Associations Between Dental Fluorosis of the Permanent and Primary Dentitions

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Abstract

Objectives: Relatively little is known about associations between primary and permanent tooth fluorosis. In this study, associations between dental fluorosis of the permanent and primary dentitions were assessed. Methods: Subjects (n=601) are in the Iowa Fluoride Study, which included fluorosis examinations of the primary and early-erupting permanent dentitions by trained dentist examiners. Relative risks, correlations, and logistic regression assessed associations between permanent tooth fluorosis and primary molar fluorosis. Results: Ten percent had primary molar fluorosis at age 5; 36% had definitive (mostly mild), 28% questionable, and 36% no permanent incisor fluorosis at age 9. Those with primary molar fluorosis were significantly more likely to have definitive permanent incisor fluorosis (76% vs. 32%), and permanent molar fluorosis (59% vs. 16%). The strong association between primary and permanent tooth fluorosis is independent of level of fluoride intake. Conclusions: Detection of primary tooth fluorosis in pre-school children should alert clinicians and parents to the high likelihood of subsequent fluorosis in the permanent dentition.

Key Words: Dental fluorosis, permanent dentition, primary dentition, associations

Introduction

In most developed nations, along with the overall decline in dental caries, there has been an increased prevalence of dental fluorosis due to the widespread use by young children of fluoride in many forms, including fluoride dentifrice (1, 2). A 1999 review estimated fluorosis prevalence in North America to be 30%-80% in fluoridated and 10%-40% in non-fluoridated areas (3).

Substantial research efforts have focused on permanent tooth fluorosis prevalence and risk factors (4, 5, 6, 7), while primary tooth fluorosis has been much less studied, especially in the United States (8, 9). One previous publication showed an increased risk of diffuse enamel defects (generally considered dental fluorosis) of the permanent incisors for those with defects of the primary molars (10).

Those with diffuse defects of the primary first molars had a 45% greater risk (RR = 1.45, 95% CI = 1.05-2.00) and those with primary second molar defects had 86% greater risk (RR = 1.86, 95% CI = 1.36-2.54) of having permanent incisors with diffuse defects. Although the only study of its kind (10), it did not study individual fluoride intake, so that it was not possible to assess whether fluoride intake alone explained fluorosis in both dentitions. This paper reports on the association between the prevalence of dental fluorosis of the early-erupting permanent teeth and the primary molars, and explores these relationships while controlling for individual fluoride intakes. It also includes some analyses of primary molar fluorosis that were conducted independently of the permanent tooth assessments.

Methods

Subjects were participants in the Iowa Fluoride Study, a cohort study following children recruited at birth from eight Iowa hospitals during 1992-95 (11). With institutional review board approval, parents provided consent for study questionnaires and dental examinations; children provided assent. At ages 4-6 years (mean 5.2), dental fluorosis exams were conducted on the primary dentition using the Tooth Surface Index of Fluorosis (TSIF) adapted for primary teeth (9), followed by exams at ages 7-12 years (mean 9.2) with the Fluorosis Risk Index (FRI) (12) for the early-erupting permanent teeth (8 permanent incisors and 4 first molars) and TSIF for primary second molars. The FRI was chosen for the assessment of the early-erupting permanent teeth because it scores fluorosis on four zones per tooth, and it was felt that scoring zones would be useful in relating fluoride intake at specific ages to fluorosis on specific tooth zones. For these analyses, three FRI zones of each buccal surface (incisal edge/cusp tip, incisal/occlusal third, and middle third, with gingival zones excluded due to less full eruption) were included. Two trained, calibrated dentists (JJW and MJK) conducted epidemiological dental examinations at both ages with portable equipment and halogen headlights. Examinations were conducted by both examiners on a subset to assess inter-ex-

aminer reliability. Primary tooth results were dichotomized at the person level (one or more affected teeth vs. none). Person level permanent tooth results were categorized as 1) definitive cases (at least one FRI score of 2 (white striations) or 3 (staining/pitting/deformity) on more than one-half of a surface zone); 2) questionable (with a maximum FRI score of 1 for less than half of a zone clearly or possibly affected by white striations); and 3) none (all zones scored as FRI = 0 (no indication of fluorosis) or 7 (non-fluoride opacity)).

