Original Article

Increased Occurrence of Dental Anomalies Associated with Second-Premolar Agenesis

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ABSTRACT

Objective: To evaluate the prevalence of dental anomalies in patients with agenesis of second premolars and compare the findings with the prevalence of these anomalies in the general population.

Materials and Methods: A Brazilian sample of 203 patients aged 8 to 22 years was selected. All patients presented agenesis of at least one second premolar. Panoramic and periapical radiographs and dental casts were used to analyze the presence of other associated dental anomalies, including agenesis of other permanent teeth, ectopia of unerupted permanent teeth, infraocclusion of deciduous molars, microdontia of maxillary lateral incisors, and supernumerary teeth. The occurrence of these anomalies was compared with occurrence data previously reported for the general population. Statistical testing was performed using the chi-square test ($P < .05$) and the odds ratio.

Results: The sample with agenesis of at least one second premolar presented a significantly increased prevalence rate of permanent tooth agenesis (21%), excluding third molars. Among the sample segment aged 14 years or greater (N = 77), occurrence of third-molar agenesis (48%) exceeded twice its normal frequency. Significant increases in occurrence of microdontia of maxillary lateral incisors (20.6%), infraocclusion of deciduous molars (24.6%), and distoangulation of mandibular second premolars (7.8%) were observed. Palatally displaced canine anomaly was also significantly elevated (8.1%).

Conclusion: The results provide evidence that agenesis of other permanent teeth, microdontia, deciduous molar infraocclusion, and certain dental ectopias are the products of the same genetic mechanisms that cause second-premolar agenesis. (*Angle Orthod.* 2009;79:436–441.)

KEY WORDS: Agenesis; Dental anomalies; Second premolar

INTRODUCTION

There is considerable evidence suggesting that genes play a fundamental role in the etiology of tooth agenesis. Grahnén[1] conducted a study on children with tooth agenesis and reported that more than 50% of siblings and relatives also presented with hypodontia, a high prevalence compared to the expected prevalence in the general population. A study of twins demonstrated a high percentage of concordance for agenesis between homozygotic twins, whereas pairs of heterozygotic twins presented discordance for this dental anomaly.[2] Vastardis[3] analyzed a large family with agenesis of all second premolars and third molars and identified a mutation in gene *MSX1* on chromosome 4p.

Moreover, there seems to be a genetic relationship in the determination of different dental anomalies, considering the high frequency of patterns of association. A single genetic defect may result in different phenotypic expressions, including such various traits as tooth agenesis, microdontia, ectopic tooth position, and delayed development of different teeth.[4] Garn and Lewis[5,6] observed that patients with agenesis of third molars presented an increased prevalence of agenesis of other permanent teeth, as well as a general reduction in tooth size. In 1992, Bjerklin et al[7] observed

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a high frequency of association in the occurrence of agenesis of premolars, ectopic eruption of permanent maxillary first molars, ectopic eruption of maxillary canines, and infraocclusion of deciduous molars, suggesting that these anomalies presented a common genetic etiology. Peck et al[8] observed high prevalence of tooth agenesis and peg-shaped lateral incisors in patients with a transposition of the maxillary canine and first premolar. They reported similar findings in samples of patients with palatally displaced canines (PDC) and transposition between mandibular canines and lateral incisors.[9,10] Baccetti[11] observed that agenesis of second premolars, microdontia of maxillary lateral incisors, PDC, infraocclusion of deciduous molars, ectopic eruption of maxillary first molars, and enamel hypoplasia are frequently related dental anomalies. Shalish et al[12] demonstrated that patients with unilateral agenesis of second premolars often exhibit distal angulation and delayed development of the unerupted contralateral second premolar.

Even though previous studies reported associations between tooth agenesis and other dental anomalies, no study investigated the frequency of dental anomalies occurring in a significantly large sample with second premolar agenesis. Therefore, this study aimed to determine the prevalence of permanent tooth agenesis, discrete ectopias, microdontia, deciduous molar infraocclusion, and supernumerary teeth in patients with agenesis of second premolars and compare the prevalence of these with the frequency expected in the general population. The null hypothesis was that subjects with agenesis of at least one second premolar do not demonstrate a significantly increased prevalence of other dental anomalies.

