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Renal Fluoride excretion in children following topical application of acidulated phosphate fluoride and sodium fluoride

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Abstract

The aim of this study was to demonstrate that if there is an increase in urinary fluoride and creatinine excretion and F/ Cr ratio after application of acidulated phosphate fluoride APF and sodium fluoride NaF fluoridated gel.

The sample chosen consisted of 80 children randomly selected, aged 9-11 years old, lived in Baghdad city with non-fluoridated water areas. The children were divided into two groups, the study group which consists of 60 children who received the topical fluoridated gel, the acidulated phosphate fluoride (APF) and the sodium fluoride (NaF).Urinary samples were taken from them before the topical application of dental fluoride gel APF and NaF and 2 hours afterwards. In an age matched control group of 20 children from the same community, who received no treatment, samples were taken at the same way. The urinary excretion of fluoride was analyzed by determining fluoride ion (F^-) level and fluoride/ creatinine (F/ Cr) ratio in the urine.

Results showed that the mean F ion before and 2 hours after acidulated phosphate fluoride application APF was (1.74 and 2.36) respectively, this difference was statistically highly significant ($p<0.001$). While the F/ Cr ratio before and 2 hours after APF application was (1.01 and 1.07) respectively, with no significant difference ($P<0.05$). The mean of F ion before and 2 hours after sodium fluoride application NaF was (1.74 and 3.18) respectively, the difference was highly significant ($p<0.001$). While the F/ Cr ratio before and 2 hours after NaF application was (1.16 and 1.33) respectively with no significant difference ($p<0.05$). In the control group no significant changes occur ($p<0.05$).

Key words: Fluoride, Sodium fluoride, Acidulated phosphate fluoride, Fluoride/ Creatinine ratio, Urinary excretion, children.

Introduction

The importance of fluoride in prevention of dental caries and promoting oral health has been widely accepted for over 60 years. Fluoride sources include water, diet, tooth paste, mouthwashes supplements and professionally applied fluoride [1, 2].

Fluoride has been considered an effective anti- caries agent when delivered in many vehicles and concentrations, including a variety of professionally applied fluoride products [3]. The anti- caries effectiveness of the fluoridated

products has been shown especially in permanent teeth and being less evident in primary teeth [4, 5]. Excessive ingestion of fluoride possess the risk of acute or chronic exposure and creates a metabolic over load without increasing protection against caries. Chronic exposure to excessive and continued ingestion of fluoride causes dental fluorosis [6]. 75 to 90% of fluoride is absorbed through duodenum and stomach, fluoride ion is eliminated through the urine [7]. The ability to swallow correctly influences the level of fluoride entering the system by means of tooth pastes [8]. The amount of fluoride found in the urine may be considered an acute reflection of the volume ingested both in the form of food and from preventive treatment [9]. Creatinine is the product of muscle creatin catabolism [10]. In the present study we evaluate the effect of oral application of sodium fluoride (NaF) and acidulated phosphate fluoride (APF) on urinary fluoride/ creatinine excretion.

Materials and Methods

80 children aged (9-11) years old, both sexes were included in this study. The participants were healthy volunteers, selected from children who visit the pedodontic clinic in collage of Dentistry Al- Mustansiria University. All children had brushed their teeth using their non- fluoridated tooth paste without special instructions. The study group divided into two subgroups, first group consists of 30 children, 15 female and 15 male who received the (APF), The second group consists of 30 children, 15 female and 15 male who received the (NaF). All children in the study group give a simple explanation about all procedure of the study and get acceptance from their parents about involve their children in this study, each child from both groups was given sterile poly ethylene cup with a capacity 100 ml and instructed to urinate in the cup. The collection procedure was supervised by member of the research team. The pre-treatment samples were identified by a numerical code, assigned to each child. The plaque were removed from all teeth of children by polishing with non-fluoridated pumice and rubber cup, after that the first group children was received the APF (4ml), which is Thixotropic gel with Xylitol and Vitamin E, consist of 1.23% fluoride ion, made in USA and manufactured by (DHARMA), the APF gel applied to all teeth (dental surfaces) with use of disposable dental trays in upright position for 4 minutes, after that the children were instructed to spit out any residual saliva into spittoon. The children should be instructed not to rinse, consume food, water or urinate until they were called to provide the second urine sample after 2 hours.

The same procedure repeated for the children who received NaF which is 2% neutral sodium fluoride gel, available in US, Canada and manufactured by Denta.

