Renal excretion of fluoride after fluoride mouth rinses in children

**ABSTRACT**

**Aim** This study was conducted to determine if there was an increase in the urinary excretion of fluoride, after the use of fluoride mouth rinses in children.

**Materials and methods** The sample consisted of 58 children aged 5-8 years, randomly selected, residents in non-fluoridated water areas. Urine samples were collected prior to mouthwash and also 2 hours after use. The control sample, which received no treatment, consisted of 16 children of equivalent age and from the same community. Urinary excretion of fluoride was analysed by determining the pH, creatinine, F- ion and fluoride (mg)/creatinine (g) (F/Cr) ratio in urine.

**Results** In the studied sample, the mean F/Cr ratio before fluoride mouth rinse was 0.26 mg/g and it rose to 1.58 mg/g 2 hours after mouth rinse. This difference of 1.33 mg/g was statistically highly significant (p<.001). In the control group no significant changes occurred. The average 2 hours afterward F/Cr ratios were 0.29 and 0.27 respectively (p=0.426).

**Conclusion** After the use of a fluoride mouthwash, in children, there is a statistically significant increase of fluoride ion in urine, which can be attributed to the application of this product.

**Keywords** Fluoride; Fluoride mouthwash; Fluoride/creatinine ratio; Urinary excretion.
The most commonly used fluoride mouthwashes are used on a weekly or daily basis. Mouthwashes of 0.2% sodium fluoride, to be used once a week or every two weeks, contain 900 ppm of F- (0.90 mg F-/ml) and are usually used in school programmes. The 0.05% sodium fluoride mouthwash, for everyday use, contains 225 ppm of F- (0.23 mg F-/ml) and is frequently used in individual programmes. Both types of rinses result in significant caries reductions, of about 30-35%. These mouthwashes were approved as safe and effective by the FDA in 1974 and by the Council of Dental Therapeutics of the ADA in 1975, as preventive agents to decrease dental caries incidence [Donley and Stookey, 2004]. Although fluoride mouthwashes efficacy against dental caries is well studied, we could not find in the literature data regarding fluoride excretion in urine, proceeding from fluoride mouthwashes topical use, as an expression of its systemic absorption. This led us to design a study in order to demonstrate that, after topical use of fluoride dental rinses by children, fluoride systemic absorption occurs and, consequently, there is an increase in urinary excretion attributable to the administration of the mouthwash.

Materials and methods

The study was conducted on a group of students, aged between 5 and 8 years, from a public school situated in a locality of the Community of Madrid, with non-fluoridated water (<0.3 ppm). A study group consisting of 58 children and a control group of 16 children were randomly selected from a list of 300 students of both genders. A different number was assigned to each child in order to identify their samples anonymously throughout the study. Inclusion criteria included an informed consent signed by the parents or guardians and that a sufficient amount of urine was provided in order to be analysed.

Exclusion criteria were the presence of kidney disease and other systemic diseases or having been previously included in a programme of fluoride mouthwashes. The project was reviewed and approved by the Research Ethics Committee of the Hospital Clínico San Carlos (Complutense University of Madrid, Spain).

Fieldwork was conducted in the school in morning periods. The children came to school after their regular food intake and hygienic habits, without previous instructions. Early in the morning, 58 children from the study group and the 16 from the control group were called and the procedure was briefly explained to them. Thereafter, a bottle of sterile polyethylene with a capacity of 100 ml was given to each one of them, indicating that they had to urinate inside it. This first urine sample was identified with the number assigned to each child and labelled “sample pre-treatment”. Subsequently, the way the rinse should be used was explained to all children, specifying that it should circulate between teeth and that swallowing should be avoided. A disposable cup containing 10 ml of 0.2 Flür-aid 0.2® mouthwash was given to each child of the study group. Each child of the control group received a disposable cup containing 10 ml of water. All children performed the rinse for 1 minute and threw out the excess in the same cup. Children returned to their schoolwork, with instructions not to rinse, ingest food or water or urinate until they were called again to collect a second urine sample. This second sample was collected at approximately 2 hours after obtaining the first. Therefore a second sterile container was given to each child, in both groups, identified with the corresponding number and labelled “sample post-treatment”. The pH and the concentrations of fluoride and creatinine were determined for each different urine samples pre and post-treatment. The pH measurements were performed using the potentiometric method and the quantifications of fluoride ion were done by potentiometry with ion specific electrode, following a serial calibration technique.

In order to determine the concentration of creatinine, a high performance liquids chromatography technique was used. The ratio F/Cr was calculated automatically. Determinations of each variable were subjected to its respective quality control (blind repetitions, repeatability control, accuracy control and precision control) and were performed in an accredited biochemical laboratory.

