Effect of Some Medicines on Caries of Deciduous Teeth

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Abstract
Background Dental caries in addition known as tooth decay is a breakdown of teeth due to actions of bacteria. The cavities may be a number of dissimilar colors from yellow to black. Symptoms may contain pain and difficulty with eating. **Aims** To determine the direct effect of the oral medicines which were used for long time by children on the teeth. To reduce the negative effect of these drugs. **Material and Methods** the study used medications that are prescribed for children for long time that administrated only orally to determine the direct effect of these drugs. The study sample included lower deciduous molars, which were obtained from children who required extraction of their mobile molars after taking the agreement of parents. Sample size was (50) freshly extracted, caries-free lower molar of patients aged 10-12 years old. Teeth were divided into five groups with 10 samples in each group, natural saliva was collected from a number of children and was added to the solution to simulate the oral cavity. The incubation period was 32 days then sectioning the samples and measure the lesion depth by polarized microscope. **Results** Verapamil produced maximum lesion depth in enamel while Dexamethasone was associated with minimum lesion depth. **Conclusion** it is obvious that all test medications affect the enamel of tooth by different degree.

Keywords: deciduous teeth, enamel, caries, medications.

Introduction

Dental caries in addition known as tooth decay, caries, is a breakdown of teeth due to actions of bacteria (Silk H, March 2014). The cavities may be a number of dissimilar colors from yellow to black. Symptoms may contain pain and difficulty with eating. Complications could include inflammation of the tissue around the tooth, tooth loss, and infection or abscess formation (Laudenbach JM and Simon Z, November 2014). The reason of caries is bacterial breakdown of the hard tissues of the teeth (enamel, dentin and cementum) this occurs as a result of acid made from food debris or sugar on the tooth surface. Simple sugars in food are these bacteria›s primary energy source and thus a diet high in simple sugar is a risk thing. If mineral breakdown is larger than build up from sources for example saliva, caries results. Risk factors comprise conditions that result in less saliva such as: diabetes mellitus, Sjogren›s syndrome and some medications. Medications that reduce saliva production comprise de antihistamines and antidepressants among others (Neville, B.W et al., 2002). Several medications have harmful effect on our health. Oral liquid pharmaceutical

dose forms such as syrups, solutions and suspensions are the therapeutic option for the management of pediatric patients. The use of these liquid preparations, despite being generally for short period, can be considered as prolonged occurrence (Babu KL et al., 2008). Particularly in patients who suffer from chronic condition, for example respiratory allergies, asthma and convulsions, or recurrent acute diseases as tonsillitis, otitis, sinusitis and allergic rhinitis (Marquezan M et al., 2007).
The employ of medicines in childhood is high particularly among children under two years old so that the constant use of medicines to treat asthma and attention-deficit or hyperactivity disorders has been rising (Headley J and Northstone K, 2007).
The truth that the tooth being affected by the use of medications is based on the hypothesis that these can diminish saliva flow and buffering capacity (Taji S and Seow-WK, 2010). Liquid formulations used for a three-month minimum period are considered a dangerous factor for increased levels of dental caries (Sahgal J et al., 2010). For this reason, children who use vitamin C supplements are 4.7 times more likely to increase dental erosion lesions (Al-Malik MI et al., 2001). So, children with chronic or recurrent health trouble who make recurrent use of medications are mainly at risk (Souza MIC et al., 2002). While caries is a sucrose-dependent disease. In addition, as numerous liquid medicines for children have low endogenous pH, they can also endorse dental erosion, mainly if they wait for prolonged period in contact with the tooth surface (Neiva A et al. 2001).

Materials and Methods

Sample size and criteria

Full details treatment plans were explained to the children›s parents and written consents were obtained prior to collection of the samples. The study sample includes lower deciduous molars, which were obtained from children who required extraction of their mobile molars Sample size was (50) freshly extracted, caries-free lower molars of children aged 10-12 years old. Teeth collected according to flowing criteria:
•Non-carious lower primary molars.
•Non-abrasion, attrition or erosion teeth.
•Any morphological anomaly tooth excluded from study.
Natural saliva was collected from a number of children and was added to the solution to simulate the oral cavity. The incubation period was 32 days then sectioning the samples and measure the lesion depth by microscope.
Samples preparation:
Teeth were scaled and polished using non fluoridated pumice and rubber cup, stored in thymol (0.1%, pH=7). In addition, teeth were examined under reflected light microscope with 10X magnification power to exclude those with any defects (Dan PP et al., 2008). Then immersion the teeth in solutions prepared from the medications (free of sugar), saliva (pH 6.5-7) and at temperature (37 ºC), then incubated for 32 days.

