Scientific Article

Taurodontism and Learning Disabilities in Patients With Klinefelter Syndrome

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Abstract

Purpose: The purpose of this descriptive clinical study was to determine the prevalence rates of taurodontism and learning disabilities in a sample of patients with Klinefelter syndrome.

Methods: Questionnaires and dental radiographs of Klinefelter syndrome patients were obtained and analyzed using previously published methods. Prevalence rates were determined for taurodontism and learning disabilities in the sample population and compared to the general population. Statistical analyses included a Fisher's exact 2-sided test to compare the prevalence rates to that found in the general population and subsequent determination of the positive predictive value.

Results: Taurodontism was found in 75% of the 24 participants. Eighty-three percent of the participants reported having a learning disability. These rates are significantly higher than the general population, as reported in the literature.

Conclusions: The positive predictive value for Klinefelter syndrome, given a male patient with taurodontism and a learning disability, is 84%. In this case, the dentist should recommend karyotyping to the patient, parent, or physician. This demonstrates how important it is for dentists to understand and assist physicians in the diagnosis of genetic disorders. (Pediatr Dent 2005;27:389-394)

KEYWORDS: TAURODONTISM, KLINEFELTER SYNDROME, LEARNING DISABILITY, KARYOTYPING

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Klinefelter syndrome is a genetic disorder that affects approximately 1.2 in 1,000 males.[1,2] The genotype of the disorder is 47, XXY, due to the presence of more than 1 X-chromosome in a male. The cytogenetic cause of the syndrome is a nondisjunction of the X-chromosome during parental gametogenesis, prior to fertilization of an egg by sperm.[1] Clinical characteristics of an adult with Klinefelter syndrome include tall stature, hypogonadism, androgen deficiency, and female traits such as wide hips and sparse facial hair.[3] A recent study by Fales demonstrated that men with the syndrome have "a difficulty in encoding verbal information into working memory (that) may underlie their executive and linguistic impairments."[4] A lower-than-average IQ is also associated with the syndrome.[5] Children diagnosed with the condition show a predilection for emotional and social problems compounded by attention deficit disorders and learning disabilities.[6]

In addition to emotional problems and learning disabilities, the syndrome is associated with a high rate of infertility and cancer.[7] If diagnosed, treatment includes counseling, special education, and hormone replacement therapy.[8] Unfortunately, Abramsky et al reported that childhood diagnosis of Klinefelter syndrome is rare. Abramsky found that only 1 of 28 males with Klinefelter syndrome was diagnosed before age 11.[2] Many men with Klinefelter syndrome, however, may, in fact, remain undiagnosed.[9] Because learning disabilities are common in children, the presence of a learning

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disability rarely suggests to health care providers the presence of Klinefelter syndrome. If some other factor could help to suggest the possibility of Klinefelter syndrome within the large number of boys with learning disabilities, it could be helpful in possibly identifying those at risk that otherwise may not be detected.

Many previously published articles describe abnormal dental and orthodontic findings in individuals with Klinefelter syndrome. For instance, several studies found a tendency toward mandibular prognathism and decreased facial height.[10-12] Other findings have included higher rates of caries and periodontal disease in affected individuals.[13,14]

Another dental condition that has been associated with Klinefelter syndrome is taurodontism.[7] Taurodontism is defined as an "increase in the apico-occlusal dimension of the pulp chamber, accompanied by an alteration in the external root configuration."[15] As compared to the general population, taurodontism is seen more commonly in conditions such as trisomy 18, ectodermal dysplasia, and syndromes such as Down, Williams, Mohr, Seckel, Lowe, trichodentoosseous, and Klinefelter.[16]

Since the early 1920s, anthropologists used the term "taurodont" to describe the morphology of certain fossilized teeth. In 1928, Shaw further classified teeth as "hypotaurodont," "mesotaurodont," and "hypertaurodont."[17] Hypotaurodontism applied to teeth with slightly enlarged pulp chambers, mesotaurodontism applied to teeth with more enlarged pulp chambers, and hypertaurodontism applied to teeth with much enlarged pulp chambers.[17]

In 1966, Keene created a method to determine whether a tooth is taurodontic.[18] In 1971, Blumberg modified this method.[19] Shifman and Chanannel, in 1978, further revised and simplified the earlier methods.[20] The method of determining taurodontism in this study was derived from 3 previously described methods. The first was Keene's, who used 2 variables to calculate what he termed the "taurodontism index."[18] The variables were defined as the height of the pulp chamber and the length from the pulp chamber roof to the longest root's apex.

