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Sex differences in dental development in children with precocious puberty related to central nervous system lesions

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Abstract

Forty-three children with precocious puberty related to central nervous system (CNS) lesions were examined. Plasma concentrations of estradiol in the females and testosterone in the males were obtained. Panoramic radiographs were used to assess dental root and crown development. All mandibular canines, premolars, and molars were included which could be visualized without apparent distortion. Dental development was retarded significantly relative to chronological age in female patients with CNS lesion-related precocious puberty. However, no significant abnormal dental development was detected in the males of the same group. The data suggest that elevated levels of estrogen associated with precocious puberty may retard odontogenesis.

Hormonal effects on developing teeth have been postulated but not demonstrated clearly.[1-4] Oral evaluations of patients with precocious puberty and with Turner's syndrome have suggested that hormones associated with the hypothalamic-pituitary-gonadal (HPG) axis may have subtle influences on dental and craniofacial development.[3,5,6]

In a previous study of 101 children with precocious puberty, we observed that dental development was normal in all diagnostic categories except idiopathic precocious puberty (IPP).[6] The children with IPP had significantly delayed dental development despite advanced skeletal age. Seeking to explain their delayed dental development, we postulated that the effect of precocious puberty in dental development and in the relationship between dental and skeletal development might differ according to sex, since 98% of our patients with IPP were girls. To evaluate this hypothesis, we examined the effect of sex on dental development in male and female children with precocious puberty due to central nervous system (CNS) lesions. This diagnostic group was chosen because it was the only one in which there were sufficient numbers of children from each sex to perform statistical analysis.

Central precocious puberty (CPP) is the result of premature activation of the HPG axis and can be either idiopathic or the result of CNS system tumors or abnormalities.[7] CPP in boys causes increased plasma testosterone, whereas CPP in girls causes increased plasma estradiol.

Methods and Materials

The authors examined 43 white patients who were referred to the National Institute of Child Health and Human Development with a diagnosis of CNS-related precocious puberty. Data from some of these patients, without analysis of possible sex differences, were included in an earlier report.[6] The diagnoses of the 29 females included hypothalamic hamartoma (14), congenital hydrocephalus (4), astrocytoma (3), neurofibromatosis (2), dermoid teratoma (1), arachnoid cyst (1), optic glioma (1) ependymoblastoma (1), Dandy-Walker syndrome (1), and Arnold-Chiari syndrome (1). The diagnoses of the 14 males included hypothalamic hamartoma (6), astrocytoma (5), neurofibromatosis (1), glioma (1), and arachnoid cyst (1). Plasma estradiol levels were obtained in the female patients and plasma testosterone levels were determined in the males.

The skeletal age was assessed for each patient using radiographs of the wrist and hand.[8] A panoramic radiograph was used to evaluate odontogenic crown and root development.[3,9] Included were all molars, premolars, and canines which showed no apparent radiographic distortion. Teeth with closed root

TABLE 1. Dental Age by Sex in Children With Precocious Puberty Related to Central Nervous System Lesions

Sex	Number of Patients	Age Range and Mean Age (Years/Months)	Number with Normal Dental Age	Number with Advanced Dental Age	Number with Delayed Dental Age	Mean Dental Age (Standard Deviation Units Relative to Normal Controls)	Significance Level*
Male	14	2Y/9M-11Y/9Y mean: 7Y/1M	2	7	5	0.20	0.56
Female	29	3Y/3M-9Y/11M mean: 6Y/10M	3	9	17	−0.48	0.02†

* Wilcoxon sign-ranked test.
† Significance level less than 0.05.

apexes were excluded, as time of closure could not be determined accurately.

The 14 male and 29 female patients in the study were grouped according to sex for analysis. Dental age was determined by expressing the radiographic appearance of each tooth relative to the mean attainment age in units of standard deviation of the mean attainment age.[9] The values recorded were added and then divided by the number of teeth evaluated to obtain an average overall dental age for each patient in standard deviation units.

