The prevalence and risk factors of fluorosis among patients in a pediatric dental practice

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Abstract

Seven hundred eight patients aged 5–19 years in a pediatric practice in North Carolina were selected using a random-start, systematic sampling procedure and enrolled in a case control study to determine risks for fluorosis. Subjects were examined by four trained examiners using the Tooth Surface Index of Fluorosis (TSIF). Information on fluoride exposures and other explanatory variables was obtained through parent interviews and mail questionnaires. Fluoride exposure was confirmed by fluoride assay of community drinking water samples. Bivariate associations for the entire sample were tested using MH χ^2 statistic. A secondary analysis controlling for fluoride in drinking water was performed using logistic regression for 233 subjects (116 drinking fluoridated water; 117 drinking fluoride-deficient water) who were lifetime residents at the same address. Nearly 78% of subjects had a TSIF score of > 0; 36.3% > 1; and 18.9% > 2. Twenty-two variables found in bivariate analyses (P < 0.15) to be associated with fluorosis were included in multivariate analyses. For subjects drinking fluoride-deficient water, fluorosis (1 or more positive TSIF scores) was associated with dietary fluoride supplement frequency (OR = 6.5) and age of the child when brushing was initiated (OR = 3.0). For subjects drinking fluoridated water, fluorosis was associated with age of child when brushing was initiated (OR = 3.1). (Pediatr Dent 17:19–25, 1995)

Understanding of fluoride exposures has increased over the last five decades and various recommendations have been made to limit fluoride intake to those levels providing the greatest benefits and the smallest risks. Public Health Service standards establish optimal levels for community water fluoridation, the dosage schedule for fluoride supplements has been revised downward in the 1970s, and fluoride levels in processed infant foods were lowered in the 1980s.

Increases in dental fluorosis in the US and elsewhere have renewed interest in evaluating fluoride exposures and their outcomes.[1-4] These observations also have stimulated recommendations to lower the fluoride supplement dosage schedule, limit toothpaste consumption in young children, and to use other fluoride products according to published guidelines.[5-7]

A number of studies have implicated supplements as a primary factor in increased prevalence of fluorosis.[8-16] Concern also has been expressed about topical fluorides as a risk factor, yet less clinical evidence exists for this exposure source compared with supplements.[8,17,18] Ripa pointed out that inadvertent swallowing of fluoride toothpaste, professionally applied topical fluoride, or fluoride rinses could cause fluorosis.[19] Others concluded that small children may accidentally swallow enough fluoride from fluoridated toothpaste to cause fluorosis development.[20] Certain foods and drinks are major sources of fluoride. McKnight-Hanes et al. point to the potential for soy-based formulas to cause fluorosis because of their fluoride-binding properties.[21] Osuji et al. found that prolonged formula feeding placed infants at risk for fluorosis.[17] Certain beverages, especially teas, contain high levels of fluoride,[22,23] and while consumption increases with age, the standard deviation within the same age groups is very large.[24,25]

Surveillance for fluorosis prevalence and its severity continue to be important, as do epidemiological studies to carefully delineate risk factors. Relatively few studies of risk factors include a comprehensive list of fluoride exposures or factors that may modify these exposures. Further, few studies simultaneously compare subjects who were drinking fluoridated water with those drinking fluoride-deficient water. Rarely have studies of fluorosis included interviews to determine fluoride exposures, a method that is more accurate than self-completed questionnaires.

A large number of fluorosis cases observed by a pediatric dentist in Asheville, North Carolina, provided the opportunity to quantify its prevalence, and to identify those factors likely contributing to its occurrence. Asheville, in western North Carolina, has been fluoridated since 1965 and has a population of 61,855 according to the 1990 census.[26] The pediatric practice is one of only two in this section of the state, and draws from a large geographic area including both fluoridated and nonfluoridated communities.

The purpose of this study was 1) to determine the prevalence and severity of enamel fluorosis occurring in patients in this pediatric dental practice in a fluoridated community in North Carolina; and 2) to identify those factors contributing to fluorosis.