Parents provided demographic information at the time of recruitment, with more limited demographic data (education level only) provided at age 5, but not age 9. Detailed questionnaires were sent five times during the first year and 2-3 times per year thereafter to assess fluoride intake (including water sources; filtration status; water, beverage and selected foods intake; use of dietary fluoride supplements and fluoride dentifrice) and report body weight. Fluoride intake methods of estimation have been described previously (11, 13, 14, 15). Briefly, combined fluoride intake for this paper was estimated by combining fluoride ingested from water, other beverages, and selected foods (11, 14); ingestion of fluoride dentifrice (15); and dietary fluoride supplements (13). Selected questions were repeated by telephone within about 10 days of the parent's completion of the original questionnaire to allow assessment of reliability. Imputed body weights were used in place of missing weights for 69 subjects (71 questionnaires representing 0.6% of the data) using linear interpolation of previous and subsequent weights for the individual subjects. Total daily fluoride intake (mg F) was divided by body weight (kg) for each returned questionnaire. Average daily fluoride intake (mg F/kg bw) was estimated for birth to 36 months and again for 36 to 72 months of age using the trapezoidal method of calculation for area-under-the-curve (AUC). While many choices of intake intervals were available for study, it was thought that 0-36 months was a reasonable

estimate of fluoride intake that would occur before full eruption and assessment of primary 2nd molar fluorosis. The 36-72 month intake is a good representation of "modifiable" fluoride intake, especially for late-erupting teeth, occurring after primary 2nd molar fluorosis assessment, but generally before eruption of the permanent dentition.

Both permanent incisor and permanent first molar fluorosis results were separately related to age 5 and age 9 assessments of the primary molars using relative risks (yes vs. questionable/none) and logistic regression. Relative risks and 95% confidence intervals were calculated according to the SAS cohort study method. Two separate logistic regressions predicting definitive permanent incisor fluorosis used 0-36 and 36-72 month AUC fluoride intake, respectively, in addition to primary second molar fluorosis at age 5. Two additional logistic regressions predicting definitive permanent first molar fluorosis also used primary second molar fluorosis assessed at age 5, as well as 0-36 and 36-72 month AUC fluoride intake, respectively. P-values less than 0.05 were considered statistically significant. Statistical analyses were performed using SAS version 9 (16).

Results

Study subjects were generally of relatively high socioeconomic status (SES), with 46% of mothers having completed 4 years of college and 72% with family income of $30,000 or more at recruitment; 51% were female, 98% had Caucasian mothers, and 44% were first children. A total of 601 individuals had examinations at both approximately age 5 and age 9, and are included in all subsequent analyses.

It was not possible to directly validate questionnaire responses. However, reliability was assessed for selected questions on an ongoing random sample of questionnaires concerning water sources, dietary fluoride supplements, and fluoride dentifrice, with results of 91% agreement on tap water source (Kappa = 0.77), 95% agreement on use of filtration

(Kappa = 0.81), 99% agreement on use of fluoride supplements (Kappa = 0.97), and 86% agreement on toothbrushing frequency (weighted Kappa = 0.79).

Person-level inter-examiner reliability was good for both age 5 primary first molar fluorosis (kappa=0.49, 96.9% agreement) and age 5 primary second molar fluorosis (kappa=0.61, 90.8% agreement). At age 9, person-level reliability was similar for primary second molar fluorosis (kappa=0.64, 94.1% agreement), and also good for permanent tooth incisor fluorosis (definitive vs. questionable/none, simple kappa=0.53, 76.5% agreement) and first molar fluorosis (simple kappa=0.60, 88.2% agreement).

