Delayed tooth eruption: association with severity of HIV infection

Mary J. Hauk DDS Mark E. Moss DDS, PhD Geoffrey A. Weinberg MD Robert J. Berkowitz DDS

Dr. Hauk is an assistant professor, Division of Pediatric Dentistry, Eastman Department of Dentistry, University of Rochester, Rochester, New York; Dr. Moss is an assistant professor, Department of Community and Preventive Medicine University of Rochester School of Medicine and Dentistry, Rochester, New York; Dr. Weinberg is an associate professor, Division of Pediatric Infectious Disease, Department of Pediatrics and Dr. Berkowitz is a professor and chief , Division of Pediatric Dentistry, University of Rochester Medical Center, Rochester, New York. Correspond with Dr, Hauk at mary_hauk@urmc.rochester.edu

Abstract

***Purpose**: HIV status is monitored by expression of clinical symptoms as well as CD4 lymphocyte counts. The purpose of this study is to assess the relationship between delayed dental eruption (DDE) and the progression of pediatric HIV infection to AIDS.*

***Methods**: A population of 70 perinatally HIV- infected children, aged 5 months to 13 years at their time of entry into the study, received dental examinations. Regression analysis between dental age and chronological age was performed. Subject CDC classification, adjusted for age, was used to determine an association between eruptive delay and severity of disease progression.*

***Results**: Data revealed no significant difference in timing of eruption based on severity of CD4 depletion alone (P=0.09). However, clinical symptom status was strongly associated with DDE (P=0.003). The relationship between symptoms and DDE persisted after controlling for CD4 depletion.*

***Conclusions**: Our study indicates that there is a correlation between the progression from HIV infection to Pediatric AIDS and DDE and that this delay is most closely linked to severity of symptoms and not CD4 depletion. (Pediatr Dent 23:260-262, 2001)*

HIV infection has significant and well-described oral manifestations in children.[1-7] It has been observed that delayed dental eruption (DDE) may be associated with HIV infection.[7] On this basis, this study assessed the relationship between DDE and the progression of HIV infection to pediatric AIDS.

Methods

Patient population

The study population consisted of 70 perinatally HIV infected children who were patients of the HIV program at Children's Hospital at Strong (Rochester, NY). This cohort consisted of 37 males and 33 females that were 5 months to 13 years of age at their time of entry into the study. The racial distribution of this group was 53% African American, 17% Hispanic, 21% Caucasian, and 9% other. Documentation of HIV infection included repeatedly positive antibody ELISA with confirmation by Western blot analysis for children greater than 18 months of age and by repeatedly positive polymerase chain reaction (PCR) for children less than 18 months of age. All of the subjects were taking anti-retroviral medications.

Evaluation of dental age

Comprehensive medical management of these patients included an oral examination at least once every 6 months. Each subject had from 1-8 oral examinations during the study period with a mean of 2.3 oral examinations per subject for a total of 158 oral examinations during the study period. At each oral examination, the number and type of erupted teeth were recorded. Dental age was assessed utilizing the criteria of Logan and Kronfeld as modified by McCall and Schour.[9] DDE was defined as dental age being 6 or more months younger than chronological age.

Evaluation of progression of HIV disease

Progression of HIV disease utilized the CDC criteria, which is based on age adjusted CD4 lymphocyte counts and clinical status (see Table 1a and 1b). The CDC classification was assigned by the pediatric infectious disease physician at the time of each oral examination.

Data collection

A total of 158 examinations were performed on the 70 subjects. An expedited IRB review was achieved to permit the use of pre-existing patient records for this study. Oral examinations included a dental charting with estimation of amount of eruption for each tooth. Each tooth was assigned a best-fit description of unerupted, and not palpable through soft tissue, unerupted but palpable through soft tissue; cusp tips visible; 1/4 of the clinical crown erupted, 1/2 of the clinical crown erupted, 3/4 of the clinical crown erupted, or clinical crown fully erupted. For the primary dentition, additional categories included 1mm mobile, 2mm mobile, 3mm mobile, and soon to exfoliate.

A tracking number for each subject and his/her charting was transferred to a data collection form. This permitted blinded assignment of dental ages to the subjects. One of the authors (MH) and a second year pediatric dental resident performed the clinical examinations and reviewed the dental records. The

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Table 1A. Pediatric HIV Classification

	Clinical categories (symptoms)			
Immunologic categories	**N: no signs/ symptoms (s/s)**	**A: mild s/s**	**B: moderate s/s**	**C: Significant s/s**
1. no evidence of suppression	N1	A1	B1	C1
2. moderate suppression	N2	A2	B2	C2
3. severe suppression	N3	A3	B3	C3

MMWR- Morbidity and Mortality Weekly Report. 43(RR-3):1-21, 1994 Mar 4.

Table 1B. Immunologic Categories Based on Age-specific CD4+ T-Lymphocyte Counts and Percent of Total Lymphocytes

	Age of Child		
Immunologic category	**<12 months uL (%)**	**1-5 years uL(%)**	**6-12 years uL(%)**
1. no suppression	>=1,500 (>=25)	>=1,000 (>=25)	>=500 (>=25)
2. moderate suppression	750-1499 (15-24)	500-999 (15-24)	200-499 (15-24)
3. severe suppression	<750 (<15)	<500 (<15)	<200 (<15)

Ibid

examiners consulted with one another at regular intervals during the study to assure adequate inter- and intra-examiner reliability.

