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RESEARCH ARTICLE

EVALUATION OF ALTERATION IN PLAQUE PH ON CONSUMPTION OF COMMONLY PRESCRIBED LIQUID MEDICINES TO CHRONICALLY ILL CHILDREN

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Abstract

Purpose: To estimate drop in plaque pH, minimum pH and maximum pH drop in first 30 mins on consumption of commonly prescribed liquid medicines to chronically ill children.

Methods: A cross- sectional study was carried out in Pediatric ward of J.K.LOAN hospital (Government Hospital), Jaipur, India on chronically ill children. Five commonly prescribed liquid medicines were selected for the study to estimate drop in plaque pH, minimum pH and maximum pH drop in first 30 mins. The products were evaluated in a randomized experiment, with 3 repetitions for each sample, and the mean was taken.

Results: Phenytoin, Theophylline and Multivitamin - multimineral syrup showed decrease in plaque pH and had minimum pH value comparable to 10% sucrose solution. Vitamin D_3 - Calcium Carbonate and Ferrous Fumarate - Folic acid syrup did not show a significant decrease in plaque pH and minimum pH was also found elevated as compared to 10% sucrose solution. Maximum pH drop was seen with Phenytoin (1.48) and Theophylline (1.41) comparable to 10% sucrose solution (1.40). The test showed that there was no significant difference between Phenytoin, Theophylline, Multivitamin - multimineral syrup and sucrose solution as the medicines behaving essentially same as 10% sucrose solution with respect to their potential to generate acids.

Conclusion: Most commonly prescribed medication to the patients of younger age group is in the form of syrup. Therefore incorporation of non sweetened or sugar- free sweeteners in the liquid medications is recommended.

Introduction

Many chronic diseases in childhood have been associated with poor oral health and increased risk of dental caries (Walton AG, Thomason JM et al 2000). Such children often have several risk factors such as poor oral health, including social disadvantage, long term exposure to sugar loaded medicines, and the fact that their dietary habits may not be optimal(Balmer R, Bu'Lock FA 2003)**.**

Liquid oral medicines are used extensively in children to aid compliance. However, some of the inactive agents used in liquid medicines can pose a threat to dental health (Foster H, Fitzgeralg J 2005). Occasional brief courses of sugar containing medicines seldom has an adverse effect on the teeth but chronic diseases like asthma, epilepsy, malnutrition, nephrotic syndrome, anaemia and diseases which require long term medications may

predispose for the occurrence of dental caries (Nunn JH, Ng SK et al 2001). Many studies have reported that children under sucrose-based liquid medications had significantly more carious teeth (Roberts IF, Roberts GJ 1979)**.** Dental caries is a chronic disease, a process that progresses very slowly in most individuals. Dental caries is a multifactorial disease that is caused by interplay of three major factors, i.e. teeth, cariogenic bacteria, and fermentable sugars. Epidemiological studies revealed the relationship between caries prevalence and sugar consumption. Dental plaque is a typical biofilm consisting of micro-organisms and their products such as adhesive glucan (Taku F 2005)**.** Reports suggest that sucrose-containing preparation produces a significantly greater drop in plaque pH than their sucrose-free counterpart (Marathaki E, Pollard MA et al 1995)**.** Plaque bacteria produce a large quantity of acids such as lactic acid from fermentable carbohydrates. Acids are entrapped between the tooth surface and plaque biofilm, then the pH of the enamel easily falls below 5.6, and loss of mineral (decalcification) from enamel is induced. This is initiation of dental caries (Taku F 2005)**.** The plaque pH estimation may be used to develop a scale of relative cariogenicity of prescriptional and non-prescriptional medicines and identify low caries risk medicinal components and their pattern (Sharma A, Deshpande S 2011)**.** There is a high need to identify the drop in plaque pH of liquid medicines so that a substitute can be added in place of cariogenic sugar if found to decrease plaque pH to less than critical pH. The need of the present study was to anchor the pre-existing association between sugar based LOM and dental caries in chronically ill children. In the present investigation the pH changes in dental plaque after using different pediatric medicines and a 10% sucrose solution were compared in a randomized trial.

