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Acidogenic and Erosive Potential of Paediatric Liquid Medications- A SEM Based Study.

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ABSTRACT

Background: Dental erosion is a complex pathology of multifactorial etiology in which chemical, biological and behavioural factors influence the erosive process. The etiology has been related to the regular use of products with low endogenous pH and high acidity including liquid medicaments. Aim: To investigate the endogenous erosive potential of commonly used pediatric liquid medicaments. **Methods**: Endogenous pH and titratable acidity of eight commonly used pediatric liquid medicaments were measured using a digital pHmeter. 54 exfoliated or extracted primary and permanent teeth without any carious lesion, maintained in pediatric liquid medicaments were observed under SEM after 1 minute and 10 minutes of time intervals. **Results**: Most of the medicaments showed etched prism pattern on primary teeth and crater formation whereas etched prism pattern was seen on all permanent enamel surfaces. **Conclusion**: Evidence of dental erosion was observed on both primary and permanent enamel.

Keywords: Erosion, Pediatric Liquid Medicaments, pH, Titratable acidity.

INTRODUCTION

Dental erosion is defined as the physical result of a localized, chronic, pathological and irreversible loss of dental hard tissue caused by acids or chelates in systematic manner without bacterial involvement.[1] Studies have pointed out the cariogenic potential of pediatric liquid medicaments (PLM), but few of them have evaluated the effect on tooth surface topography taking into consideration the pH and titratable acidity of these medicaments. Hence, this study was aimed to evaluate, in vitro, the effect of pediatric liquid medicaments on the topography of primary and permanent enamel and the influence of pH and titratable acidity on their erosive effect.

MATERIALS AND METHODS

Eight commonly used pediatricliquid medicamentswere selected for the study [Table 1]. Artificial saliva was used as control. Endogenous pH and titratable acidity of the pediatric liquid medicaments were measured using a digital pH meter. Titratable acidity of the study and control medicaments were determined by adding increasing amounts of 0.1N sodium hydroxide (NaOH) solution.

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Table 1: Pediatric Liquid Medicaments used in the study

Analgesics	Drug A	Ibuprofen and Paracetamol suspension
	Drug B	Acelofenac and Paracetamol suspension
Antibiotics	Drug C	Amoxycillin oral suspension
	Drug D	Cefixime oral suspension
Antihistamines	Drug E	Chlorpheniramine maleate and Codeine phosphate
	Drug F	Diphenhydramine hydrochloride
Multivitamins	Drug G	Multivitamin, Multimineral and Protein
	Drug H	Multivitamin and Multimineral

Procedure:

Measurement of pH

For each medicament, the pHwas measured using a digital pH meter. At the start of each session, the electrode was calibrated using test solutions of known pH.20 ml of each freshly prepared dilution was placed in a glass beaker on a thermostatically controlled electric hotplate at 370C. Before reading its pH, each sample was mixed thoroughly using a magnetic stirrer for 1 minute. Each dilution was

tested three times to give a mean measurement. Between readings, the electrode was rinsed in distilled water to ensure that no cross-contamination occurred.

Measurement of titratable acidity

For each medicament, titratable acidity was measured by placing 20 ml of each dilution in a glass beaker placed on a thermostatically controlled electric hotplate at 370C. Then 0.1 M sodium hydroxide (NaOH) solution was gradually pipetted into the beaker until the pH reached neutrality. Each sample was stirred continuously to ensure thorough mixing. The volume of NaOH required to raise the pH of each sample to neutrality was recorded. This process was carried out three times for each dilution and a mean measurement was recorded.

Preparation of samples for observation under SEM:

A total of 54 teeth samples were prepared to evaluate the erosion on primary (27 teeth) and permanent teeth (27 teeth) by regular intake of commonly used Pediatric Liquid Medicaments using Scanning Electron Microscope (SEM). The 54 study samples were divided into a Control group (n=6) and a Study group (n=48). Of the 6 teeth in the control group, 3 teeth were primary and 3 were permanent. Artificial saliva was taken as the control. Of the 48 teeth in the Study group, 24 were primary and 24 were permanent. 24 teeth in each group were subjected to the four groups of study PLM (Analgesics, Antibiotics, Antihistamines and Multivitamins) (n=6). As there were two PLM, in each of the study group, 3 teeth samples were allotted to each group.Specimens of enamel were derived from recently extracted, caries-free primary and permanent teeth.Following extraction, each tooth was carefully scraped of any remaining tissue with a scalpel. It was then rinsed in copious amounts of distilled water and stored in normal saline at room temperature till the experiments were performed. The crown was sectioned from the root and cut vertically to produce approximately equal sections of enamel. In order to minimize variation in enamel prism orientation, every attempt was made to cut sections from the same coronal area. Specimens were then immersed in 100ml of each PLM solution for 1minute and 10 minute.All specimens were thereafter coated with gold using a sputter coater. Following this, SEM analysis was performed to assess the topography of enamel surface after each treatment period for the four tested PLM groups (2 Analgesics, 2 Antibiotics, 2 Antihistamines and 2 Multivitamins) and for the Control group.