In a study of 247 Caucasian males, Keene found taurodontism in only 3% of the cases. In a second study, Blumberg also measured specific variables, such as the distance from the pulp chamber's roof to the longest root's apex.[19] Blumberg felt, however, that Keene's method did not account for age or caries, either of which could alter the position of the pulp chamber's roof. Blumberg's complex analysis included a new stable variable—the distance from the cementoenamel junction (CEJ) to the highest point of the pulp chamber floor. In a third study, Shifman and Chanannel revised and simplified the earlier methods, and their technique was used in this study.[20]

The prevalence rate of taurodontism in the general population is low and is reported to vary with ethnicity.[21] Daito et al found taurodontism to be less than 1% in 2,300 Japanese boys without chromosomal disorders.[21,22] Shifman and Chanannel found a prevalence of 6% in an Israeli general population sample.[20] The sample included males and females between the ages of 20 and 30 years. It is possible that their study included patients with sex-chromosomal disorders, thereby altering the true prevalence rate in normal subjects. Conversely, it has been found to occur in 11 of 12 patients (92%) exhibiting X-chromosomal aneuploidy.[21]

Taurodontism is not commonly used as an indicator for childhood diagnosis of Klinefelter syndrome.[23] In 1985, however, Cichon and Pack described the case of a 22-year-old male in which they diagnosed Klinefelter syndrome based on several important clues such as testicular atrophy and taurodontism.[16] Similarly, in 1989, Darbyshire and Witkop chose to karyotype a 9-year-old male with "slim build, long lower body, moderately long fingers, and the presence of taurodontic teeth."[23] The patient was diagnosed with Klinefelter syndrome.

The purposes of this pilot study were to:

1. establish the prevalence rates of taurodontism and learning disabilities in a Klinefelter syndrome population;
2. show that the combination of a learning disability and taurodontism are valuable predictors to consider karyotyping a boy for Klinefelter syndrome.

Methods

Subjects

Experimental design and recruitment protocols were approved by the Institutional Review Board at the University of Connecticut Health Center, Farmington, Conn. Participants were recruited in the following manner: An announcement of the study was placed on the Web site of an international support group for Klinefelter syndrome, Klinefelter's Syndrome Associates[24]; Klinefelter syndrome patients from the Division of Human Genetics at the University of Connecticut were asked to participate.

Procedures

Parents and/or patients who volunteered to participate were asked to complete a questionnaire to ascertain their genetic diagnosis (karyotype), presence of a learning disability, and information about their dentists. The participants were surveyed to determine when and why they were diagnosed and/or tested for Klinefelter syndrome. Dentists were then contacted and asked to submit copies of dental radiographs. These radiographs consisted of panoramic, bitewing, and periapical radiographs. Radiographs were excluded if the pulp chambers were obscured by metal prostheses such as crowns and bridges. The radiographs were analyzed by 2 examiners.

Using the Shifman and Chanannel method, measurements were made on all permanent molars using a precision ruler (Schaedler Quinzell Inc, Parsippany, NJ).[20] The following 3 variables were measured in the permanent molars:

1. V1—the distance from the lowest point of the pulp chamber roof to the highest point of the pulp chamber floor.
2. V2—the distance from the lowest point of pulp chamber roof to the longest root's apex.
3. V3—the distance from the line connecting the CEJs to the highest point of the pulp chamber floor (Figure 1).