Materials and method

The present study was conducted at J.K Loan Hospital, Jaipur, Rajasthan. Before scheduling the present study the required ethical clearance was obtained from the concerned hospital authorities. The consent of the parents/guardians was taken on the consent form. The subjects participated in the study were selected according to the following criteria: children aged 6-12 years, children who were on syrup medication and admitted children who were clinically stable, children suffering from- Anemia, Malnutrition, Epilepsy, Nephrotic syndrome and Asthma. While the exclusion criteria were: children who were on tablet formulation also, children who were critically ill and the parents/guardians who did not give the consent.

Forty- six children who were chronically ill and on long- term liquid oral medication were selected for the study. Those were children suffering from Anemia, Malnutrition, Epilepsy, Nephrotic syndrome and Asthma. Medicines were selected on the basis of the disease included in the study. Out of which six patients were on Calcium and vitamin D syrup, five patients on Iron and Folic acid, five patients on Phenytoin Oral Suspension, six patients on Theophylline and six patients on Multivitamin - multimineral syrup (total eighteen) were asked to swish with their respective medicines. Similarly eighteen patients rinsed with 10% sucrose solution.

Subjects were instructed to abstain from oral hygiene practice for 48 hours so that sufficient plaque would have accumulated. All experiments on each subject were carried out in the morning to minimize the variation in salivary flow and its composition. On the test day a sample of 5ml of drug was dispensed to the children and asked to swish it around the mouth for a min and spit it out (Sunitha S, Prashanth GM 2009).

To determine resting plaque pH at baseline, sample of approximately 1 mg of plaque was collected using harvesting method (Sunitha S, Prashanth GM 2009) and at time intervals of 5, 10, 15 and 20 mins. Each patient was asked to rinse with their respective medicine. For every measurement the collected plaque was thoroughly mixed with 10 ml of distilled deionized water in the vials. The pH was measured using Hanna digital pH meter which was calibrated by standard buffer solution at pH 4 and pH 7. To control the bias, pH measurement was done within 5 to 10 s. Plaque was harvested as far as possible from the same site (buccal surfaces of maxillary molars).

Statistical analysis

At 80% study power and alpha level of 0.05 sample size of 46 patients is required for difference of means to be detected of 0.1 in pH from resting pH at day 1 to after 30 minutes assuming expected standard deviation within groups of 0.1568 in pH as per results of pilot study. (paired t- test)

For each medicine and each case the values *of plaque pH, minimum pH and maximum pH drop* were computed. Corresponding to different medicines/control solutions, the values of mean and standard deviation were calculated. Using these mean and standard deviations, the test of significance was conducted through the unpaired Student 't' test.

Change in mean plaque pH from baseline (resting plaque pH) to pH at 30 min was *triplicated*. 't' value for comparison of minimum pH value and maximum pH drop between different test medicines and control solutions was analyzed using unpaired't' test.

Results

The test result showed decrease in plaque pH following 1 min rinse with Phenytoin, Theophylline and Multivitamin – multimineral syrup at different time interval which was comparable to 10% sucrose solution. Vitamin D3 - Calcium Carbonate and Ferrous Fumarate - Folic acid syrup did not show a significant decrease in plaque pH as compared to 10% sucrose solution (Table 2, Figure 1).

The test showed that Phenytoin (5.48), Theophylline (5.533) and Multivitamin - multimineral (5.657) syrup had minimum pH value comparable with 10% sucrose solution (5.51). While minimum pH of Vitamin D3 - Calcium Carbonate (6.68) and Ferrous Fumarate - Folic acid syrup (6.46) was elevated as compared to 10% sucrose solution (Figure 2).

Maximum pH drop was seen with Phenytoin (1.48) and Theophylline (1.41) syrup comparable to 10% sucrose solution (1.40). Multivitamin - multimineral syrup showed maximum pH drop of 1.29. Vitamin D3 - Calcium Carbonate and Ferrous Fumarate - Folic acid syrup showed lesser drop in maximum pH i.e. 0.25 and 0.46 respectively (Figure 3).