Methods

A practice-based case control study design similar in many respects to medical epidemiological studies using patients attending a single hospital or multiple hospitals as sources of cases and controls was used. Unlike a population-based case control study, this design prevents generalizations about causal factors, or actual prevalence and severity of fluorosis, beyond this dental practice.

Two methods were used to identify cases. First, 200 patients in the practice known to have fluorosis were enrolled. Second, a stratified, random-start systematic sample of patients age 6 years and older was selected from more than 4,000 active records. This sample provided a group of subjects from which controls were selected, and additional cases either unknown to the practice or undiagnosed because the clinician may have used different criteria than those used by the research team. To provide the necessary sample size, every fourth record was retrieved, and subjects were enrolled into the study if they had at least one erupted permanent tooth and had not been previously selected as a case. This sampling ratio was to provide the desired 3:1 ratio of controls to cases.

This random sample also allowed us to determine the prevalence estimates for the entire patient pool. When sampling, any record that had been previously identified as having fluorosis was recorded for later use in calculating prevalence. By limiting the prevalence calculations to only those subjects whose records were retrieved during the random sample, we were able to determine prevalence estimates within the practice. This was done by dividing those subjects with fluorosis by those records retrieved from the random sample and also examined by the research team.

Examinations for enamel fluorosis were performed in the dental office by four examiners using the Tooth Surface Index of Fluorosis (TSIF) classification system.[27] Examiners were blind to the case status of subjects. TSIF scores were assigned to labial and lingual surfaces of anterior teeth, and to buccal, lingual, and occlusal surfaces of posterior teeth where teeth were fully erupted and surfaces were restoration free. Surfaces were not dried or cleaned prior to examination, and dental lights were used for illumination. Examiners were assisted by trained recorders employing direct data entry. Criteria developed by Russell[28] were used to differentiate milder forms of fluorosis from nonfluoride enamel opacities.

The study team conducted a pretest of examination methods in a high-fluoride area.[29] Final training and calibration of study examiners were conducted by one of the developers of the TSIF according to objectives set by the World Health Organization.[30] Replicate examinations were performed on a 13% sample or about one in seven subjects to determine intra- and interexaminer reliability during data collection using Kappa statistics.[31] To the extent possible, examiners were blind to replicate examinations.

Two questionnaires, one administered by interview, the other by mail, were used to gather information on fluoride exposures. These questionnaires were developed from an etiologic model of enamel fluorosis derived from a literature review and after reviewing questionnaires used by other researchers.[2,8,12,13,17] Questions that could be answered quickly and with little recall, and sensitive questions such as educational attainment and income were included in the interview to increase response rates. Questions requiring more recall, or those requiring respondents to seek additional information, such as fluoride prescriptions, were incorporated into the 101-item mail questionnaire. Display cards showing response categories for educational attainment, salary ranges, and toothpaste amounts were shown to respondents to increase response rates and accuracy. Levy's method was used to elicit amounts of toothpaste used on the child's brush.[32] Survey instruments were pretested on a sample of 10 dental professionals, some having children similar in age to those included in the study. Final modifications in the survey instruments were made after a pilot test with 15 parents of patients in a pediatric dental office in a different North Carolina city.

Trained interviewers met with parents at the time of their child's examination visit in a room separate from the examinations to eliminate any bias. Interviewers were blind as to the case or control status of the parents' children. At the conclusion of the interview, parents were given the mail questionnaire and a bottle to obtain a home water sample, and instructed to return the completed questionnaire and water sample within a week. After 3 and 5 weeks, follow-up telephone calls were made to remind parents. Prior to the interview parents were informed through a newsletter that a study would be conducted to determine if tooth discoloration was a problem. However, risk factors for any discoloration present on their childrens' teeth were never discussed. Questionnaires were edited for completeness and accuracy and coded where necessary. Water fluoride assays were performed by the NC State Laboratory using the complexion method. Data were entered into a computer, verified 100%, and Statistical Analysis System (SAS) summary data sets created.