20 children involved as control group, the plaque were removed by using non- fluoridated pumice and the urine sample were collected before polishing their teeth and after 2 hours. The fluoride ion and creatinine were measured in the same way.

The fluoride ion determination was performed using the potentiometric method with ion specific electrode following the serial calibration technique, (WTW InoLab PH 7110 Using fluoride electrode- 1052 F, Germany).

Creatinine concentration was measured using high performance liquid chromatography devices and equipment.

Statistical analysis was carried out; the F/Cr ratio was calculated

automatically. A t-test with paired data was used in order to compare two mean values within subject measures.

Results

Table 1 showed the average urinary fluoride ion and creatinine levels before (Cr1, F1) and after (Cr2, F2) APF application in the study and control group, highly significant difference were found between (Cr1, Cr2 and F1, F2) for the study group $p<0.01$. No significant difference were found in the control group $p<0.05$. Table 2 illustrated the average F/ Cr ratios for both urine samples, before (F/ Cr1) and after (F/ Cr2) APF application taken from both groups. The study group was statically non-significant $p<0.05$. No significant differences were found between F/Cr ratios from the first and second urine samples in the control group. Table 3 showed the average urinary fluoride ion and creatinine levels before (Cr1, F1) and after (Cr2, F2) NaF application in the study and control groups. Highly significant difference between Cr1, Cr2 and F1, F2 for the study group $p<0.01$. No significant difference were found in the control group $p<0.05$. Table 4 illustrated the average F/ Cr ratios for both urine samples, before (F/ Cr1) and after (F/ Cr2) NaF application, taken from both groups. No significant difference were found between F/ Cr ratios from the first and second urine samples in the study group $p<0.05$, also no significant difference were found in the F/ Cr ratios for the control group $P<0.05$.

Discussion

The kidney accumulates fluoride more than other organ in human body, so the main route for fluoride excretion is through the kidney. This study was concentrated on the measuring of fluoride level in urine as well as the action of kidney's by measuring the creatinine levels for children aged between (9-11) years old, and found a significant increase of fluoride level in the group treated with NaF more than the group treated with APF this was due to the fact that sodium ion is more soluble than phosphate ion [(11)]. It must be pointed out here that we did not find any existing studies on the absorption of fluoride applied topically in the form of gel, which require spot urinary samples for determination of the F/ Cr ratio, one of the reasons for using this method was that the F/ Cr ratio is a particularly reliable indicator when studying groups of individuals [(12)]. The F/Cr ratio is considered to be equivalent to total 24 hour fluoride excretion, however, while the concentration in urine over 24 hour allows an accurate reading of total fluoride excretion over this time period, such measurement does not accurately reflect the increase in excretion, because 24 hour readings don't distinguish increase in secondary fluoride concentrations from fluoride present in dentifrice or diet [(13)]. The authors compared this study with those of other investigations in which Fluoride/ Creatinin (mg/g) ratio and fluoride levels (mg/l) were analyzed in the urine of subjects treated with other fluoride supplements. This study agreed with another study carried out by Ekstrand etal 1980 who administered doses of 3 to 5 Duraphat to 4 children aged 4,5,12 and 14 based on their age. Before applying the varnish, the mean concentration of fluoride in urine over 12 hours was 0.1 mg F in younger children and 0.2 mg F in the older children. Following the application of varnish, the urine concentrations increase to 0.5 mg F over 12 hours in the two younger children and 1.1 mg F in the older children. The plasma F levels were

well below those considered to be toxic [14]. This finding is in consistence with that observed by Pessan etal 2005 who observed a significant increase in fluoride levels in urine following the application of approximately 4.52 mg fluoride in the form of varnish (Duraphat) and a return to baseline conditions within 24 hours in a sample of 11 children between the ages 4 and 7 years who used fluoridated tooth paste [15].). Also this study agreed with Olympios etat 2009 who Carried out an investigation on a sample of 7 children of 5 years of age who brushed their teeth with placebo tooth paste for 7 days, concluded that, after the application of Duraphat fluoride varnish, the increase in the urinary excretion of fluoride was significant but returned to baseline levels at 48hours [16]. This study also agreed with Garcia etal 2014 on 58 children aged 5-8 years old, results showed a highly significance increase in fluoride concentrations after application of fluoridated mouth rinses [17]. This research disagree with Garcia-Comb 2009 on 100 children aged between 5-8 years old, living in zone with non-fluoridated water, in which the F l/Cr ratio in the urine before and 2 hours after brushing with fluoride tooth paste was 0.61 mg/g and 1.25 mg/g respectively ($p<0.001$) [13].