The age 5 primary tooth fluorosis prevalence rates were 2.2% for the first molars and 9.8% for the second molars. Prevalence rates for fluorosis of the permanent incisors (age 9) were 36.3% definitive, 27.3% questionable, and 36.4% none, while fluorosis prevalence for the permanent first molars was 20.0% definitive, 25.5% questionable, and 54.6% none. Almost all dental fluorosis was mild, with only 8 individuals (~1%) with moderate (dark staining)/severe (pitting) permanent tooth fluorosis (FRI score of 3) and only 2 (~0.3%) with severe primary tooth fluorosis (TSIF score of 5).

There were significant relationships between both age 5 and age 9 primary tooth and permanent incisor fluorosis (Table 1), although they were stronger for age 9 primary second molars. The relative risks of permanent incisor fluorosis were 2.4, 2.4, and 2.8 for age 5 primary first molar, age 5 second molar, and age 9 second molar fluorosis prevalence, respectively, relative to those without primary tooth fluorosis (all p<0.001). The relative risks of permanent first molar fluorosis (Table 2) were 4.1, 3.8, and 4.5 for age 5 primary first molar, age 5 second molar, and age 9 second molar fluorosis prevalence, respectively (all p < 0.0001). These permanent incisor and first molar fluorosis relationships with primary molar fluorosis were all statistically signifi-

cant. It should be noted, however, that although primary tooth fluorosis is an important predictor, permanent tooth fluorosis occurred relatively frequently, even without primary tooth fluorosis. For example, among subjects without age 5 primary second molar fluorosis, 32% had definitive fluorosis on permanent incisors and 16% had definitive fluorosis on permanent first molars. Nevertheless, primary second molar fluorosis had good predictive value for permanent incisor fluorosis (positive predictive value (PPV) = 0.76, negative predictive value (NPV) = 0.68) and permanent first molar fluorosis (PPV = 0.59, NPV = 0.84).

It is not surprising to see the strong association between permanent and primary tooth fluorosis, since both are associated with elevated fluoride intake. In order to assess the association between permanent and primary tooth fluorosis that is independent of fluoride intake, multiple logistic regression was used. The multiple lo-

gistic regression analyses related permanent incisor fluorosis to primary molar fluorosis, fluoride intake AUC from birth to 36 months, SES (at birth and age 5), gender, and age at the examination (none of these last three were significant, nor were any pairwise interactions). A simplified model using only primary molar fluorosis and 0-36 month fluoride intake AUC is presented graphically in Figure 1, revealing significant increases in fluorosis prevalence with higher fluoride intake and primary tooth fluorosis (both P<0.001). The interaction between fluoride intake and primary molar fluorosis was non-significant and not included in the models. Those with primary molar fluorosis were much more likely to have permanent incisor fluorosis at all levels of fluoride intake, as demonstrated by the large odds ratios estimated from the logistic equation (9.8 after adjusting for 0-36 month fluoride intake). For example, in Figure 1 at daily intake levels from birth to 36 months of

0.04 mg F/kg bw, those with primary molar fluorosis had about a 77% probability of permanent incisor fluorosis vs. 25% without primary molar fluorosis. At 0.08 mg F/kg bw, the probabilities were about 88% and 43%, respectively.

Similar logistic regression analyses were conducted using 36-72 month AUC fluoride intake instead of 0-36 month AUC. Results were similar, with both 36-72 month AUC and primary second molar fluorosis status significantly related to permanent incisor fluorosis (OR=11.2), but the slope of the relationship between permanent incisor fluorosis and fluoride intake was somewhat gentler (data not shown). Models including both 0-36 month and 36-72 month AUC fluoride intake simultaneously were not developed further due to problems arising from their correlation (r=0.50).

Multiple logistic regression analysis related permanent first molar fluorosis to primary molar fluorosis and

Table 1
Relationships between permanent incisor and primary molar fluorosis

Primary Molar Fluorosis		Percentage with Primary Tooth Fluorosis	n	Permanent Incisor Fluorosis			Relative Risk for Definitive Fluorosis (vs. Questionable/None)	
				Definitive	Questionable	None	RR	95% CI
Age 5	Yes	2	13	85	8	8	2.4	1.9-3.1
1st Molar	No	98	588	35	28	37		
Age 5	Yes	10	59	76	12	12	2.4	2.0-2.9
2nd Molar*	No	90	542	32	29	39		
Age 9	Yes	13	80	81	8	11	2.8	2.3-3.3
2nd Molar	No	87	521	29	30	40		

*All 13 subjects with primary first molar fluorosis also had primary second molar fluorosis.