The test showed that there was no significant difference between Phenytoin, Theophylline, Multivitamin - multimineral syrup and sucrose solution as the medicines behaving essentially same as 10% sucrose solution with respect to their potential to generate acids. Highly significant difference was found between Vitamin D3 - Calcium Carbonate and Ferrous Fumarate - Folic acid syrup and sucrose solution, as they did not behaved same as 10% sucrose solution (Table 3)

Table 1: List of medicines according to the active ingredients, sugar content and manufacturer

Sr. no.	Active Ingredients	Available sugar content given on label of medicine	Manufacturer
1	Ferrous Fumarate, Folic acid	-	Medicamen Biotech Ltd
2	Multivitamin, multiminerals	Liquid Glucose, Sugar	Galpha Laboratories Limited
3	Phenytoin	-	Ciron Drugs and Pharmaceutical Pvt. Ltd
4	Vitamin D_3, Calcium Carbonate	-	Medicamen Biotech Ltd
5	Theophylline	-	Cipla Ltd.

Table No. 2 Mean plaque pH for test medicines/ 10% sucrose solution at resting pH and following 1 minute rinse at different time interval

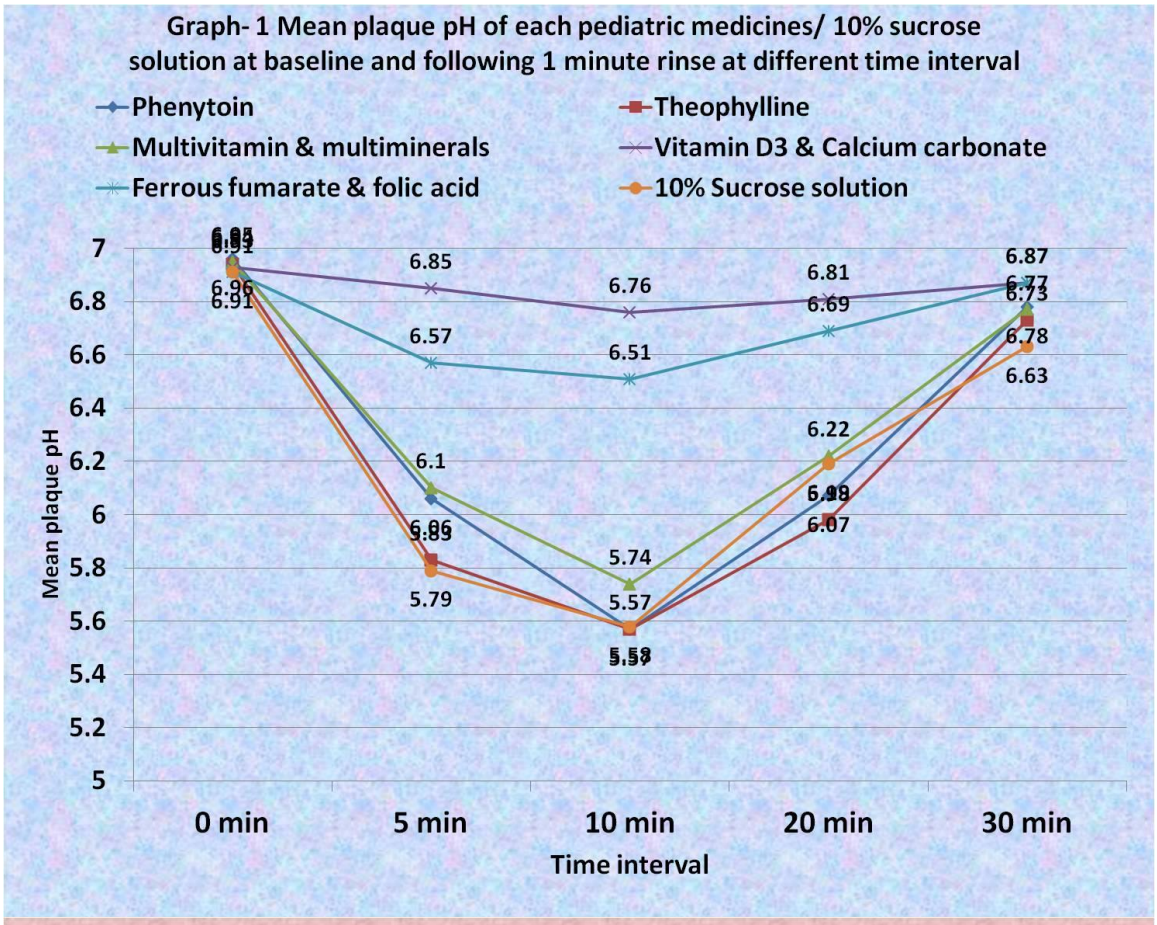
Name of Medicine/Control solution		Resting pH	5 min. pH	10 min. pH	20 min. pH	30 min. pH
Phenytoin	Mean	6.96	6.06	5.57	6.07	6.78

