In this study it could be observed that part of the pediatric medicines analyzed has low pH able to initiate the dental demineralization by direct action above the enamel surface, without direct influence on the oral microbiology. This chemical feature determines medicines' erosive potential. Although the development of erosion is also influenced by the enamel type, temperature and acid exposition time (12).

Passos et al. (13) observed in the sample the mean ± SD of endogenous pH and compared between groups: endocrine, nutrition and blood group had lower mean (3.8 ± 1.0 and 4.3 ± 1.8, respectively), while anti-infective and cardiovasculary system group had mean pH higher than the critical value (5.5) to enamel desmineralization. The mean pH of iron sulfate had high influence on the mean pH of nutrition and blood groups (minimum and maximum pH 2.3 ± 0.01 and 3.6 ± 0.2, respectively). The pH ± SD in the respiratory group was high (5.71±0.89), but did not differ of the anti-infective group (6.85 ± 2.10). The latter has differed from nutrition and blood (p= 0,002) and endocrine (p= 0,001) groups. The pH values for cardiovascular system and endocrine groups were statistically different (p= 0.04).

An aggravation, considering the medicines of this study, is the fact that they are administered during years and in high frequency, from 1 to 4 times a day. This high frequency of daily ingestion, associated to lower levels of mineralization, reduce thickness and maturation of the deciduous teeth (12,14). In addition, permanent teeth has just erupted and the low pH, associated the low fluoride concentration are factors that aggravate the oral health of children.

Many of the pH values observed in this study are compared to several soft drinks, fruit juices and teas considered potentially erosive (10,12, 14-16). Especially, the iron sulfate showed to have higher cariogenic and erosive potential, similar to that observed by Maguire et al. (17). The lower pH and fluoride concentration are similar to the acidity of the coke-based drinks (15).

Liquid medicines with pH <5.5 can acidify the dental biofilm by diffusion process, promoting adequate environment to the reproduction of pH-strategist microorganisms, thus substantially favoring acids production as consequence of their intense metabolism and resulting in the enamel demineralization by indirect medicines action.

In the combat to the cavity and erosion in daily challenge of consuming pediatric liquid medicines, saliva has a protecting action as long as they have mineral potential in the beginning stages of dental erosion (12). However, this is questionable, as in apatite erosion crystals are lost layer by layer and none or few mineralized crystals can be expected. Possibly, the higher action of the saliva as protection is related to the formation of the enamel pellicle acquired that reduces the demineralization effect of medicines in the enamel surface (18).

Medicines on powder for suspension with "dilute in water" indication should have the fluoride concentration increased in regions where water is fluorided. This increase in the fluoride consumed increases the dental fluorosis risk. The Azitromicine suspension and the Nitrofurantoine solution presented high fluoride concentration, generating the need of a differentiated analysis from the point of view of the dental fluorosis risk for children between 6-7 years old (19).

The Azitromicine presented elevated pH value, choice determined its non erosive feature. The Nitrofurantoin presented low endogenous pH, which may initiate the dental demineralization process, however, this solution makes available in the oral cavity an elevated fluoride concentration with low pH interfering positively in the calcium fluoride globules formation (9).

The fluoride protective effect in most medicines cannot be considered effective by the low values observed, similar to the physiologic concentration in the saliva (0.02 to 0.05 mg/L), in the plaque (0.03 mg/L) and in the plaque fluid (0.01 to 0.02 mg/L) (20).

As a preventive action, fluoride concentration in saliva might be kept in great therapeutic level, in other words, in an approximate concentration of 0.1 ppm. This is possible with the regular use of fluoride dentifrice (11) in association with topic-application fluoride gel (21).

The of long-term medicines ingestion is frequently associated exclusively to the benefit promoted to the general health of children, but it is observed that if preventive actions are not incorporated as a protocol after the ingestion of these medicines they can cause harmful effects to the oral health.

In summary, our data showed that among the pediatric medicines evaluated, endocrine and nutrition and blood medicines (iron sulfate), 2-4 times a day posology and syrup formulations presented the lowest pH and fluoride concentration values, resulting in factors that predict highest cariogenic and erosive potential. Thus, the results presented support the cariogenic potential of pediatric medicines (1-4) and will serve as base to future studies which clinically will investigate the erosive potential presented by these long-term medicines. In addition, other researches are required to investigate variables such as calcium and phosphate in pediatric medicines.