For each of the analysed variables, pH, F- and creatinine, it was processed, together with each batch, 10% of duplication of the collected samples, as well as blank samples, in order to perform an internal quality control on the precision. Two aliquots paths of certified urine samples were processed together with some of the sample batches for fluorides, of low and high levels respectively, in order to check the accuracy of the determinations. Control charts were also constructed in order to validate the results of each batch. If the results in the control samples exceeded the acceptance ranges, all results of the corresponding series were deleted.

Table 1 shows the average urinary pH and creatinine levels before (pH 1, Cr 1) and after (pH 2, Cr 2) mouthwash application in the treatment and control groups. No significant changes were found in those measurements.

Results

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Table 1 shows the average urinary pH and creatinine levels before (pH 1, Cr 1) and after (pH 2, Cr 2) mouthwash application in the treatment and control groups. No significant changes were found in those measurements.
Table 2 shows the average F/Cr ratios for both urine samples, before (F/Cr 1) and after (F/Cr 2) mouthwash application, taken from both groups. The difference of 1.33 mg/g found in the treatment group was statistically significant (p < .001). No significant differences were found between the F/Cr ratios from the first and second urine samples in the control group.

**Discussion**

To determine fluoride concentration in urine, many authors use the total excretion of fluoride in urine 24 hours after, but this method does not reflect with precision the increase in the excretion of fluoride as a result of the use of fluoridated mouthwash. In this study, as in previous studies conducted by our team on urinary excretion of fluoride [García-Camba de la Muela et al., 2009; Garcia-Hoyos et al., 2012], we employed the ratio fluoride/creatinine because its values are considered equivalent to those found in urine samples of 24 hours, when creatinine concentrations are normal (between 0.5 and 3.0 g/l) [Kertesz et al., 1989; Zohouri et al., 2006; Székely et al., 2008] and because the ratio fluoride/creatinine is particularly reliable when groups of individuals are studied [Szekely et al., 2008].

Because the authors could not find other studies in the literature that reflect the presence, in urine, of fluoride from topical application of a fluoride mouthwash, we compared our findings with those of other investigations in which fluoride/creatinine (mg/g) ratio and fluoride levels (mg/l) were analysed in the urine of subjects receiving other fluoride supplements.

In the present study, 10 ml of mouthwash Fluor-Aid 0.2®, containing 0.2% sodium fluoride at 900 ppm F-, were used. The F/Cr ratio, in the study group urine sample at baseline was 0.26 mg/l (SD=0.19) and 0.29 mg/l (SD=0.24) for the control group. As expected, the difference between them was not significant. These values are lower than those reported by other authors, who analysed the fluoride in the urine of individuals receiving fluoride supplements. This can be explained by the fact that this investigation was performed in a community with non-fluoridated water. In the present study, the second urine sample, collected 2 hours after the application of fluoride mouthwash, showed highly significant results (p <0.001) in the study group, and no changes were observed in the control group. The results for F/Cr obtained in the second urine sample of the study group are higher than the ones found by Declercq et al. [1995] in a group of 700 children aged between 2 months and 14 years who lived near an aluminium smelter, industrial process which involves the emission of fluoridated derivatives into the atmosphere, as a result of the use of the compound Na3 Al F6 in the electrolytic reduction process of aluminium. In this study an F/Cr ratio of 0.52 mg/g in urine single samples was obtained. They also assessed the urinary excretion of fluoride in two other groups of children from the same community. The first group, who drank mineral water rich in fluoride

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Average g/l</th>
<th>95% Confidence interval</th>
<th>St Dev.</th>
<th>Minimum</th>
<th>Maximum</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr 1</td>
<td>1.22</td>
<td>1.12 - 1.32</td>
<td>0.50</td>
<td>0.20</td>
<td>2.50</td>
<td></td>
</tr>
<tr>
<td>Cr 2</td>
<td>1.10</td>
<td>0.97 - 1.23</td>
<td>0.66</td>
<td>0.10</td>
<td>3.10</td>
<td>0.20</td>
</tr>
<tr>
<td>pH 1</td>
<td>6.24</td>
<td>6.11 - 6.38</td>
<td>0.68</td>
<td>5.00</td>
<td>7.80</td>
<td></td>
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<tr>
<td>pH 2</td>
<td>6.36</td>
<td>6.21 - 6.50</td>
<td>0.72</td>
<td>5.00</td>
<td>7.90</td>
<td>0.21</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Control group</th>
<th>Average g/l</th>
<th>95% Confidence interval</th>
<th>St Dev.</th>
<th>Minimum</th>
<th>Maximum</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr 1</td>
<td>1.28</td>
<td>0.97 - 1.58</td>
<td>0.58</td>
<td>0.20</td>
<td>2.30</td>
<td></td>
</tr>
<tr>
<td>Cr 2</td>
<td>1.04</td>
<td>0.77 - 1.32</td>
<td>0.52</td>
<td>0.20</td>
<td>1.80</td>
<td>0.15</td>
</tr>
<tr>
<td>pH 1</td>
<td>6.00</td>
<td>5.58 - 6.42</td>
<td>0.79</td>
<td>5.00</td>
<td>7.50</td>
<td></td>
</tr>
<tr>
<td>pH 2</td>
<td>6.12</td>
<td>5.71 - 6.54</td>
<td>0.77</td>
<td>5.00</td>
<td>7.40</td>
<td>0.57</td>
</tr>
</tbody>
</table>