Results

Table 1 provides the age range, mean age, and descriptive dental age statistics by sex. A positive standard deviation score indicated that dental development was accelerated relative to normal subjects while a negative score indicated that dental development was delayed. The Wilcoxon sign-ranked test was used to test the hypothesis that the standard deviation is symmetric about zero for the two sexes.[10] The hypothesis of symmetry about zero is equivalent to no abnormal development. This test revealed that dental development was significantly delayed in female patients with CNS-related precocious puberty ($P = 0.02$) but there was no significant abnormal dental development in males ($P = 0.56$).

Table 2 gives the mean differences between dental and chronological age and between skeletal and chronological age. The average difference between dental and chronological age was positive for male patients and negative for females. The average skeletal age was 4.5 years ahead of chronological age for males and 3.5 years for females ($P = 0.001$ for both sexes). By contrast, the dental age was significantly behind the chronological age for female patients with CNS-related precocious puberty ($P = 0.01$), whereas there was no difference between dental and chronological age in male patients ($P = 0.31$).

Linear correlation of dental age, as described by Moorrees et al.,[9] minus chronological age versus skeletal age minus chronological age was performed (Table 2). The correlations were positive for both sexes. Neither correlation coefficient was significantly different from zero ($P > 0.15$) when they were considered separately. However, when data from both sexes were combined the correlation coefficient was 0.39 which was significant ($P = 0.02$). Figures 1 and 2 demonstrate the plasma concentration of estradiol in the female patients and testosterone in the males of this study. All the patients exhibited sex steroid levels normally associated with puberty.[11]

TABLE 2. Skeletal and Dental Age Versus Chronological Age by Sex for Children with Precocious Puberty Related to Central Nervous System Lesions

Sex	N	Mean Difference Between Dental and Chronological Age (Years)	Mean Difference Between Skeletal and Chronological Age (Years)	Correlation Coefficient
Male	14	0.21	4.54†	0.35
Females	29	−0.35*	3.46†	0.28

* Significantly different from zero by the paired t-test ($P = 0.01$).
† Significantly different from zero by the paired t-test ($P < 0.001$).

Discussion

The current study showed that sex influences the effect of precocious puberty on dental development. The girls with CNS-related precocious puberty had significantly delayed dental development similar to the girls with idiopathic precocious puberty in our earlier study, whereas boys with the same diagnoses had normal dental development. These findings suggest that in precocious puberty the sex of the affected child is a determining factor as to whether

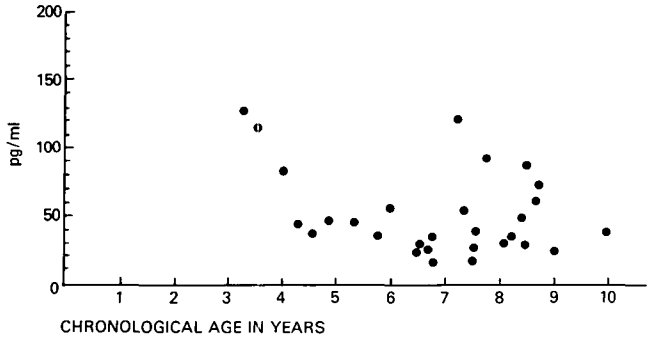

FIG 1. Plasma estradiol concentrations in females with CNS-related precocious puberty. Normal puberty values: 5–125 picograms (pg)/milliliter (ml).[10]

dental development will be normal or delayed. In no instance was dental development found to be accelerated.

It would appear that odontogenic development is unaffected by the release of pituitary gonadotropins which are common to both males and females. The gonadotropins stimulate the gonads to release testosterone in males and estrogen in females. The data suggest that testosterone does not influence the developing teeth as no abnormal dental development was observed in males. It appears, however, that pubertal concentrations of estrogen actually delay tooth formation while simultaneously advancing skeletal maturation significantly.

It is well recognized that teeth normally develop and erupt at an earlier age in females than males. Most of the permanent teeth develop prior to puberty, which occurs at a mean age of 11.6 years in males and 11.0 years in females.[12] Prior to the onset of puberty, estrogen secretion is relatively low in females. However, the initiation of puberty results in an elevated level of estrogen production by the ovaries. The female child who experiences precocious puberty produces an increased estrogen level prior to the age of 8 years and as early as 1 year of age.