Concentration of medication and Sample grouping

Most medications in children are dosed according to body weight (mg/kg) or body surface area (mg/m2) (BSA). The Doses is expressed as mg/kg/day. Dosing also varies by indication.
•Group A: teeth suspended in methotrexate solution (1980mgcontaminated with saliva).
•Group B: teeth suspended in azathioprine solution (1800mg contaminated with sa-

liva).
•Group C: teeth suspended in verapamil solution (180mg contaminated with saliva).
•Group D: teeth suspended in dexamethasone solution 1800mg contaminated with saliva.
•Group E: teeth suspended in fluoxetine solution 600mg contaminated with saliva.

Microscopical evaluation of demineralization

At end of incubation phase, the samples were washed with deionized water, after that the samples were cut in cross section labiolingual by thin section –cut off saw, followed by each cut-sample was grind by grinding machine and polishing from non-cutting side until the enamel slice reach thickness of (250μm) using caliper, after that each cut sample fixed on microscopically slide from the cutting side via canda plasm and hot plate (Amandeep Singh, 2006). This process was done in coordination with college of science/department of earth science/university of Baghdad.
The enamel slices were examined under polarized light microscope (orthoplan, 071884). Lesion depth (μm) was measured for each slide using eyepiece graticule supplied with polarized microscope. The lesion depth represents the distance from surface zone till deepest zone of body lesion (Hicks MJ, 1993). Photomicrographs were captured using special digital camera and images were digitalized on computer (Figures 1-5).

Figure (1): Photomicrograph exhibited caries –like lesion of sample suspended on methotrexate.

Figure (2): Photomicrograph exhibited caries –like lesion of sample suspended on azathioprine.

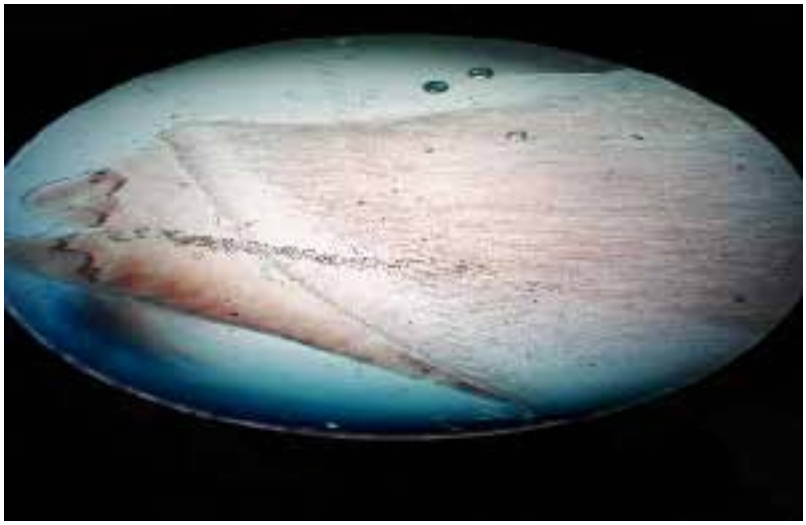
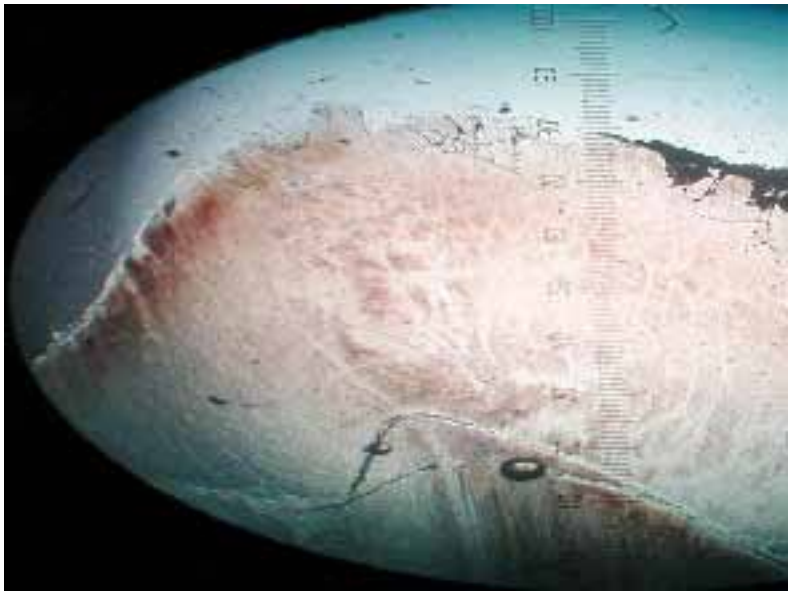