A total of 57 explanatory variables were grouped into four categories to simplify interpretations of the analyses and recommendations resulting from the study. The first category, biological variables, included: gender, tooth eruption schedule, illnesses of child, antibiotic therapy of child, and illnesses of mother during pregnancy. The second category, socioeconomic variables, included: education level both of person interviewed and spouse, household income, and marital status of person interviewed. A third category had 21 variables indicating fluoride exposures including fluoride status of home drinking water, supplement use,

fluoride toothpaste use during each year from birth to 6 years of age, fluoride mouth-rinse use, and participation in a school fluoride mouth-rinse program. The remaining 27 variables included in the final category were those behaviors that could modify exposure to fluorides, or provide nontherapeutic fluoride exposures. Among these variables were: time spent outside the home for each two-year interval from birth to 6 years of age, age at first dental visit and frequency of visits, if the child was breast- or bottle-fed, type of prepared formula used, and tea consumption. Also included in this category were a number of variables related to brushing, such as: parent brushing of child's teeth and age when it began; and for each two-year interval from birth to 6 years of age, if the child brushed, if toothpaste was used, and if the child was allowed to place the toothpaste on the brush.

A case was defined as a subject having one or more surfaces with an index score greater than 0. Cases and controls were compared based on the proportion having a history of exposures to the fluoride sources under study. Bivariate and multivariate analyses were performed using SAS. In the bivariate analyses, each exposure variable was evaluated using Chi-square and Mantel-Haenszel statistics. Variables determined to be associated with fluorosis ($P \le 0.15$) were included in multivariate analyses. The number of independent variables included in any regression model was kept at a ratio of 1:10, i.e., one variable for every 10 observations.[33] For all analyses, alpha was set at 0.05. Stepwise logistic regression was employed to determine the joint effects of exposure variables while simultaneously controlling for other explanatory variables. In these multivariate analyses, models were analyzed for two separate groups — children drinking fluoride-deficient water since birth and children drinking fluoridated water since birth. These analyses were limited to the subgroup for whom lifetime water histories could be verified, i.e., those with continuous lifetime use of a single water source, and with fluoride assay results from this water supply. This stratified regression analysis allowed for direct control of exposure to a major source of fluoride, which is important for interpreting results and making policy recommendations.

Results

Sample results

The sample of patient records yielded a total of 804 patients of whom 552 (68.7%) were examined and whose parents were interviewed. Clinical examination results and parent interviews were available for 156 (78%) of the original 200 cases. Self-completed questionnaires and water samples were returned for 593 (84%) of the 708 examined subjects, providing complete information (clinical examinations, parent interviews, parent self-completed questionnaires, and drinking water fluoride assay results) for 593 (59.1%) of the 1,004 subjects included in the study. The subgroup to be used for logistic regression analyses included 233 children with

	0	1	2	3	4–7
TABLE 1. PERCENTAGE DISTRIBUTION OF INDIVIDUAL SURFACES AND MAXIMUM PERSON TSIF SCORES FOR ALL SURFACES AND LABIAL SURFACES OF MAXILLARY ANTERIOR TEETH					
Surfaces (N = 18,645)					
All	64.6	25.4	6.4	3.2	0.4
Labial maxillary anterior teeth	42.5	43.1	9.2	4.1	1.1
Person Maximum Score (N = 708)					
All	22.2	41.5	17.4	14.3	4.6
Labial maxillary anterior teeth	30.8	47.4	13.7	5.4	2.7

verified water fluoridation histories, of whom 116 were drinking fluoride-deficient drinking water and 117 fluoridated water.

Examiner reliability

The 92 replicate examinations conducted during data collection indicated good to excellent agreement for the four examiners.[34] The weighted Kappa statistic using the TSIF surface score as the unit of analysis averaged 0.93 (SE = 0.03) and 0.69 (SE = 0.02) for intra- and interexaminer comparisons, respectively.

