Effect of gastric contents on the bioavailability of fluoride in humans

Elliot R. Shulman, DDS, MS Margaret Vallejo, BS, MS

Abstract

The purpose of this study was to determine the effect of milk and solid foods on fluoride absorption. Ten adult volunteers received the following four treatments after being NPO for 8 hr: 1) 2.2 mg NaF, 2) 2.2 mg NaF and lunch, 3) 2.2 mg NaF and milk, and 4) lunch only. Samples of blood were taken at baseline and at up to 180 min after fluoride administration. Fluoride absorption was calculated for all four treatment groups. Milk was found to reduce fluoride absorption by 13%, while the presence of food reduced the absorption by 47%. The presence of food also delayed fluoride absorption, and significantly reduced the peak level of fluoride in serum.

Introduction

Fluoride taken systematically during tooth development has been shown to reduce the incidence of dental caries. The uptake of many drugs is affected by food present in the stomach at the time of drug administration. Currently, there are no dietary guidelines provided to patients concerning the administration of fluoride supplements.

Several studies have been performed to determine the bioavailability of fluoride for absorption when placed in a solution of milk. Simons (1965) reviewed studies in rats and humans using radioactive fluoride in milk at a concentration of one or four ppm as compared to similar concentrations of fluoride in water. He noted that although fluoride absorption was slightly slower from the milk solution, ultimately, the amount absorbed was the same.

Ericsson (1958) noted that the absorption of fluoride was reduced greatly by the simultaneous ingestion of inorganic salts or solid foods. Using rats, he showed that F^{18} absorption was inhibited when placed in a milk solution. Through diffusion studies, he also showed that fluoride did not completely diffuse through milk. He postulated that this could occur as a result of coagulation of the milk and/or the liberation of calcium ions due to the digestion of the milk. The resulting acidification gives rise to calcium fluoride, which is of low solubility and is not absorbed well.

Jowsey and Riggs (1978) investigated the effect of free calcium ions on fluoride absorption. Nine female adults received oral fluoride supplements with or without calcium carbonate. The authors were able to show that the serum levels were 22% lower when the fluoride was administered with calcium carbonate. Since prior studies had shown that calcium gluconate did not cause the same effect, they concluded that the decreased absorption likely was due to the alkaline state of the carbonate.

The influence of milk on fluoride absorption in humans has been studied by Shannon (1977), Ekstrand and Ehrnebo (1979), Spak et al. (1982), Trautner and Siebert (1986), and Trautner and Einwag (1989). They found that significantly less fluoride was absorbed when the fluoride was administered simultaneously with milk or dairy products.

The influence of food intake on fluoride absorption was first studied by Ekstrand and Ehrnebo (1979). Although they observed a decrease in fluoride absorption with solid foods, all the foods were dairy products and were not typical of a normal meal.

Trautner and Einwag (1987) studied the administration of sodium fluoride in the form of tablets or solutions given immediately following a standard breakfast. They found a decrease in absorption, with peak blood fluoride levels similar to those reported by Trautner and Siebert (1986).

Trautner and Einwag (1989) showed that although milk significantly decreased the absorption of fluoride, the addition of a standard breakfast nearly reversed this effect, contrary to the results reported by Ekstrand and Ehrnebo (1979).

All research to date has studied the simultaneous administration of fluoride with milk or solid foods. It would be of interest to find out what happens if the fluoride supplement is consumed long after food has been consumed.

The purpose of this study was to attempt to confirm the findings of Ekstrand and others on the influence of milk and solid food on fluoride absorption using a larger patient population. The study also was designed to determine the effect of administering fluoride after the consumption of milk or solid foods on fluoride bioavailability.

Methods and Materials

Ten healthy male adult volunteers 18–35 years of age participated in this study. The subjects were evaluated under four different testing sessions, with the order of presentation of the sessions randomized for each subject. Written informed consent was obtained for all subjects.

The subjects abstained from the use of fluoridated products, including toothpaste, one day prior to each session. A nonfluoridated toothpaste (Pepsodent—Lever Brothers, New York, NY) was supplied to each subject. The subjects were NPO after midnight on the day of each session.