Data analysis

The data were examined for any relationship between DDE and CDC classification of HIV infection for the entire population. In addition, this same analysis was performed on the population stratified by race and gender to control for differences in these sub-populations that may have confounded our results. None of the charts needed to be discarded due to a lack of information because dental eruption is part of the routine examination for all patients of the pediatric HIV clinic.

Multiple logistic regression analyses were performed using generalized estimating equations (GEE) to assess effects of the subject's clinical status and CD4 counts on the presence of DDE. Multivariate analysis was used in order to separate out independent effects of CD4 depletion and severity of symptoms. In addition, the GEE analysis permitted us to control for repetition of subjects since some of the children enrolled in the study were examined more frequently than others.

Results

Findings are summarized in the Tables 2-4. Evaluation of the data demonstrated that there was a statistically significant association between DDE and severity of symptoms (P=0.003; Table 2). There was also a statistically significant relationship between DDE and CD4 depletion (Table 3). However when controlled for severity of symptoms (utilizing GEE logistic regression), CD4 depletion was not associated with DDE (P=0.19; Table 4). An analysis was performed to detect any difference in gender or race distribution of eruptive delay relative to CDC classification and CD4 count. There was no statistical difference in DDE for male or female participants (P= 0.81). In addition, there was no association between DDE and race (P= 0.82).

Table 2 shows those children with mild or moderate symptoms have an average delay in eruption of about 7 months (0.6 of 1 year). Those with severe symptoms have an average delay of 14 months. The pattern was similar in Table 3, but the trend was not statistically significant. Table 4 shows the results of the multiple logistic regression model. The model indicates that compared to children with no symptoms, the odds of having a 6 month delay in dental eruption increase by a factor of 1.3, 1.8, and 2.3 as severity of symptoms progressed to mild, moderate, and severe, respectively.

Discussion

Analysis of the data demonstrated no statistically significant association between CD4 depletion and DDE. However, severity of symptoms was strongly associated with DDE. The results of these analyses indicate that DDE is associated with clinical symptoms and not CD4 depletion. The results of the multivariate analysis show that when both CD4 count and severity of symptoms are used as independent predictor variables for DDE that the severity of clinical symptoms is the better predictor.

Limitations of this study include the reliance on a clinical examination alone to determine the subject's dental age, which limits the precision of our study by impairing our ability to

Table 2. Mean Delay in Dental Eruption (Years) According to Symptoms

CDC symptom score	N	Mean Delay (years)	Min.	Max.
No symptoms (N)	13	0.000•±1.09	-2.66	1.75
Mild symptoms (A)	78	0.61±1.08	-2.75	3.75
Moderate symptoms (B)	26	0.57±0.67	-0.33	2.67
Severely symptomatic (AIDS) (C)	41	1.20±1.07	-0.67	4.25

GEE regression P-value=0.003 for relationship between CDC symptom score and probability of eruption delay of 6 months or more. Correlation = exchangeable • -4.58×10^{-9}

Table 3. Mean Dental Eruption Delay in Years According to CD4 Depletion

CDC score of CD4 depletion	N	Mean Delay (years)	Min.	Max.
Mild or no depletion CDC score = 1	38	0.45±0.75	-1.42	2.25
Moderate depletion CDC score = 2	44	0.63±0.86	-0.5	3.75
Severe depletion CDC score = 3	76	0.87±1.27	-2.75	4.25

GEE regression P-value = 0.09 for relationship between CD4 depletion score and probability of eruption delay of 6 months or more. Correlation = exchangeable

assign a dental age when teeth were not actively erupting. Radiographic analysis would have increased the accuracy of the dental ages assigned to each subject. To compensate for lack of radiographic analysis in situations where a range of dental ages was possible, the dental age closest to the chronological age was used to minimize the risk of incorrectly declaring a subject as having DDE.

Another limitation of this study is the discrepancy in race distribution of our population and the standardized eruption tables. This population consisted of a large proportion of African American and Hispanic subjects. It has been documented in previous studies that African American and Hispanic children exhibit advanced dental development.[11-15] However, currently available tables were developed with predominantly Caucasian subjects.[16] Evaluation of an age, race, and gender matched control group would provide a more accurate estimate of the extent of DDE in our patient cohort.

Table 4. Results of the GEE Logistic Regression for Subject's Clinical Symptoms and CD4 Counts on Eruption Delay of 6 Months or More

Comparisons	Coefficient	Standard Error	*P*-value
Severity of CD4 depletion	0.083	0.119	*P*=0.48
Severity of clinical symptoms	0.280	0.109	*P*=0.01

Correlation = exchangeable Number of observations = 158
Number of subjects = 70
Observations per subject: Minimum = 1 Average = 2.3 Maximum = 8

Conclusions

This study extends earlier findings that indicate HIV infection is associated with DDE. The current study supports the concept that HIV infection in and of itself is not associated with a delay in dental eruption but rather, the onset of clinical symptoms is.

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