RESULTS

pH of the pediatric liquid medicaments

[Table 2] shows that The pH value of analgesic group (Drug A & Drug B) was lower compared to antibiotics (Drug C & Drug D) and multivitamins (Drug G & Drug H).Antihistamines (Drug E & Drug F) had significantly lower pH values when compared to antibiotics (Drug C & Drug D) and multivitamins (Drug G & Drug H). Analgesics and antihistamines had the lowest pH values whereas antibiotics and multivitamins showed higher pH values.

Table 2: pH value of pediatric liquid medicaments

Group	Description	pH Value
Drug A	ANALGESICS	4.54
Drug B		4.57
Drug C	ANTIBIOTICS	5.56
Drug D		4.93
Drug E	ANTIHISTAMINES	4.49
Drug F		4.65
Drug G	MULTIVITAMINS	5.56
Drug H		4.92

Titratable acidity of pediatric liquid medicaments

[Table 3] illustrates that the analgesics (Drug A& Drug B) had significantly higher titratable acidity compared to antibiotics (Drug C & Drug D) and multivitamins (Drug G & Drug H). Antihistamines had a higher titratable acidity compared to antibiotics and multivitamins.

Table 3: Titratable acidity value of pediatric liquid medicaments

Groups	Description	Titratable acidity value
Drug A	ANALGESIC	118.00
Drug B		113.00
Drug C	ANTIBIOTICS	57.33
Drug D		93.67
Drug E	ANTIHISTAMINE	110.33
Drug F		106.33
Drug G	MULTIVITAMINS	51.67
Drug H		96.33

Effect of different study groups on primary enamel observed under SEM at different time intervals

Surface changes on primary enamel treated with various Pediatric Liquid Medicaments were observed under SEM at 1 minute and 10 minutes [Table 4]. The etched enamel prism pattern was seen on all the primary enamel surfaces irrespective of the immersion time intervals. Sporadic rod ends were seen more at the end of 1 minute whereas crater formationwas not observed at the end of 1 minute for any group except Drug H (Multivitamins). For most of the medicaments, etched prism pattern and crater formation were observed at the end of 10 minutes. Control group did not show any changes at all-time intervals.

Table 4: Effect of different study groups on primary enamel observed under SEM at different time intervals

PLM	Group	Sample	1 Minute			10 Minutes		
			Sporadic Rod Ends	Etched Enamel Prism	Crater Formation	Sporadic Rod Ends	Etched Enamel Prism	Crater Formation
SALIVA	Control	1	¥			¥		
		2		¥			¥	
		3	¥			¥		
ANALGESICS	Drug A	1	¥				¥	
		2		¥				¥
		3		¥			¥	
	Drug B	1		¥			¥	
		2		¥				¥
		3		¥			¥	
ANTIBIOTICS	Drug C	1	¥					¥
		2		¥			¥	
		3		¥				¥
	Drug D	1	¥					¥
		2		¥		¥		
		3	¥				¥	
ANTIHISTAMINE	Drug E	1		¥				¥
		2		¥			¥	
		3	¥				¥	
	Drug F	1		¥		¥		
		2		¥			¥	
		3		¥			¥	
MUTIVITAMINS	Drug G	1	¥					¥
		2			¥		¥	
		3	¥			¥		
	Drug H	1		¥			¥	
		2	¥				¥	
		3			¥			¥

¥: erosion seen/present

Table 5: Effect of different study groups on permanent enamel observed under SEM at different time intervals

PLM	Group	Sample	1 minute			10 minutes		
			Sporadic Rod Ends	Etched Enamel Prism	Crater Formation	Sporadic Rod Ends	Etched Enamel Prism	Crater Formation
SALIVA	Control	1	¥			¥		
		2	¥	¥			¥	
		3						¥
ANALGESICS	Drug A	1	¥			¥		
		2		¥			¥	
		3	¥				¥	
	Drug B	1		¥				¥
		2			¥		¥	
		3		¥			¥	
ANTIBIOTICS	Drug C	1	¥				¥	
		2		¥				¥
		3			¥			¥
	Drug D	1		¥		¥		
		2	¥				¥	
		3	¥				¥	
ANTIHISTAMINES	Drug E	1		¥		¥		
		2		¥				¥
		3			¥		¥	
	Drug F	1		¥		¥		
		2		¥			¥	
		3	¥					¥
MUTIVITAMINS	Drug G	1	¥				¥	
		2		¥			¥	
		3	¥			¥		
	Drug H	1		¥			¥	
		2	¥			¥		
		3			¥		¥	