Prevalence of fluorosis

Table 1 shows the distribution of TSIF scores for surfaces and subjects. Of the 18,645 tooth surfaces scored in the 708 examined subjects, 35% had TSIF scores of 1 or greater, and 10% had scores of 2 or greater. When limited to the labial surfaces of the maxillary anterior teeth, both the prevalence and severity were greater than when all surfaces were considered.

Based on the maximum score for all surfaces, 77.8% of subjects had TSIF scores > 0. This prevalence estimate was only slightly higher and not significantly different from the 74.1% derived from the random sample taken when records previously selected as cases by the pediatric dentist were considered in calculating prevalence of the entire practice.

Bivariate analysis results

Of the 57 variables analyzed for their association with the prevalence of fluorosis, 29 were found to have a *P*-value of ≤ 0.15, and 19 at *P* ≤ 0.05.

Age of subjects when their first permanent anterior tooth erupted was the only biological factor associated with fluorosis at *P* ≤ 0.05. Unexpectedly, children who experienced early eruption (prior to age 5) were more likely to have fluorosis than children with average eruption (age 5 to 7) and even more so than children who experienced late eruption (age 8 or older). In the socioeconomic category, household income and education

TABLE 2. RESULTS OF STEPWISE LOGISTIC REGRESSION ANALYSIS BY EXPOSURE TO FLUORIDATED DRINKING WATER

Variable	β Value	Standard Error	Odds Ratio	PROB
Fluoridated Drinking Water (N = 115)				
Intercept	1.0986	0.0482	—	0.0071
Toothpaste use < 2 yrs vs ≥ 2 yrs	1.1394	0.5523	3.1249	0.0391
Fluoride-Deficient Drinking Water (N = 113)				
Intercept	-0.2595	0.4304	—	0.5465
Supplement freq. Daily vs < daily	1.8667	0.5593	6.4669	0.0008
Toothpaste use < 2 yrs vs ≥ 2 yrs	1.1136	0.4964	3.0453	0.0249

level of the mother were significantly associated with higher TSIF scores.

Nearly half of the fluoride exposure variables were significant, particularly those measuring exposure to fluoridated drinking water and dietary fluoride supplements. Of the 593 water samples returned, 51.1% indicated that the child was presently drinking fluoridated water. Although only a little more than one-third (N = 233) of these children were lifetime residents who would be continuously exposed to the level of fluoride indicated by the assay results, those currently drinking water with optimal levels of fluoride nevertheless were found to have higher TSIF scores. The association between drinking water and fluorosis for each year from birth until age 6 was significant except for the years birth to 1 (P = 0.051) and 2 to 3 (P = 0.162).

Based on the 593 mail questionnaires returned, 46.2% of children had used dietary supplements, of whom 65% took them daily. Having had dietary supplements prescribed, having taken them during the first or second year of life, and their frequency of use all were associated with fluorosis. Children who began using fluoride toothpaste before age 2 years were more likely to have fluorosis than those who began at 2 or older. Fluoride mouth-rinse use (P = 0.099) and participation in a school fluoride mouth-rinse program (P = 0.056) were not significant.

Six of the 27 variables in the behavioral category were associated with fluorosis. Whether the bottle-fed babies were given milk or soy formula was significant, but in contrast to results of previous studies, we found that children fed milk-based formulas were more likely to have fluorosis than those fed soy-based formulas. Tea, which was consumed by approximately 59% of children, was associated with fluorosis. The remaining variables in this final category measured toothbrushing

behaviors. Parental tooth-brushing, whether the child's teeth were brushed between birth and 2 years of age, and frequency of brushing from ages 2 to 6 years were associated with fluorosis. More than 99% of parents reported that their children used a fluoride toothpaste.

Multivariate analysis results

Table 2 shows results of the logistic regression analysis performed for the two subgroups formed based on verified exposure to fluoridated drinking water. The results for children drinking fluoridated water were different from those drinking fluoride-deficient water throughout their lives. Children who drank fluoridated water and initiated brushing with a fluoridated toothpaste before age 2 were 3.1 times more likely to develop fluorosis than those who waited until at least 2 years of age. Likewise children who drank non-fluoridated water and started using fluoride toothpaste prior to age 2 were three times more likely to develop fluorosis than those who started later. Further, in the nonfluoridated model, children who took fluoride supplements daily were 6.5 times more likely to have fluorosis than those who did not take supplements daily.