Each session began at the same time, one week apart. Each patient had a heparinized catheter (18 gauge 1 3/4 in—Critikon, Tampa, FL) placed in an accessible arm vein. After 15 min, 3 cc of blood was drawn and discarded. A 5-cc sample of blood then was taken to determine a baseline plasma fluoride concentration. Two cc of normal saline and 100 units of heparin (Wyeth Labs, Philadelphia, PA) were used to flush the catheter each time blood was drawn.

In Session A, two 1.1 mg sodium fluoride tablets were swallowed by each subject. Blood samples were drawn at 15, 30, 45, 60, 90, 120, 150, and 180 min after fluoride ingestion. The catheter then was removed.

In Session B, the subjects were treated similarly to those in Session A. However, subjects in Session B consumed a lunch during a 15 min period; 30 min later, they ingested two 1.1 mg sodium fluoride tablets. Blood samples were then taken from the subjects at the same time intervals as in Session A.

Session C was similar to Session A, except that the subjects were given 6 oz of whole milk to ingest 15 min prior to the fluoride administration. Blood samples again were drawn at the same time periods after fluoride administration.

Session D was similar to Session B, except no fluoride tablets were consumed after lunch. The milk used in this study contained no fluoride.

The lunches consisted of a 2.8 oz roast beef sandwich, a turkey sandwich (both on white bread with a total of 1 tbsp of mayonnaise), 20 gm of potato chips, 1 cup of orange juice (248 gm), and 1 apple.

Specimens were collected in evacuated tubes containing powdered ethylenediamine tetraacetic acid as an anticoagulant. These tubes contained no detectable fluoride. The plasma obtained by centrifugation was stored frozen until analysis. Analyses of ionic fluoride concentrations present in the plasma were done as outlined by Whitford and Reynolds (1979). The technique was validated in conjunction with Dr. Whitford's laboratory. The Orion Model 94-09 ion-selective electrode (Orion Research, Inc., Boston, MA) for fluoride analysis was used.

Fluoride values were calculated for each patient by subtracting the baseline values at each session. The amount of fluoride absorbed was determined by calculating the area under the absorption curves less the baseline level, using the trapezoidal rule. Analysis of Variance (ANOVA) was used to determine significant differences. Post-hoc comparisons were made using the Neuman-Keuls test. All significance levels used were set at $P < .05$.

Results

Fig 1 illustrates mean fluoride absorption curves for all four treatments. Typically, the peak fluoride levels were similar in subjects receiving fluoride alone or both milk and fluoride. The consumption of lunch appeared to reduce the peak levels significantly and delay the timing of maximum fluoride absorption.

The amount of fluoride absorbed for each patient treatment session is shown in Table 1 (see next page). The values represent the area under the curve in cm^2. Consumption of a lunch without fluoride supplementation did not result in any appreciable fluoride absorption over baseline levels. The mean values for fluoride

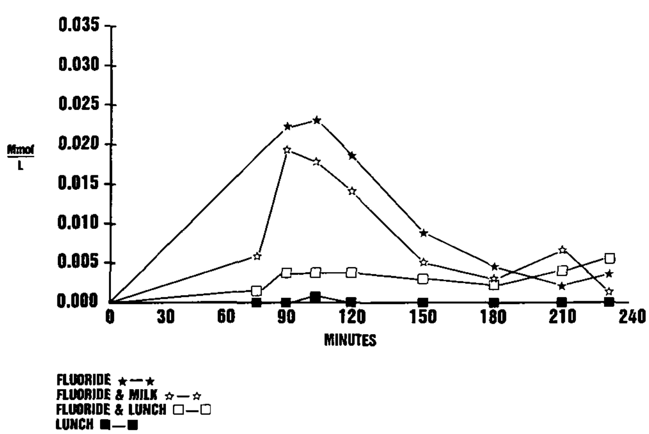

Fig 1. Mean fluoride absorption curves for the four treatment groups.