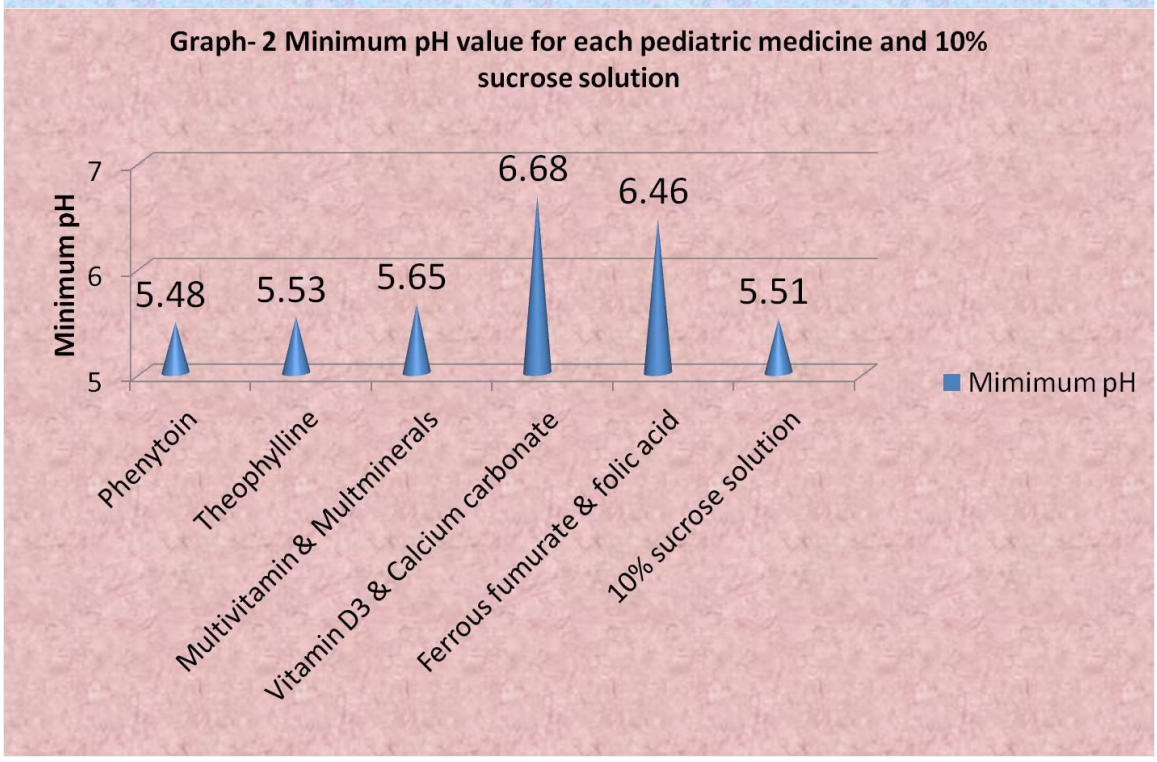
	SD	0.03	0.32	0.05	0.17	0.12
Theophylline	Mean	6.94	5.83	5.57	5.98	6.73
	SD	0.04	0.04	0.02	0.08	0.05
Multivitamin & multimineral	Mean	6.95	6.1	5.74	6.22	6.77
	SD	0.02	0.38	0.46	0.28	0.07
Vitamin D_3, Calcium Carbonate	Mean	6.93	6.85	6.76	6.81	6.87
	SD	0.03	0.04	0.09	0.07	0.02
Ferrous Fumarate, Folic acid	Mean	6.91	6.57	6.51	6.69	6.87
	SD	0.02	0.39	0.53	0.29	0.02
10% Sucrose solution	Mean	6.91	5.79	5.58	6.19	6.63
	SD	0.02	0.07	0.14	0.05	0.11