**TABLE 1** Creatinine levels and pH in urine samples from the study and control groups before and after application of fluoride mouthwash.

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Average mg/l</th>
<th>95% Confidence interval</th>
<th>St Dev.</th>
<th>Minimum</th>
<th>Maximum</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>F/Cr 1</td>
<td>0.26</td>
<td>0.21 - 0.31</td>
<td>0.19</td>
<td>0.06</td>
<td>1.03</td>
<td></td>
</tr>
<tr>
<td>F/Cr 2</td>
<td>1.58</td>
<td>1.23 - 1.93</td>
<td>1.33</td>
<td>0.20</td>
<td>6.29</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Control group</th>
<th>Average mg/l</th>
<th>95% Confidence interval</th>
<th>St Dev.</th>
<th>Minimum</th>
<th>Maximum</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>F/Cr 1</td>
<td>0.29</td>
<td>0.17 - 0.42</td>
<td>0.24</td>
<td>0.11</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>F/Cr 2</td>
<td>0.27</td>
<td>0.17 - 0.37</td>
<td>0.19</td>
<td>0.08</td>
<td>0.83</td>
<td>0.42</td>
</tr>
</tbody>
</table>
showed a F/Cr ratio of 0.69 mg/g; in the second group, who was taking a daily fluoride tablet containing unspecified fluoride ion, the ratio was 0.82 mg/g [Declercq et al., 1995]. These results are also superior to those obtained by García-Camba in their study of 100 children between 5-8 years old, living in a zone with non-fluoridated water, in which the F/Cr ratio in urine before and 2 hours after brushing with fluoride toothpaste was 0.61 mg/g and 1.25 mg/g respectively (p <0.001) [García-Camba de la Muela et al., 2009]. The study of García-Hoyos et al. [2012] on urinary excretion of fluoride in children between 5-8 years of age who lived in a non-fluoridated water area, showed that the F/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).

The results obtained in the second urine sample of the study group are similar to those reported by Zohouri et al. [2006] that evaluated fluoride excretion in urine in a group of 7 children aged between 16-36 months (mean 32 months), residing in a community with fluoridated water, recording a F/Cr ratio in urine of 1.49 mg/g. Meanwhile, Kertesz et al. [1989], in a study on 326 children aged between 8-13 years, living in a Hungarian community with fluoridated water, reported an average ratio of 1.51 mg/g. In another study by Seixas et al. [2000] on adults who worked at an aluminium smelter, the F/Cr baseline ratio ranged between 1.3 and 3.0 mg/g.

Ekstrand, et al. [1980], in their study on fluoride varnish in 4 children aged 4, 5, 12 and 14 years, found that after an application of 3 mg in the younger and 5 mg in the elderly, fluoride urinary concentration/12 hours increased from 100 to 500 µg F/12h in the younger and 200 to 1,100 µg F/12h in the elderly. In another study of fluoride varnishes, Pessan et al. [2005] applied 4.5 mg of Duraphat® varnish to 11 children aged between 4-7 years old, living in an area with fluoridated water and using fluoride toothpaste. The results showed a significant increase in the fluoride concentration in urine, recovering baseline levels at 24 hours. Olympios et al. [2009], in a sample of 7 children of 5 years of age, who lived in an area with fluoridated water and that brushed their teeth with a placebo toothpaste for 7 days, concluded that, after the application of 0.2 ml of Duraphat® fluoride varnish, the increase in the urinary excretion of fluoride was significant but returned to baseline levels at 48 hours.

**Conclusion**

The results of this study indicate that, after the use of fluoridated mouthwashes in children, there is a significant increase in the F/Cr ratio in urine regarding the levels obtained in the analysis prior to treatment. The increase in the F/Cr ratio in urine, associated with the use of fluoridated mouthwashes, leads us to conclude that part of the mouthwash passes to the systemic route.

**References**