Figure (3): Photomicrograph exhibited caries –like lesion of sample suspended on verapamil.

Figure (4): Photomicrograph exhibited caries –like lesion of sample suspended on dexamethasone.



Statistical Analysis

The one-way analysis of variance (ANOVA) is used to determine whether there are any significant differences in lesion depth means between five independent (unrelated) groups. The one-way ANOVA compares the means between the groups and determines whether any of those means are significantly different from each other. Specifically, it tests the null hypotheses: $H0:\mu1=\mu2=\mu3=\ldots=\mu k$

The data obtained during the course of study were analyzed using Excel; Microsoft office 2010, Windows 7 Ultimate. Descriptive statistics consist of: mean, standard deviation, minimum and maximum be calculated for each group. A post hoc test used to establish which certain groups differed from other (Mahbubul A, 2013).

Results

The descriptive statistics of test groups including mean, standard deviation and standard error were calculated (Table 1).All test medications caused some degree of dental caries. The results show the verapamil more cariogencitythan other test medications.

Table (1): descriptive statistics of test groups.

Group	Sample size	Rank of Mean (µm)	SD	SE
Verapamil	10	570.605	467.5	148
Methotrexate	10	365.01	275.4	87.14
Azathioprine	10	354.525	209.8	66.4
Fluoxtine	10	285.6	247.6	78.36
Dexamethasone	10	116.765	51.29	16.23

Comparison between medication was done in pairs using post hoc test with respect to lesion depth in enamel and most of the test medications exhibited statistically significant ($p \leq 0.05$) difference between each other.

Table (2) demonstrates comparison among mean of test medication, the results show there is no significant difference between methotrexate and verapamil, methotrexate and azathioprine while the difference is significant between azathioprine and verapamil, methotrexate and fluoxtin, azathioprine and dexamethasone, azathioprine and fluxotine, verapamil and dexamethasone, dexamethasone and fluoxtine while the significant difference is high between methotrexate and dexamethasone and between verapamil and fluoxtine

Table (2): Demonstrating correlation analysis between test medications.

Test medications	*p*-value	Significance
Methotrexate and Verapamil	0.102	NS
Methotrexate and Azathioprine	0.09	NS
Azathioprine and Verapamil	0.023	S
Methotrexate and fluoxtine	0.007	S
Methotrexate and dexamethasone	0.001	HS
Azithroprine and Dexamethasone	0.007	S
Azithroprine and Fluoxtine	0.017	S
Verapamil and Dexamethasone	0.017	S
Verapamil and Fluoxtine	0.001	HS
Dexamethasone and Fluoxtine	0.025	S

Discussion

The frequent use of oral medicines put children at risk of dental caries and erosion, as demonstrated by various clinical studies (Taji S and SeowWK, 2010) (Maguire A, 1996) In a survey conducted, found that the dental health of children taking long-term liquid medication to be worse than their siblings in relation to anterior teeth decay in deciduous dentition (Maguire A, 1996) In this study it was obvious that exposure of enamel to high concentration of medications used in this study lead to affect the sound enamel with different lesion depth. The mean of lesion depth ranged between (116.765µm-570.6µm). Comparison among samples mean of (5) groups of test medications and these groups have same experimental period and specific concentration for each one. The results confirmed that there was significant difference between highest mean of lesion depth (verapamil), lowest mean of lesion depth (dexamethasone) were the mean in verapamil was (579.605µm), and mean in dexamethasone was (116.765µm). According to these results, the verapamil have highest cariogencity, while dexamethasone has lowest cariogencity, this can be explain by the fact that the endogenous pH of verapamil was (5.7) while the pH of dexamethasone (7.1).