This finding also disagree with that obtained by Garcia etal 2012 on urinary excretion of fluoride after the application of fluoride varnish (Duraphat) in 42children aged between 5-8 years old who lived in non-fluoridated water area, showed that the Fl/Cr ratio in urine before and 2 hours after varnish application was 0.42 mg/g and 1.38 mg/g respectively ($p<0.001$) [18]. In this study 2 hours urinary excretion was chosen as the response variable to evaluate the bioavailability of fluoride from the products tested.

Conclusion

The results of this study indicated that, after application of the fluoridated gel APF and NaF, there is a highly significant increase in the fluoride and creatinine levels in the urinary excretion especially with NaF, this lead to conclude that NaF gel passes to the systemic route. Also this study showed no significant increase in the F/ Cr ratio for both APF and NaF fluoridated gel $p<0.05$.

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Table -1- Creatinine and fluoride levels in urine samples from the study and control groups before and after application of acidulated Phosphate fluoride APF.

	Average	Confidence interval 95%	std	Min.	Max.	P.value
treatment						
Cr1 with APF	1.80	0.31—0.79	0.42	1.10	2.70	0.000***
Cr2 with APF	2.36	0.31—0.80	0.52	1.10	3.40	
Fluoride1 with APF	1.74	0.27—0.97	0.82	0.47	3.30	0.001**
Fluoride2 with APF	2.36	0.27—0.97	0.50	1.48	3.13	
Control						
Cr1 with APF	1.32	0.21—0.34	0.25	1.11	2.0	0.629
Cr2 with APF	1.39	0.21—0.34	0.33	1.13	2.30	
Fluoride1 with APF	0.28	0.05—0.32	0.12	0.168	0.500	0.162
Fluoride2 with APF	0.42	0.06—0.33	0.26	0.166	0.880	

Table-2- F/Cr ratios in urine samples from the study and control groups before and after application of acidulated phosphate fluoride APF.

	Average	Confidence interval 95%	std	Min.	Max.	P.value
treatment						
Fl/Cr1 ratio with APF	1.01	0.17—0.280	0.50	0.2320	1.86667	0.663
Fl/Cr2 ratio with APF	1.07	0.18—0.281	0.38	0.54118	2.11538	
Control						
Fl/Cr1 ratio with APF	0.223	0.053—0.186	0.098	0.084	0.38393	0.257
Fl/Cr2 ratio with APF	0.289	0.054—0.187	0.149	0.1469	0.56296	

Table-3- Creatinine and fluoride levels in urine samples from the study and control groups before and after application of Sodium fluoride NaF.

	Average	Confidence interval 95%	std	Min.	Max.	P.value
treatment						
Cr1 with NaF	1.95	0.21—0.78	0.58	1.00	3.10	0.001**
Cr2 with NaF	2.45	0.21—0.79	0.54	1.80	4.60	
Fluoride1 with NaF	1.74	0.875—1.987	0.77	0.58	3.61	0.000***
Fluoride2 with NaF	3.18	0.872—1.990	1.311	1.49	6.21	
Control						
Cr1 with NaF	1.44	0.266—0.330	0.35	1.130	2.300	0.824
Cr2 with NaF	1.41	0.267—0.331	0.28	1.10	2.00	
Fluoride1 with NaF	0.35	0.163—0.301	0.23	0.170	0.950	0.538
Fluoride2 with NaF	0.42	0.164—0.303	0.26	0.167	0.870	

Table-4- F/Cr ratios in urine samples from the study and control groups before and after application of Sodium fluoride NaF.

	Average	Confidence interval 95%	std	Min.	Max.	P.value
treatment						
Fl/Cr1 ratio with NaF	1.16	0.10—0.45	0.47	0.64762	3.00833	0.211
Fl/Cr2 ratio with NaF	1.33	0.10—0.45	0.59	0.7040	2.93684	
Control						
Fl/Cr1 ratio with NaF	0.246	0.104—0.222	0.142	0.09565	0.56548	0.459
Fl/Cr2 ratio with NaF	0.304	0.106—0.223	0.200	0.13917	0.70732	