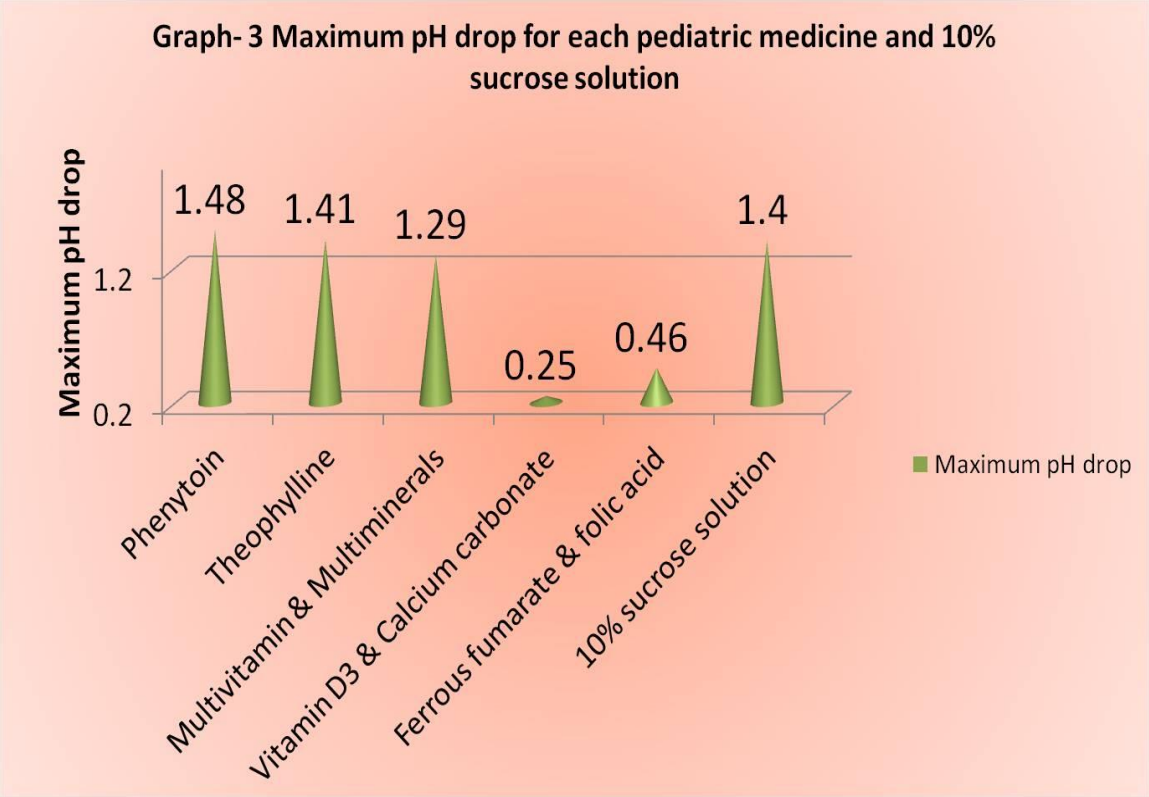
Table 3 ‘t’ value for comparison of minimum pH value and maximum pH drop between different test medicines and 10% sucrose solutions