Teeth were included for analysis if V1 and V2 and/or V3 were able to be determined. According to Shifman and Chanannel, a tooth was taurodontic if the ratio of V1 to V2 was greater than 20 and if V3 was greater than 2.5 mm. If the radiograph did not include the apex, the tooth was deemed taurodontic if V3 was greater than 2.5 mm. Measurements were performed independently by 2 of the authors using the same method and instruments. The authors then discussed their disagreements in measurements. Because they independently found taurodontism in the same patients, there was no need to exclude those patients from the study.

Participants or their parents were asked whether or not they had a learning disability. This was intentionally subjective because the results would be compared to a control group that was assessed by questionnaire as well.[25] Prevalence rates for taurodontism and learning disabilities were calculated for the sample using Microsoft Excel (Microsoft Corp, Seattle, Wash). A new control group was not formed because of the chance for skewed statistical comparisons. In other words, the low prevalence rate of taurodontism found in the general population may lead to the underexpression or nonexpression of that trait in a control group. Additionally, there was the chance that a male control subject was actually an undiagnosed 47, XXY. Hence, prevalence rates for the 2 conditions in the general population were obtained from literature sources.[20,25]

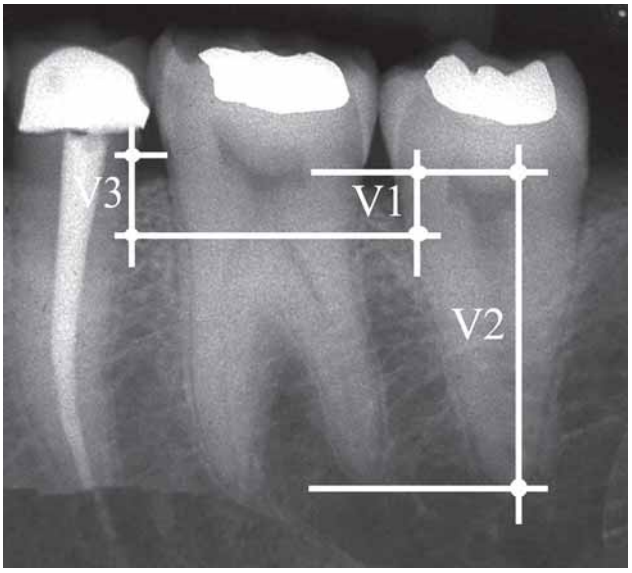

Figure 1. V1—the distance from the lowest point of the pulp chamber roof to the highest point of the pulp chamber floor. V2—the distance from the lowest point of the pulp chamber roof to the longest root's apex. V3—the distance from the line connecting the cementoenamel junction to the highest point of the pulp chamber floor.[20]

Statistical analysis

Fisher's exact 2-sided tests were performed to compare the prevalence rates of taurodontism and learning disabilities to that of the general population, as stated in the studies cited later. A positive-predictive value for Klinefelter syndrome was then determined.

Results

Eighty people responded to the announcement of the study. Of those that provided addresses, 34 returned questionnaires with consent to contact their dentists. Thirty dentists were asked for copies of the participants' dental radiographs. Twenty-seven copies were received. Three sets of radiographs were excluded from the study because the pulp chambers were obscured by metal prostheses or the apices were not visible.

The average age of the participants was 19 years, 5 months, with a range of 3 to 56 years. Twenty-two of the participants were 47, XXY. One participant was a mosaic, and 2 were 48, XXYY variants.

In 2 cases, only primary teeth were present. In both of those cases, the teeth were deemed to be taurodontic due to an increased pulp chamber height compared to the neighboring teeth. Two sets of radiographs did not show the apices of the teeth and were determined to be taurodontic because the variable V3 (distance from CEJ to the pulp chamber floor) was greater than 2.5 mm.

Two examiners recorded small differences in measurements but determined the presence of taurodontism in the same patients' radiographs. Their overall results were, therefore, the same. The Spearman-Brown coefficient, a measure of reliability, was calculated. For all 12 measurements, this value was 0.949. Spearman-Brown coefficients over 0.90 are considered excellent. The distribution and prevalence rates of taurodontism in molars are shown in Table 1.