Table 1. Amount of Fluoride Absorbed*

Patient	Fluoride	Fluoride and Milk	Fluoride and Lunch	Lunch
A	0.80	1.68	1.61	0
B	1.19	1.60	1.76	0
C	2.39	1.65	0.92	0.17
D	1.26	0.85	0.26	1.68
E	3.44	1.27	0	0
F	1.80	1.54	0	0
G	1.71	2.11	1.29	0
H	0.91	2.54	1.59	0
I	1.38	0	0.75	0
J	1.40	0.97	0.46	0.35
Mean	1.63 ± .79	1.42 ± .70	0.86 ± .68	0.22 ± .53

Fluoride and Milk vs. Fluoride and Lunch: $P < .05$
Fluoride and Milk vs. Lunch: $P < .05$
Fluoride vs. Lunch: $P < .01$

* Area under curve cm^2

absorption when milk was consumed were 13% less than was seen in subjects given fluoride alone. This difference was not statistically significant. The addition of lunch to the fluoride supplement reduced absorption by 47%. This was found to be significant ($P < .05$) when compared to the milk and fluoride group, but not to the group given fluoride alone ($P = .1$). Fluoride absorption observed in the *lunch alone* group was significantly less than either the *fluoride alone* or *fluoride and milk* groups.

Table 2 illustrates the mean peak levels of fluoride absorption (and timing) for all four treatment groups. No significant differences were found in the peak values for the *fluoride* or *fluoride and milk* groups. The addition of lunch significantly reduced the peak ($P = .01$) from these other two groups to a level not much different than when no fluoride was administered with the lunch.

The timing of the peak value of absorption was not statistically different when comparing the *milk and fluoride* to the *fluoride alone* group. However, the addition of lunch significantly delayed the peak level. Six of 10 patients showed an average delay of 10 min, while four patients never showed any fluoride absorption during the time period studied. These latter patients dropped the overall mean showed in Table 2 to 65.3 min.

Discussion

The present study found that milk consumed prior to fluoride supplements reduces fluoride absorption by 13%, compared to supplements consumed on a fasting stomach.

Where previous studies by Ekstrand and Ehrnebo (1979) showed a 31% reduction, Spak et al. (1982) found a 28% reduction, and Trautner and Einwag (1989) found a 30% reduction, why did this study not show a significant reduction? This is most likely due to the differences in methodology for the studies. Milk was not administered simultaneously with the fluoride supplement, but rather 15 min before the fluoride supplement in this study. According to Whitford and Pashley (1984), a more acidic gastric pH favors fluoride absorption. Milk may reduce fluoride absorption by altering the pH to a more basic value. By waiting 15 min after milk consumption, the gastric contents may have had time to return to a more acidic pH, favoring absorption.

Another theory proposed by Spak et al. (1982) suggests that milk may coat the gastric wall and reduce the absorption of fluoride. The study by Trautner and Einwag (1989) appears to confirm this theory. The 15 min delay in this study would have allowed most of the milk to empty from the stomach, according to Paraskevopoulos et al. (1988). This would explain the reduced effect of the milk on fluoride absorption in this study.

The fluoride tablets were not chewed but rather swallowed whole in this study. While not all previous studies delineate how the tablets were consumed, chewing the tablet might increase the amount of fluoride absorbed when taken on a fasting stomach. Milk might then show a greater effect on reducing fluoride absorption as compared to this higher baseline figure.

Food in the present study was found to reduce significantly and delay fluoride absorption by 47%. This is in agreement with the results of Ekstrand and Ehrnebo (1979) of 46% and those of Trautner and Siebert (1986) of 4–89%. A delay of 30 min also was found in the peak absorption level. This again concurs with results by Trautner and Einwag (1987) of 1 hr, and Trautner and Einwag (1989) of 40 min.

Why does solid food have such a large effect on fluoride absorption as compared to milk? The most plausible theory was proposed by Spak et al. (1982). The larger quantity of food consumed decreases the speed of

Table 2. Peak Concentration of Fluoride

	Cmax $\left(\frac{Mmol}{L}\right)$	Tmax *(min)*
Fluoride	.024 ± .008*	99.8 ± 10.0*
Fluoride and Milk	.020 .009*	96.0 10.5*
Fluoride and Lunch	0.008 .008	65.3 56.8
Lunch	0.002 ± .005	12.0 ± 38.0

(*$P < .01$)

emptying of the stomach. This allows the food to stay in the stomach longer and act as a physical barrier, preventing fluoride absorption by the mucosal surface.

Although this study was done in adults, the results also should be applicable to children. Even though a younger child may absorb more fluoride, the effects of milk and food in the basic process of fluoride absorption should be similar.