Comparison between	Minimum pH	Maximum pH drop
Phenytoin & Sucrose solution	0.38^{NS}	0.91^{NS}
Theophylline & Sucrose solution	0.28^{NS}	0.02^{NS}
Multivitamin & multimineral & Sucrose solution	1.98^{NS}	0.92^{NS}
Vitamin D_3, Calcium Carbonate & Sucrose solution	15.82^{**}	15.58^{**}
Ferrous Fumarate, Folic acid & Sucrose solution	6.68**	6.97^{**}

NS: Not significant, *Significant ($P<0.05$), **Highly Significant ($P<0.001$)


Graph- 1 Mean plaque pH of each pediatric medicines/ 10% sucrose solution at baseline and following 1 minute rinse at different time interval
Phenytoin
Theophylline
Multivitamin & multiminerals
Vitamin D3 & Calcium carbonate
Ferrous fumarate & folic acid
10% Sucrose solution
Mean plaque pH
7
6.8
6.6
6.4
6.2
6
5.8
5.6
5.4
5.2
5
6.85
6.76
6.81
6.87
6.57
6.51
6.69
6.1
6.22
5.74
5.79
5.57
6.07
6.63
0 min
5 min
10 min
20 min
30 min
Time interval


Graph- 2 Minimum pH value for each pediatric medicine and 10% sucrose solution
Minimum pH
7
6
5
5.48
5.53
5.65
6.68
6.46
5.51
Mimimum pH
Phenytoin
Theophylline
Multivitamin & Multminerals
Vitamin D3 & Calcium carbonate
Ferrous fumurate & folic acid
10% sucrose solution



Discussion

Dental caries is slowly becoming a health problem which can be attributed to use of various therapeutic product, food and beverages which are acidic in nature. The etiology of dental caries is multifactorial, but sucrose normally plays a major role because of the ability of the micro-organisms in dental plaque to convert this important dietary constituent into various organic acids. In order for sugar to be metabolized by dental plaque, it must first dissolve in the oral fluids and then diffuse into the plaque (Lagerlof F, Dawes R et al 1985).

An assessment of acid production from carbohydrate by dental plaque bacteria can be used to assess the cariogenicity of dental plaque from a particular site. It is now well recognized that acid production following a sucrose challenge differs both between patients and between sites in the same patient (Weatherell JA, Duggal MS et al 1988, Laurence JW 2006).

Acid production within plaque affects the nature and composition of the dental plaque microflora. Bacteria with a high tolerance for acid (aciduric bacteria) which can also produce large amounts of acid can selectively overgrow within the microflora of supragingival plaque. This includes organisms within the mutans streptococci grouping as well as lactobacilli. In fact, the numerical emergence of mutans streptococci in dental plaque is often preceded by other types of aciduric bacteria. Many streptococci are relatively acid tolerant, while highly aciduric bacterial species are few in number (Laurence JW 2006). The caries process can be described as loss of mineral (demineralization) when the pH of plaque drops below the critical pH value of 5.5; the critical value for enamel dissolution is 5–6, and an average pH of 5.5 is the generally accepted value (Sharma A, Deshpande S 2011, Dong YM, Pearce EI et al 1999, Touger-Decker R, Loveren C 2003). Site-specific differences in human dental plaque pH after sucrose rinsing have also been detected (Weatherell JA, Duggal MS et al 1988).

Hence, evaluation of alteration in plaque pH to assess the cariogenicity becomes necessary. The present study evaluated plaque pH of commonly prescribed five liquid medicines to children admitted at J.K Loan Hospital, Jaipur.

Any food is been considered to be acidogenic if it produces a similar pH response as that of 10% sucrose solution (Sunitha S, Prashanth GM et al 2009). Thus, the plaque pH fall following the drug intake was compared with the fall in pH following the consumption of 10% sucrose solution.