Discussion

Case-control studies are useful to identify risk factors for conditions with a long latency period such as fluorosis, but have the disadvantage that subjects' recall can be faulty. To help increase response accuracy, a number of questions were asked in a face-to-face interview. Cue cards were used when appropriate. Of the eight recent US and Canadian studies on fluoride supplements and fluorosis, only one based exposures on parent interviews.[17] This study is subject to recall bias as well. Parents who know their children have fluorosis may overestimate fluoride exposures. No efforts were made to control for this potential bias. Future studies might need to include control patients with enamel defects with an etiology other than fluoride.

The finding that three of four patients in this practice had fluorosis is striking. Since this study used a practice-based case control design, generalizations beyond this single practice can not be made. Yet the fluorosis estimates found in the present study suggest that the prevalence and severity in the geographic area from which this practice draws patients may be higher than expected based on past and current estimates.[8, 35-37]

Szpunar and Burt[3] concluded that an increase in the prevalence of enamel fluorosis has occurred, but that it is unaccompanied by any appreciable increase in severity. Of concern, however is the emergence of a small number of moderate to severe cases in some communities — a level of severity that was previously nonexistent.[4] Of the 708 children in our study, 4.6% presented with TSIF scores of 4 or greater, which is considered severe fluorosis because of its esthetic implications and loss of enamel. Eight percent of lifetime

residents in a fluoridated household had severe fluorosis, compared with 2.6% for children with lifetime residence in nonfluoridated households. Williams and Zwemer found 14% with severe fluorosis in an optimally fluoridated city, but only 1.4% in the less than optimally fluoridated area around the city.[37] Due to the prevalence and severity of fluorosis found in this practice, further surveys are in progress in the local community and state to determine estimates for the community, and whether pockets of fluorosis exist in other parts of the state.

An additional advantage of this study is that it incorporated both fluoridated and nonfluoridated communities. As expected, fluoridated drinking water was associated with dental fluorosis. Each of the single-year age groups from birth to 6 was significant except for the first ($P = 0.051$) and third years of life ($P = 0.16$). Besides water fluoridation, previous studies identified fluoride supplement use as the most consistent risk factor for fluorosis.[8–16, 38] Our findings agree with these studies. In bivariate analyses, having had supplements prescribed, the frequency of their use, and having taken them during the first two years of life all were associated with fluorosis presence. Regression results indicate that only their frequency was important in those not drinking fluoridated water.

The reported use of supplements by 46% of the sample was higher than the general population. According to the 1989 National Health Interview Survey, from 15 to 16% of the general population used supplements from birth to 4 years of age, after which use gradually declined to approximately 3% for ages 15–17 years.[39] Levy[25] reported that an average of 37% of children recruited from a University's clinics received supplements during several measurement time points during the first 18 months of life.

In our sample, pediatricians and family practitioners comprised 65.7% of providers writing fluoride supplement prescriptions, similar to the estimate reported by Woolfolk et al.[13] Furthermore, we found that 14.5% of children drinking fluoridated water were prescribed supplements. Two other studies reported that 14.8[40] and 18.1%[41] of children drinking fluoridated water also reported using supplements.