Table 2
Relationships between permanent first molar and primary molar fluorosis

| Primary Molar Fluorosis		Percentage with Primary Tooth Fluorosis	n	Permanent First Molar Fluorosis (%)			Relative Risk for Definitive Fluorosis (vs. Questionable/None)	
				Definitive	Questionable	None	RR	95% CI
Age 5	Yes	2	13	77	23	0	4.1	2.9-5.8
1st Molar	No	98	588	19	26	56		
Age 5	Yes	10	59	59	29	12	3.8	2.8-5.0
2nd Molar*	No	90	542	16	25	59		
Age 9	Yes	13	80	61	24	15	4.5	3.4-5.9
2nd Molar	No	87	521	14	26	61		

*All 13 subjects with primary first molar fluorosis also had primary second molar fluorosis.

Figure 1
Logistic Regression Prediction of Permanent Incisor Fluorosis
Using Primary 2nd Molar Fluorosis Indicator
and AUC Fluoride Intake from Age 0 to 36 Months
N=349

	Odds Ratio	(95% C.I.)
Primary 2nd Molar Fluorosis	9.8	(3.9,24.7)
Fluoride Intake (0.01 mgF/kg)	1.2	(1.1,1.4)
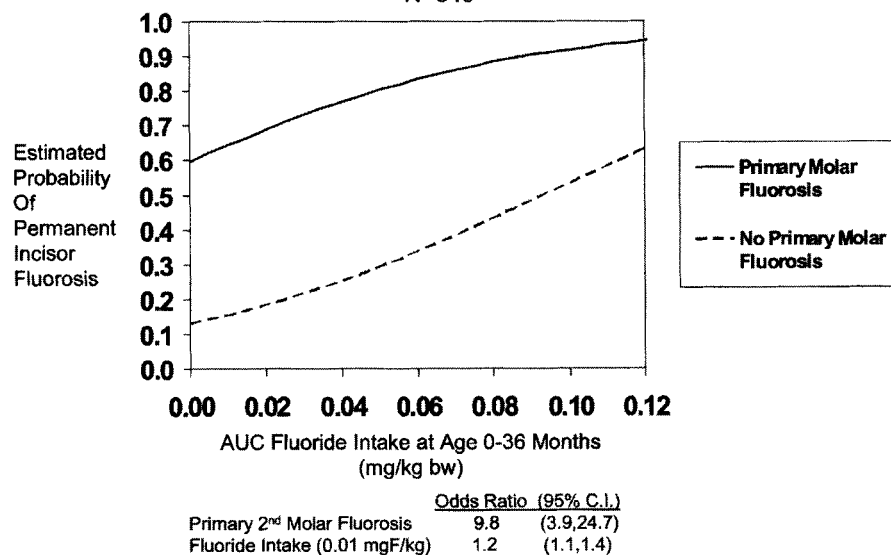
Figure 2
Logistic Regression Prediction of Permanent First Molar Fluorosis
Using Primary 2nd Molar Fluorosis Indicator
and AUC Fluoride Intake from Age 0 to 36 months
N=349