Mean plaque pH for test medicines

In the present study, Phenytoin, Theophylline and Multivitamin - multimineral syrup showed fall in pH after the drug was rinsed for one min corroborating the findings of previous investigations (Marathaki E, Pollard

MA 1995, Sharma A, Deshpande S 2011, Sunitha S, Prashanth GM et al 2009, Srinivas N, Reddy VV 1994, Lokhen P, Birkeland JM et al 1995, Rekola M 1989). While Vitamin D3 - Calcium Carbonate and Ferrous Fumarate - Folic acid showed findings similar to Mentes A (2001).

Minimum pH value for test medicines

Minimum pH is defined as the lowest pH recorded during the test session on three different consecutive days in triplicate. Minimum pH of Phenytoin was found to be less than 5.5 (critical pH) corroborating the findings of Mentes A (2001) and Sharma A, Deshpande S (2011). Minimum pH of Vitamin D3 - Calcium Carbonate and Ferrous Fumarate - Folic acid, was found to be more than critical pH corroborating the findings of Mentes A (2001).

Maximum pH drop for test medicines

Maximum pH drop is defined as the difference between the initial prerinse plaque pH (resting pH) and minimum plaque pH obtained.

Maximum pH drop was seen with Phenytoin and Theophylline syrup. Finding of the study was consistent with the findings of previous investigations (Sharma A, Deshpande S 2011, Lokhen P, Birkeland JM et al 1975). The mean maximum pH drop was lowest with Vitamin D3 - Calcium Carbonate and Ferrous Fumarate - Folic acid, corroborating the findings of Lokhen et al (1975).

The liquid medications have a great potential for causing dental caries when inappropriately used. Majority of children did not brush their teeth after taking drugs. A long-term use of sugar-containing drugs has been considered a cause of dental caries in children. The increase of prescribed medicine intake and of self-medication in developed countries exposes a growing number of children to medication caries, which can be considered a public health problem. More extensive measurements on numerous medications are needed to be defined, that which characteristics lead to plaque pH alterations (Sunitha S, Prashanth GM et al 2009).

Summary and Conclusion: The present study demonstrated that there was no significant difference between three medications (Phenytoin, Theophylline and Multivitamin – multimineral syrups) and 10% sucrose solution with respect to their potential to generate acids. The manufacturer of these medicines should take necessary steps to reduce the pH level of these medicines.

Recommendations: Pediatrician and dental personnel should advice the mothers and caretakers to introduce oral hygiene practices after the consumption of the medication. Taking into consideration the present results, which have demonstrated the erosive potential of medicines commonly prescribed to chronically ill children, we recommend the following steps to mitigate any problems associated with their use:

1. The manufactures should formulate the medicines so as to make them less erosive to the teeth.
2. Instructions to the parents should be provided about the presence of sugar (sucrose) not only in foods & beverages, but also in medicines and its cariogenic potential.
3. The importance of rinsing the mouth with plain water after taking syrups should be told to parents.
4. Health practitioners should prescribe non−cariogenic form of syrups.
5. The patient who needs to be on long term liquid oral medicines should be advised for regular dental check up.
6. All medicines should contain a data sheet showing the type of sweetener and, if it is cariogenic, its concentration and pH should be labeled, with a warning sign (harmful for teeth).
7. Drug manufactures should be encouraged to replace sucrose by non cariogenic sweeteners.
8. All Children using liquid oral medication should brush their teeth twice a day using toothpaste containing at least 500 ppm fluoride. They should spit the toothpaste and should not swallow it.
9. Sealants should be applied and maintained in the pits and fissures of molars where there is increased caries-risk. The condition of sealants should be reviewed at each check-up. Glass ionomer sealants should only be used when resin sealants are unsuitable.
10. A fluoride varnish (e.g. Duraphat) may be applied every four to six months to the teeth of high caries risk children such as those children on long term liquid oral medication(Scottish Intercollegiate Guidelines Network 2012).

Conflict of interest: None declared.

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