Effect of different study groups on permanent enamel observed under SEM at different time intervals

The etched prism pattern was seen on all the permanent enamel surfaces irrespective of the immersion time. Sporadic rod ends were more at the end of 10 minutes whereas crater formation was less commonly seen at both time intervals. Control group did not show any changes at all-time intervals [Table 5].

DISCUSSION

Erosive lesions with multi-causative etiology are signs of dental hard tissue disease that has become commonly evident in today's society. Erosive damage to the permanent teeth in early childhood may compromise the dentition for the child's entire lifetime and this will certainly require expensive dental treatments in adult life.[2] The etiology of erosion is related to different behavioural, biological and chemical factors and it can have either extrinsic or intrinsic causes.

According to Costa et al. (2006) it has been related to the regular use of products with low endogenous pH, high acidity and absence or low concentrations of ions including those of calcium, fluoride and phosphate in their composition.[3]

The long-term ingestion of medicines 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 intake of these medicines they can cause harmful effects to the oral health. The most frequent therapeutic classes of children's liquid medicines according to Neveset al.(2007) are analgesics and antipyretics (98.8%), antibacterial (88.4%) and antitussives (67.4%) mostly in the form of suspensions and syrups.36 Menezeset al. (2010) concluded Antibiotics (45.6%), Antihistamines (33.3%), Non-Steroidal Anti Inflammatory Drugs (23.8%) and Multivitamins (21%) to be the most commonly prescribed medicaments in children.[4]

Menezeset al. (2010) showed that mostpediatric medicines (52.6%) had been prescribe in liquid form (suspension or syrup) for which elimination from the oral cavity occurs more slowly compared to tablets and capsules.[4] The acidogenicity of these liquid preparations depends on pH, titratibility, buffering capacity and organic acid present in the medications. Many of the liquid syrups are maintained in acidic pH as the solubility of weak acids and bases is pH dependent making acidic preparations necessary for drug dispersion (Addyet al. 2000).[5] Additionally, these acidic medicines often taste pleasanter, which may enhance patient compliance, especially in children. Sugar based syrups are often used as alternatives to tablets in younger children to increase palatability and patient acceptance.[6]

There is clear association between sugar containing oral medicines and dental caries and the effect is greater if they are taken at night or at bedtime when the protective buffering and cleansing effects of saliva are reduced as the salivary flow rate falls (Neveset al. 2007).[7]

Very few studies have been conducted in our environment to evaluate the effect of the pH and titratable acidity of commonly prescribed Pediatric Liquid Medicaments on the tooth surface topography. Hence the present study was conducted to know the acidogenic potential of commonly used Pediatric Liquid Medicaments (PLM) in our society and their erosive effect on tooth enamel.

Erosion in deciduous teeth has only been sparsely reported in the literature with few considering an important question of whether deciduous teeth are more prone to erosion than permanent teeth. Therefore, in the present study, the erosive effect of the study medications was seen both on primary as well as permanent teeth enamel.

Rugg-Gunnet al. (1998)attributedthree properties of a medicament contributing to its erosive potential: 1) the amount of acid available (titratable acidity); 2) the amount of acid actually present (the concentration of the H+ ion or the pH); and 3) the relative strength of the acid or ease with which the acid will give up free H+ ions (the pKa).[8] Hence in the present study the erosive properties of the PLM were investigated by determining their endogenous pH and titratable acidity and their effecton the primary and permanent enamel surface were studied using Scanning Electron Microscope (SEM).