	Odds Ratio	(95% C.I.)
Primary 2nd Molar Fluorosis	7.8	(3.6,16.8)
Fluoride Intake (0.01 mgF/kg)	1.3	(1.2,1.5)
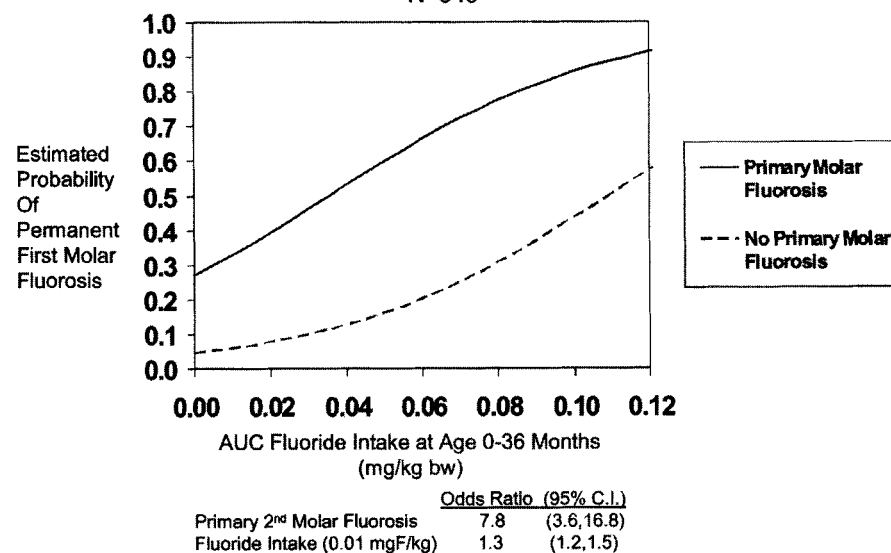
fluoride intake AUC from birth to 36 months (Fig. 2). SES (birth and age 5), gender, and age at the examination did not contribute significantly and, therefore, are not included. Primary molar fluorosis and fluoride intake were both significant (p < 0.001). However, the interaction between fluoride intake and primary molar fluorosis was non-significant, and not included in the model. Subjects with primary molar fluorosis were much more likely to have permanent first molar fluorosis at all levels of fluoride intake, as demonstrated by the large odds ratio estimated from the logistic equation (7.8 after adjusting for 0-36 month fluoride intake). As shown in Fig. 2, at 0.04 mg F/kg bw 0-36 month AUC, those with primary

second molar fluorosis had a predicted 53% probability of permanent first molar fluorosis vs. 13% for those without primary second molar fluorosis. At 0.08 mg F/kg bw, the predicted probabilities were 77% and 31%, respectively, for subjects with and without primary second molar fluorosis. Logistic regression analysis using 36-72 month AUC fluoride intake, in addition to primary second molar fluorosis status, showed similar results.

Discussion

There was a strong association between mostly mild primary and permanent tooth fluorosis prevalence. This is generally consistent with the results of Milsom et al. (10) who used a different index to study 8- and 9-year-olds' eight primary molars and eight permanent incisors. When considering all their study children who had varied numbers of teeth present, those with diffuse enamel defects (fluorosis) of primary first molars had a significant relative risk of 1.45 (95% CI, 1.05 to 2.00) and those with defects of second primary molars had a relative risk of 1.86 (95% CI, 1.36 to 2.54) for permanent incisor fluorosis. When limiting analyses to the smaller subset with all permanent incisors and primary molars present in the mouth, the relative risks for permanent incisor fluorosis were 1.88 (95% CI, 1.19 to 2.98) for primary first molar defects and 2.27 (95% CI, 1.45 to 3.54) for second molar defects.

The authors had previously assessed primary molar fluorosis at age 5 years (9), prior to permanent incisor eruption. Those with primary first molar and second molar fluorosis at age 5 had substantially higher relative risks of 2.4 (95% CI, 1.9 to 3.1) and 2.4 (95% CI, 2.0 to 2.9) for permanent incisor fluorosis. Only second primary molars were re-examined at about age 9; the age 9 prevalence of fluorosis was greater at 13% vs. 10% at age 5, and the relative risk was greater using these results (RR = 2.8, 95% CI, 2.3 to 3.3). This additional examination of primary second molars at age 9 was conducted to see how stable the results from age 5 exams

would be. There are several possible examination-related explanations for the higher prevalence. First, it is easier to see the full buccal surface of primary molars in older children. Second, fluorosis is always more evident when the teeth are drier, and the age 9 primary tooth exam occurred after gauze was used to partially dry the teeth and immediately after the permanent teeth were assessed, so the mouth was open longer and the teeth generally drier. Also, evidence of permanent first molar fluorosis adjacent to the primary second molar and permanent incisor fluorosis could have created a bias toward fluorosis diagnosis compared to the age 5 exams which took place prior to most permanent tooth eruption. The relative risks of permanent molar fluorosis with primary molar fluorosis were greater than for permanent incisors, but there are no comparable results from Milsom et al. (10).