The overall prevalence rate of taurodontism for the 24 participants was 75%. The prevalence rate of learning disabilities, as reported by the 24 participants, was 83%.

Table 1. Distribution and Prevalence Rates of Taurodontism

	Maxillary first molars	Mandibular first molars	Maxillary second molars	Mandibular second molars	Primary molars	Patients with taurodontic teeth
Numbers	6/18	8/21	8/13	6/14	3/4	18/24
Prevalence	0.333	0.381	0.615	0.429	0.7500	0.750

As aforementioned, a Fisher's exact 2-sided test compared the prevalence rates of taurodontism in the general population (surveyed by Shifman and Chanannel) to the study sample.[20] Another test compared the prevalence rates of learning disabilities in the general population (surveyed by Halfon et al) to the study sample.[25] The *P* values for both tests were less than .005. By comparing the separate and concurrent prevalence rates of taurodontism and learning disabilities in the general population to the Klinefelter syndrome sample in this study, the positive predictive value was calculated. The positive predictive value for Klinefelter syndrome, given the presence of taurodontism and a learning disability, was calculated at 84%.

Discussion

The 75% prevalence rate for taurodontism in this study was not as high as that found by Jaspers and Witkop (92%).[21] It is higher, however, than the study by Varrela and Alvesalo, who examined 30 Finnish males with Klinefelter syndrome and found taurodontism in 30% of their mandibular molars.[26] The rate in the present study is also much higher than those reported in the literature for the "general population." As stated earlier, taurodontism was found to occur in less than only 1% of 2,300 Japanese boys without chromosomal disorders.[22]

Learning disabilities are commonly found in those with syndromes such as Turner and Klinefelter. Many articles describe the preponderance of speech, auditory processing, and arithmetic and general learning disabilities in Klinefelter syndrome patients. The specific mechanism of learning disabilities in 47, XXY patients is unknown. Some believe, however, that they are related to problems with language processing. Graham et al described the deficits as "...problems in rate and order processing of auditory stimuli, problems in the understanding of complex grammatical constructions, and problems in oral language production that include deficits in morphology, word-retrieval abilities, and oral narrative construction."[27] In a comprehensive literature review, Samango-Sprouse stated "although no formal studies have been undertaken, boys with XXY appear to have difficulty with attention in school settings based on anecdotal information such as parental reports and review of school records."[28] As stated earlier, in a study by Linden, 57% of 14 affected boys demonstrated academic difficulties.[5]

As expected, the prevalence rate (83%) of reported learning disabilities in the study population is much higher than that of the general population. Interestingly, the prevalence rate of learning disabilities in the general population is unclear due to the lack of an accepted definition of "learning disability." One study from the National Institute of Child Health and Human Development at the National Institutes of Health stated that approximately 5% of all public school students are identified as having a learning disability.[29] The authors of that study also stated that "learning disability is not a single disorder but includes disabilities in any of 7 areas related to reading, language, and mathematics."[29] Lyon et al found a prevalence rate of 2% for learning disabilities in the general population. Another study of mental health conditions reported a prevalence rate of 0.38% in 10,000 males under the age of 18.[25] The latter study used parental questionnaires, similar to those used in the present study, to determine the presence of a learning disability.

By comparing the separate and concurrent prevalence rates of taurodontism and learning disabilities in the general population to the Klinefelter syndrome population in this study, the positive predictive value was calculated. The positive predictive value for Klinefelter syndrome, given the presence of taurodontism and a learning disability, is 84%. In other words, if a male patient has taurodontism and a learning disability, 84% of the time this patient will also have Klinefelter syndrome.

As noted previously, early diagnosis of Klinefelter syndrome in children is rare. It has been suggested that the combination of low testicular volume, azoospermia, and elevated gonadotropins in male children may be indicative of Klinefelter syndrome.[30] This observation may be of little value, however, in children, and can be easily overlooked. Dental radiographs require less intervention and are commonly taken in children as part of their routine dental examinations.