Further research needs to be done on the effect of the timing of milk and food consumption prior to fluoride administration. How much time must be allowed to digest a meal prior to consuming a fluoride tablet in order not to significantly affect fluoride absorption? Can the fluoride be taken prior to a meal and not have its absorption significantly affected? If so, how close to a meal can it be taken? Many questions have yet to be answered on this subject.

Conclusions

This study found that milk does not significantly reduce fluoride absorption when taken 15 min prior to fluoride administration. On the other hand, solid food taken 30 min prior to fluoride supplements significantly reduces the amount absorbed. When prescribing fluoride supplements, instructions should be provided to administer them without any solid foods and as far away from a prior meal as possible. The consumption of fluoride supplements at bedtime or 1 hr prior to eating might be most beneficial to the patient. Fluoride supplements should not be added to milk or formula for consumption.

The authors thank Mr. Geoffrey A. Patrissi for his invaluable support in statistical analysis and Mr. Clodomiro Paoli for his untiring analytical efforts.

The opinions and assertions contained herein are those of the authors and are not to be construed as representing the policy or position of the US Air Force or the Department of Defense.

Dr. Shulman is chairman, department of pediatric dentistry, USAF Medical Center Keesler, Keesler AFB, MS. Captain Vallejo was officer in charge of chemistry at the clinical research Laboratory, USAF Medical Center Keesler, Keesler, AFB, MS at the time of this study and currently is instructor of chemistry at the USAF Academy, Colorado Springs, CO.

Ekstrand J, Ehrnebo M: Influence of milk products on fluoride availability in man. Eur J Clin Pharmacol 16:211-15, 1979.

Ericsson Y: The state of fluorine in milk and its absorption and retention when administered in milk. Acta Odontol Scand 15:51-77, 1958.

Jowsey J, Riggs LB: Effect on concurrent calcium ingestion on intestinal absorption of fluoride. Metabolism 27:971-74, 1978.

Paraskevopoulos JA et al: Effect of composition of gastric contents on resistance to emptying of liquids from stomach in humans. Dig Dis Sci 33:914-18, 1988.

Shannon IL: Biochemistry of fluoride in saliva. Caries Res 11:206-25, 1977.

Simons JH: Fluorine Chemistry. New York: Academic Press, 1965, Vol 4, p 140.

Spak CJ et al: Bioavailability of fluoride added to baby formula and milk. Caries Res 16:249-56, 1982.

Trautner K, Einwag J: Factors influencing the bioavailability of fluoride from calcium-rich health-food products and CaF_2 in man. Arch Oral Biol 32:401-6, 1987.

Trautner K, Einwag J: Influence of milk and food on fluoride bioavailability from NaF and Na_2FPO_3 in man. J Dent Res 68:72-77, 1989.

Trautner K, Siebert G: An experimental study of bioavailability of fluoride from dietary sources in man. Arch Oral Biol 31:223-28, 1986.

Whitford GM, Pashley DH: Fluoride absorption: the influence of gastric acidity. Calcif Tissue Int 36:302-7, 1984.

Whitford GM, Reynolds KE: Plasma and developing enamel fluoride concentrations during chronic acid-base disturbances. J Dent Res 58:2058-65, 1979.

To bag or not to bag? Infectious waste disposal

Increased awareness of infectious diseases has caused federal, regional, and local governments to enact legislation regarding the disposal of infectious wastes.

Because of this new awareness, healthcare facilities and healthcare workers face numerous definitions of categories of wastes and methods for their disposal. Disposing of waste items may, depending on the regulation, require special containers with biohazard labels (often referred to as red bags), and special disposal procedures and sites. Some regulations require sterilization of infectious wastes before disposal. Concern about potential infection is so great that, in a few regulations, any waste items containing even a drop of blood are considered infectious and therefore require special handling. In some instances, if the rules are to be interpreted strictly, a blood-stained bandage could be considered infectious.

The Environmental Protection Agency, in its consideration of infectious wastes, mentions four factors to be considered when determining if waste is infectious: the presence of a pathogen of sufficient virulence; the dose of the pathogen; the portal of entry; and the resistance of the host.

Consult your state and local regulations for specific proper disposal methods.