The odds ratios associating permanent and primary tooth fluorosis are statistically and clinically significant and are greater than those found by Milsom et al. (10). However, there are several important considerations in interpreting these results and explaining why concordance is not even greater. Because primary tooth dental fluorosis generally is more difficult to diagnose, it is likely that some misclassification occurred, with potential to affect the relative risks. In addition, the FRI requires at least one-half of a zone to be clearly affected in order to be scored as definitive fluorosis, underestimating fluorosis prevalence. The primary molars and early-erupting permanent teeth have only partial overlap of the tooth formation periods, with the permanent teeth continuing longer, so one would not expect full concordance.

Moreover, the association between primary molar and early-erupting permanent tooth fluorosis was still statistically significant after controlling for fluoride intake from 0-36 months or 36-72 months, suggesting primary tooth fluorosis is an independent predictor of permanent tooth fluorosis. The overlap of fluoride intake during the same developmental pe-

riod can only partially explain this and there could be other factors modifying this association between primary and permanent tooth fluorosis. These include slight differences in the process of tooth formation between primary and permanent teeth, genetic factors (17) and differences in individual metabolism and susceptibility. In addition, amoxicillin use during infancy has been linked to dental fluorosis in this same cohort (18, 19), so that amoxicillin use could be a factor. Of course, it is also plausible that critical portions of tooth formation in the respective teeth (primary second molars and permanent maxillary central incisors and permanent first molars) did not occur during the same time period, at least for some individuals.

The use of different indices for primary and permanent tooth exams (TSIF and FRI, respectively) should also be considered. It is also possible that the estimates of fluoride intake were differentially incomplete or underestimated and could have affected results. It was not feasible to directly validate the fluoride intake estimates, although reliability was generally favorable on follow-up telephone assessment.

Additional research is warranted to better understand exactly why permanent teeth are at greater risk of dental fluorosis. Also, the association between primary and permanent tooth fluorosis could be different in settings with different fluoride intake and dental fluorosis patterns. Nevertheless, the relationship between primary and permanent tooth fluorosis, independent of fluoride intake, suggests that some other factor(s) influences fluorosis development.

Study findings suggest that identification of primary molar fluorosis during the pre-school years should alert clinicians and parents to the strong likelihood of fluorosis in the permanent incisors. When primary tooth fluorosis is detected at this age, providers should assess their young child patients' fluoride intake, and for those with elevated intake, parents can be warned and various recommendations can be made to reduce the intake for the child and any younger

siblings. It could, thus, be possible to have a limited impact on the final stages of mineralization of permanent central incisors and first molars among the children examined. Reductions in fluoride intake would help prevent fluorosis of later-erupting teeth (2nd molars, canines and premolars), which can be of some esthetic importance. Identification of primary tooth fluorosis in an older child could potentially be very valuable in avoiding excessive fluoride ingestion for the younger siblings, for both earlier- and later-erupting teeth. Therefore, providers should counsel parents of young children with primary molar fluorosis about appropriate amounts of fluoride ingestion for infants and young children in order to best balance the caries-preventive benefits of fluoride with risks of dental fluorosis.

In summary, permanent maxillary central incisor and first molar fluorosis prevalence are strongly associated with primary molar fluorosis prevalence, as well as fluoride intake. Identification of primary tooth fluorosis should alert clinicians and parents to the increased likelihood of fluorosis in the esthetically important permanent incisors. Study data suggest that other factors besides fluoride intake are important. Possibilities include both genetic and other factors related to individual fluoride metabolism and tooth development.

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