Table 2. Prevalence of Taurodontism in a Population With Klinefelter Syndrome vs the General Population

	Klinefelter syndrome population (N)	General population	Total
Taurodontism	18*	31	49
No taurodontism	6	519	525
	24	550	574

*Fisher's exact 2-sided test; $P<.005$.

Table 3. Prevalence of Learning Disabilities in a Population With Klinefelter Syndrome vs the General Population

	Klinefelter syndrome population (N)	General population	Total
Learning disabilities	20*	38	58
No learning disabilities	4	9,962	9,966
	24	10,000	10,024

*Fisher's exact 2-sided test; $P<.005$.

The presence of taurodontic teeth should prompt the dentist to determine if the patient has other characteristics of Klinefelter syndrome, particularly a learning disability. The concurrence of these findings may help the family consider further evaluation for this chromosomal disorder, after discussion with the patient's physician. Chromosomal analysis or karyotyping involves collection of a tissue sample, most commonly venous draw of a patient's blood to examine a typical cellular cytologic collection of genes. Syndromes, such as Klinefelter syndrome, may result from a deletion, insertion, or rearrangement of a partial or entire chromosome. This may involve a single or multiple genes. Genetic consultation prior to chromosomal analysis is indicated, especially since the possible diagnosis requires counseling and other support systems that the dental team is not prepared to handle.

Children may benefit from early diagnosis of Klinefelter syndrome. As one study found, behavioral adjustment and school performance were significantly better in 4 boys diagnosed earlier in life than in 4 boys diagnosed later.[7] Additionally, early treatment with low-dose testosterone may help with behavior and may lead to more normal development of sexual characteristics.[31]

Conclusions

Based on the findings of this pilot study, the following conclusions can be drawn:

1. The prevalence rates of taurodontism and learning disabilities in Klinefelter syndrome patients are higher than the unaffected population by a statistically significant amount.
2. The results indicate further investigation of Klinefelter syndrome individuals. For instance, a full study to examine the rates of taurodontism and learning disabilities in the general population could reinforce the conclusion that they are strong indicators for Klinefelter syndrome.
3. Even with these preliminary results, it is important for dentists to associate the presence of taurodontism with a learning disability and then to consider the possible diagnosis of Klinefelter syndrome. A dentist may then discuss with the primary care physician the karyotyping of undiagnosed children.

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Abstract of the Scientific Literature

Propolis: a Promising New Storage Media Following Avulsion

Length of extra-alveolar time and type of storage media are both significant factors that can affect the long-term prognosis of replanted teeth. The purpose of this study was to use a Collagenase-Dispase assay to investigate the potential of a new storage media, Propolis, in maintaining viable periodontal ligament (PDL) cells on simulated avulsed teeth. Seventy freshly extracted human teeth were divided into 5 experimental groups and 2 control groups. The positive and negative controls corresponded to a 0-minute and an 8-hours dry time, respectively. The experimental teeth were stored dry for 30 minutes and then immersed in 1 of the 5 media (Hank's balanced salt solution [HBSS], milk, saline, Propolis 50%, and Propolis 100% for 45 minutes). The number of viable PDL cells were counted with a hemocytometer and analyzed. Statistical analysis demonstrated that both Propolis groups kept significantly more PDL cells viable compared to either milk, saline, or HBSS. Within this study's parameters, it appears that Propolis may be a better alternative to HBSS, milk, or saline in terms of maintaining PDL cell viability after avulsion and storage.

Comments: Propolis, an antibacterial and anti-inflammatory resinous beehive product, has never been tested for its potential benefits on PDL cells of an avulsed tooth. This study showed that Propolis may be able to maintain PDL cell viability better than HBSS, milk, or saline. Further research would determine a standard formulation for therapeutic use and the benefits of having a storage media with antibacterial and anti-inflammatory abilities. FSS

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