Some oral medicines are usually given at bedtime with subsequent tooth brushing or water rinse, and oral clearance is usually also compromised during sleep. Therefore it seems reasonable to evaluate how exposure time could influence erosive dental patterns. The choice for 1 min and 10 min were proposed according to Babuet al. (2008).[9] In their study erosion was also evaluated at 8 hours but in the present study it was not considered as it seemed more aggressive as stated by Pierro et al. (2010).2They stated the severity of erosion seen at 8 hours immersion period in the study by Babuet al.(2008) could be due to the great difference between the time periods, which could have been enough to promote saturation of the liquid medium.[9]

Results of the present study showed that all the PLM evaluated showed a pH value less than or equal to 5.5. These results were in accordance to the study conducted by Maguire et al. (2007) on the erosive potential of 97 medicines used regularly and long term by children who showed that 57% had an endogenous pH below 5.5.[10] In a study

conducted by Greenwoodet al. (1984), the liquid syrups recorded an acidic pH as low as 2.86.6 Agarwal et al.(2010) stated that 50% of most commonly prescribed liquid oral medicines showed high sugar percentage and 90% of the medicines showed pH below the critical value of 5.5.[11] According to Passoset al. (2011), 25.3% of tested formulations presented pH below 4.5 and the pH values varied from 2.3 to 10.6.[12] Sunithaet al. (2009) found that that endogenous pH of all the drugs considered were acidic in nature with the cough syrup being below the cariogenic critical pH.[13] In the study conducted by Lima et al. (2007), 74.2% of the drugs examined had pH lower than 5.5.[14] Similarly study by Grenby (1995) showed pH of throat lozenges in the range of 2.6-3.7, which was attributed to the flavouring agents.[15] Nunn et al. (2001) assessed the pH of commonly prescribed drugs used by children and found that all but two of the drugs tested had a pH well below the critical pH of 5.5 for enamel demineralization.[16] Pediatric medicines which have low pH are able to initiate the dental demineralization by direct action above the enamel surface. Liquid medicines with pH < 5.5 can acidify the dental biofilm by diffusion process, promoting adequate environment to the reproduction of pH-strategist microorganisms.

However, it is well known that the pH gives only the initial concentration of H+ ions, and does not represent the presence of undissociated acid in the medium.[17] Valinotiet al. (2008)using two acidic medicines with pH close to the same value showed, under SEM, that one medication caused more surface alterations.[18] According to the authors, the dissimilar results of these medicines were due to the differences in the titratable acidity between the medicines. Based on this, the authors concluded that higher titratable acidity contributes more than pH to the changes produced in the enamel surfaces. Titratable acidity can be claimed as a more accurate measure of the total acid content present in substances. Ions like calcium, phosphate and fluoride have a protective effect against erosion. However, in a study conducted by Pierroet al. (2010) it was stated that despite the presence of fluoride and calcium in the antihistamine liquid formulation, their ionic concentrations were not high enough to prevent the erosive effect viewed in the enamel surfaces.[2] They observed that the high titratable acidity overcame the probable positive effects of ions F-, Ca++ and PO43-on preventing enamel erosion. In the present study, on evaluating the titratable acidity, it was observed that the mean titratable acidity of Drug A (analgesic) (118.00 ± 5.57) was highest while Drug G (multivitamin) (51.67 ± 4.73) was the least.

The erosive effects of these Pediatric Liquid Medicaments on the primary and permanent enamel surface were studied using Scanning Electron Microscope (SEM). The study demonstrated erosive effect for all PLM on the primary and permanent enamel when viewed under the SEM. The etched prism pattern was seen on all the tooth surfaces irrespective of the immersion time intervals. Sporadic rod ends were seen more at the end of 1 minute whereas crater formation was not observed at the end of 1 minute for any group except Drug G and Drug H (multivitamins). In most of the medicaments we observed etched prism pattern and crater formation at the end of 10 minutes. Silverstoneet al. (1975) have described three basic types to etching pattern i.e. type-I, type –II, type-III. Prism pattern which was observed in our study was similar to type-I etching pattern where the prism core material was preferentially removed leaving the prism periphery relatively intact "HONEY COMB'/ PRISM APPEARANCE''. They also stated that this type-I etching pattern can be easily explained by noting that the crystals reach the enamel surfaces at different inclinations in the rods as compared to the inter rod areas.19 Our SEM micrographs showed that the surface was smooth, slightly etched, revealing faint outlines of scales. Enamel rods were clearly opened and the edges of the sections were deep enough to be visible under SEM.[19] Additionally, in the current study irregular pattern of pit like erosion areas were seen in all specimens varying from site to site probably depending on the prismatic versus aprismatic nature and composition of the affected enamel.

Nevertheless, based on SEM observations alone, no conclusions can be drawn on the degree or severity of erosion. SEM analyses are therefore mainly used to visualize the pathology and should not be used in isolation, without any quantitative methods.

CONCLUSION

The present study illustrates the acidogenic and erosive potential of commonly prescribed Pediatric Liquid Medicaments. Therefore greater care should be taken while prescribing these medications and parents and professionals should enhance their knowledge about the acidogenic and cariogenic potential of Pediatric Liquid Medicaments which are used in our day to day practice.

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