The medications with low pH have greater potential for causing dental caries. Pediatric syrups with low pH have ability to initiate the dental demineralization by direct action on enamel surface, without any influence on the oral microflora. The development of erosion was also influenced by the enamel type, temperature and acid exposure time (Passos IA and Sampaio FC, 2011).

The endogenous pH of a medication can be rapidly changed intraorally by salivary buffers. Alternatively, sugars metabolized by bacteria to acid products decrease the pH within an adherent bacterial-rich plaque that is relatively unavailable to salivary buffering. Low pH near the tooth surface causes ionic dissolution from the hydroxyapatite crystals and eventually carious lesions (Feigal RJ et al. 1986). An in vivo study has shown that pediatric medications causes a drop in plaque pH that is sufficient to cause decalcification within 2 – 10 minutes following its initial exposure to the teeth (Sunitha S et al., 2009).

The present research provided evidence that the studied medicines could potentially affected deciduous tooth enamel after successive immersion cycles. The enamel surfaces presented with different lesion depth, which resulted from the mineral loss caused by medicine intake. Enamel thickness in deciduous teeth, lesser mineralization levels and a lesser structural arrangement are the chief differences between deciduous tooth enamel compared with that of permanent teeth. On the other hand, some controversy remains relating to the vulnerability of deciduous teeth to caries and erosion process compared with permanent teeth (Low IM et al., 2008; Sonju AB et al., 1997).

Some in vitro researches reported that medications can affect enamel hardness, and cause morphological and roughness alterations (Costa CC et al., 2006; Valinoti AC et al., 2010). However, the results of these studies are restricted to a small number of medicines, and the literature is limited of articles that study the effects of medications on permanent and deciduous tooth enamel (Valinoti AC et al., 2010).

The experimental period (32 days) was chosen to simulate what would occur above a long treatment. It is possible that longer treatment-induced damages to tooth structures will be larger than those observed in this study. On the other hand, the medications used in this study chosen because of their routine use in treating widespread

childhood disorders; this attractive finding was agreed with other study (Camila Scatena et al., 2014). Were reported that experimental period (28) and selected mostly prescribed medications for children.
After measure the lesion depth of test medication sample by polarizing light microscope, it was found that verapamil has the highest mean of lesion depth (570.605µm), mean that it is more cariogenic among test medications. Pain - tooth or teeth is reported only by a few people who take Verapamil Hydrochloride (Irfan C et al., 1996).
Methotrexate has mean of lesion depth (365.01µm), Children submitted to antineoplastic management present numerous late effects in several organs and systems, as well as the oral cavity; these effects are caused by anticancer medications. Dental abnormalities are the more common sequelae of treatment for childhood cancer (Camila Scatena et al., 2014)
Some authors actually reporting that caries rate for most children are not markedly affected by chronic liquid medication intake (Sahgal J et al., 2010). Therefore, it is understandable that dissolution of enamel caused by medications is due to number of factors like low pH and chemical composition of the medicine. In addition, frequency of consumption of the syrup and the time of intake may also add to the potential caries challenge.
The results showed that fluoxetine increase the risk of dental caries when measure the lesion of depth of test samples, dental caries is side effect of the tricyclic antidepressants and other anticholinergic psychoactive drugs (Bassuk E and SchoonoverS1978).
Perhaps, the degree of enamel loss caused by the medications in this laboratory study could be greater than clinical situations as the oral environment cannot be exactly simulated. In oral cavity, the enamel surface is covered by a protective pellicle and/or plaque layer and subjected to flushing, buffering and remineralizing effects of saliva (Jeremy R et al., 2005).

Conclusion

The test medications in this study can cause teeth problems and considered potential risk factors for the development of dental caries; verapamil has high cariogenic potential among test medications.

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