On the basis of these findings, educational interventions to prevent inappropriate dietary fluoride supplement prescriptions need to be directed toward primary care physicians. These findings also support recommendations resulting from several conferences calling for a review of the dietary fluoride supplements dosage schedule.[5, 42–44] Most recently, the ADA Council on Therapeutics approved a new fluoride supplementation schedule. It recommended that fluoride supplementation not begin until 6 months of age, daily doses of 0.25 mg be given until age 3 years, 0.50 mg from age 3 to 6 years, and 1.00 mg from age 6–16 for areas fluoridated at less than 0.3 ppm fluoride.[6]

A number of behavioral factors were related to fluorosis, in bivariate analysis, but only early toothbrushing remained important in multivariate analysis. From bivariate results the odds of having fluorosis increased when brushing was initiated with younger children and when brushing frequency increased. Osuji et al.[17] found children who initiated brushing before 25 months of age were 11 times more likely to develop fluorosis than those who began brushing later. Milson and Mitropoulos[18] indicated that fluoridated toothpaste was the only major source of fluoride in their study to have caused fluorosis. While only a few clinical studies have implicated fluoridated toothpaste in fluorosis, several studies have shown that children inadvertently swallow substantial amounts of paste while brushing.[45–50] Using Ripa's estimate, 0.268 mg of fluoride could be ingested by a child brushing twice a day using 1,000 ppm fluoride toothpaste.[51] Parents should either brush their child's teeth or supervise the brushing through age 6. While the amount of toothpaste used at a single brushing was not significant in this study, parents and children nevertheless should be instructed as to the amount of paste placed on the toothbrush.[5, 17, 50–53]

Conclusion

Results of the regression analysis in which fluoride in drinking water was controlled show that two of 22 variables were found to be significant. For subjects drinking fluoride-deficient water, fluorosis was associated with fluoride supplement frequency and the age of the child when brushing was initiated. For subjects drinking fluoridated water throughout their lives, fluorosis was associated with the age of the child when toothbrushing was initiated. These findings suggest that supplements and brushing at an early age place children at increased risk for enamel fluorosis. Dietary fluoride supplements increase the risk of fluorosis for those in nonfluoridated areas by more than six-fold. Children who begin using toothpaste before age 2 — regardless of whether their drinking water is fluoridated — increase their odds of having fluorosis by approximately three times. By controlling the fluoride exposure variables and the behavioral risk factors — in particular fluoride supplements and toothpaste — the benefits of fluoride can be achieved with limited fluorosis.

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Magnetic resonance imaging measures brain abnormalities in people with schizophrenia

MRIs show schizophrenic patients with decreased total brain tissue and more cerebrospinal fluid

People with schizophrenia may have trouble processing information, formulating concepts, and organizing their behavior because they appear to have less frontal lobe brain tissue than healthy individuals, according to a recent article in the *Journal of the American Medical Association*.

Nancy Andreasen, MD, PHD, Department of Psychiatry, University of Iowa Hospitals and Clinics, Iowa City, Michael Flaum, MD, Assistant Professor of Psychiatry, University of Iowa, and colleagues studied the structural brain images of 52 patients diagnosed with schizophrenia and 90 healthy volunteers by using magnetic resonance imaging (MRI).

Dr. Flaum presented the findings today at an AMA media briefing on mental health.

The researchers say MRI opens a new door to the study of schizophrenia because "it allows investigators to safely examine brain tissue in relatively young patients without concern for the effects of aging, chronic or acute disease process, fixation, and other potential sources of artifact," which have been a concern in post-mortem studies.

Dr. Flaum says the findings lend further support to the idea that "schizophrenia should be conceptual-ized more as a 'brain disease' than as a 'mind disease'."

Dr. Flaum says that "in addition to the generalized brain abnormalities observed in schizophrenia, recent MRI studies suggest that specific regions (of the brain) may be particularly affected, including the frontal lobes and the thalamus. The frontal lobe normally integrates multimodality information and performs a variety of higher-level cognitive and emotional functions. The thalamus is a structure deep in the center of the brain, which appears to serve as a major relay station between the frontal lobes and all other parts of the brain. Deficits in these brain structures may explain why patients with schizophrenia often have significant deficits in formulating concepts and organizing their thinking and behavior."

Investigators are now trying to determine the pathological process that produces brain tissue deficit and elevated cerebrospinal fluid volume, as well as determining at what point the injury occurs.

The researchers note that "many investigators studying the pathophysiology of schizophrenia suspect that the seeds that produce this illness are planted as the brain develops in utero or when injuries occur during delivery or the early postnatal period."