These data suggest the hypothesis that estrogen may have a biphasic effect on the developing dentition. It may accelerate tooth development at prepubertal levels, explaining the earlier tooth eruption in girls compared to boys, but retard development at the elevated levels associated with puberty. The third molars are the only teeth primarily formed postpuberty. Our findings suggest that the development of these teeth would be delayed in girls as compared to boys. This is supported by previous observations.[9] This would be analogous to the biphasic effect of estrogen on skeletal growth, in which early pubertal levels stimulate growth whereas late pubertal or adult levels inhibit growth.[13,14]

Our findings provide a possible hormonal-related explanation of the long held clinical impression that the dentition in females develops earlier than in males. However, these differences are subtle and individual orofacial growth and development remains the primary consideration in determining when to initiate orthodontic therapy.

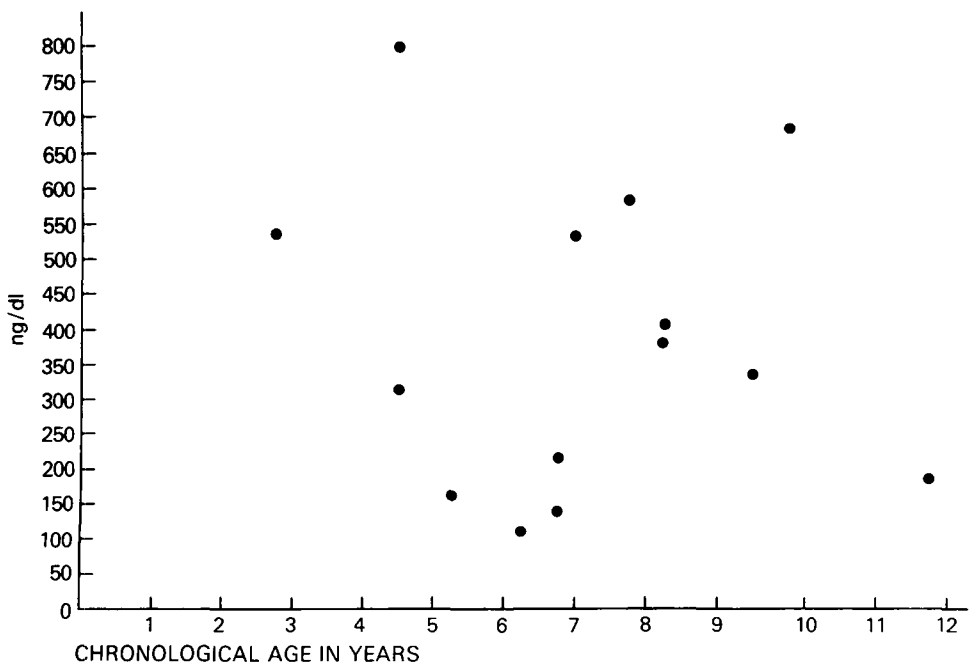

FIG 2. Plasma testosterone concentrations in males with CNS-related precocious puberty. Normal puberty values: 80–1000 nanograms (ng)/deciliter (dl).[10]

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Quotable Quote: AIDS cases to rise dramatically

Scientists for the U.S. Public Health Service (PHS) predict that the number of AIDS cases and deaths will increase more than tenfold by 1991 and that the virus will spread widely outside New York and San Francisco, infecting a larger segment of the heterosexual population.

Reporting on a conference of 85 private and government experts on AIDS, PHS officials said the number of Americans afflicted with the disease would rise to 270,000 by the end of 1991, with a total of 179,000 deaths. As many as 1.5 million Americans, including heterosexuals, would carry the disease—up from about 500,000 to 1 million today. As of June 9, 1986, the government had recorded 21,517 cases of AIDS and 11,713 deaths from the disease.

The cost of caring for AIDS patients nationwide would range from $8 to $16 billion a year, PHS predicted. The PHS report on the conference said care of an AIDS patient would cost at least $46,000 a year by 1991, though other estimates range as high as $150,000.