References

References with links to Crossref - DOI

1. Feigal RJ, Jensen ME, Mensing CA. Dental caries potential of liquid medications. Pediatrics. 1981;68:416-9.
2. Roberts IF, Roberts GJ. Relation between medicines sweetened with sucrose and dental disease. Br Med J. 1979;2:14-6.
3. Maguire A, Rugg-Gunn AJ, Butler TJ. Dental health of children taking antimicrobial and non-antimicrobial liquid oral medication long-term. Caries Res. 1996;30:16-21.
4. Sahgal J, Sood PB, Raju OS. A comparison of oral hygiene status and dental caries in children on long term liquid oral medications to those not administered with such medications. J Indian Soc Pedod Prev Dent. 2002;20:144-51.
5. Nunn JH, Ng SK, Sharkey I, Coulthard M. The dental implications of chronic use of acidic medicines in medically compromised children. Pharm World Sci. 2001;23:118-9.
6. Zero DT. Etiology of dental erosion--extrinsic factors. Eur J Oral Sci. 1996;104:162-77.
7. Durward C, Thou T. Dental caries and sugar-containing liquid medicines for children in New Zealand. N Z Dent J. 1997;93:124-9.
8. Peres KG, Armênio MF, Peres MA, Traebert J, De Lacerda JT. Dental erosion in 12-year-old schoolchildren: a cross-sectional study in Southern Brazil. Int J Paediatr Dent. 2005;15:249-55.
9. Featherstone JD. Prevention and reversal of dental caries: role of low level fluoride. Community Dent Oral Epidemiol. 1999;27:31-40.
10. Behrendt A, Oberste V, Wetzel WE. Fluoride concentration and pH of iced tea products. Caries Res. 2002;36:405-10.
11. Campus G, Lallai MR, Carboni R. Fluoride concentration in saliva after use of oral hygiene products. Caries Res. 2003;37:66-70.
12. Amaechi BT, Higham SM, Edgar WM. Factors influencing the development of dental erosion in vitro: enamel type, temperature and exposure time. J Oral Rehabil. 1999;26:624-30.
13. Passos IA, Sampaio FC, Martínez CR, Freitas CH. Sucrose concentration and pH in liquid oral pediatric medicines of long-term use for children. Rev Panam Salud Publica. 2010;27:132-7.
14. Fejerskov O, Stephen KW, Richards A, Speirs R. Combined effect of systemic and topical fluoride treatments on human deciduous teeth--case studies. Caries Res. 1987;21:452-9.
15. Edwards M, Creanor SL, Foye RH, Gilmour WH. Buffering capacities of soft drinks: the potential influence on dental erosion. J Oral Rehabil. 1999;26:923-7.
16. West NX, Maxwell A, Hughes JA, Parker DM, Newcombe RG, Addy M. A method to measure clinical erosion: the effect of orange juice consumption on erosion of enamel. J Dent. 1998;26:329-35.
17. Maguire A, Baqir W, Nunn JH. Are sugars-free medicines more erosive than sugars-containing medicines? An in vitro study of paediatric medicines with prolonged oral clearance used regularly and long-term by children. Int J Paediatr Dent. 2007;17:231-8.
18. Nekrashevych Y, Stösser L. Protective influence of experimentally formed salivary pellicle on enamel erosion. An in vitro study. Caries Res. 2003;37:225-31.
19. Fejerskov O, Manji F, Baelum V. The nature and mechanisms of dental fluorosis in man. J Dent Res. 1990;69 Spec No:692-700.
20. Tanaka M, Margolis HC. Release of mineral ions in dental plaque following acid production. Arch Oral Biol. 1999;44:253-8.
21. Van Rijkom H, Ruben J, Vieira A, Huysmans MC, Truin GJ, Mulder J. Erosion-inhibiting effect of sodium fluoride and titanium tetrafluoride treatment in vitro. Eur J Oral Sci. 2003;111:253-7.

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