MATERIALS AND METHODS

A sample of 203 Brazilians with agenesis of one or more second premolars was selected from the orthodontic patient files of a university dental school and eight private dental offices. The subjects ranged in age from 8 to 22 years at the time of construction of the diagnostic records used in this study. The total sample consisted of 134 females and 69 males, a sex ratio of 2F:1M. Given the widely heterogeneous backgrounds within the Brazilian population, a rough estimate of the ethnic makeup of the sample was derived subjectively from facial photographic records: white (84%), black (13%), and Japanese (3%).

Panoramic radiographs, periapical radiographs, and dental casts were used to investigate the presence of the following dental anomalies:

1. Agenesis of permanent teeth
2. Supernumerary teeth
3. Microdontia of maxillary lateral incisors
4. Infraocclusion of deciduous molars
5. Three types of tooth ectopia
   a. PDC
   b. Distal angulation of mandibular second premolars
   c. Mesial angulation of mandibular second molars

The critical age of 14 years was considered to be confirmation of the absence of third molars.[5] This criterion was used to restrict the sample for evaluation of third-molar agenesis to only those with diagnostic records at greater or equal to 14 years of age. Infraocclusion of deciduous teeth was determined by visual inspection.[11] Diagnosis of palatally displaced maxillary canines followed the radiographic parameters suggested by Lindauer et al,[13] confirmed by interpretation of periapical radiographs using the tube shift technique, a method of object localization using two projections with significantly different x-ray tube angulations. Based on the findings of Ericson and Kurol[14] that an attempt to determine the eruption path of maxillary canines radiographically is generally of little value in children younger than 10 years, subjects whose only diagnostic records were from an age under 10 years were omitted from the sample in evaluating for PDC. Diagnosis of distal angulation of mandibular second premolars followed the criteria described by Shalish et al,[12] using the inferior border of the mandible as a base line. The maxillary lateral incisor was considered as presenting microdontia when the maximum mesiodistal crown diameter was smaller compared to the same dimension of opposing mandibular lateral incisor in the same patient. This category also included conical or peg-shaped maxillary lateral incisors.

The results were analyzed with the chi-square test for goodness of fit in order to compare the frequency of dental anomalies in the sample with previously published reference values. These comparison reference data came from studies that had samples more racially and ethnically homogeneous than the experimental sample for the present study. Previous investigations have shown concordance among ethnicities or racial groups in the general frequencies of dental anomalies observed in this study. For hypothesis testing in this study, the 5% level of significance was employed. The odds ratio (OR) was calculated at the 95% confidence interval to measure the strength of associations between agenesis of second premolars and the presence of other dental anomalies investigated.

RESULTS

In the sample of 203 patients with agenesis of second premolars, there was a significantly higher prevalence of agenesis of other permanent teeth (OR = 5.6), excluding third molars, compared to reference

Table 1. Prevalence Rate of Tooth Agenesis and Supernumerary Teeth in Subjects with Second Premolar (P2) Agenesis, Compared with Reference Values

Dental Anomaly	Prevalence Rate in P2 Agenesis Sample	Reference Values		Difference Chi-Square (*P*-value)	Odds Ratio	95% Confidence Interval
		Prevalence Rate	Study (Year)			
Tooth agenesis (excluding third molars)	21.2% (43/203)	5.0% (53/1064)	Grahnén[1] (1956)	73.20 (<.001)	5.63	(3.65–8.70)
Maxillary lateral incisor agenesis	16.3% (33/203)	1.9% (109/5738)	Le Bot & Salmon[15] (1977)	173.21 (<.001)	10.02	(6.60–15.23)
Third molar agenesis	48.1% (37/77)	20.7% (427/2061)	Bredy et al[16] (1991)	32.64 (<.001)	3.54	(2.24–5.6)
Supernumerary teeth	3.0% (6/203)	3.9% (39/1000)	Baccetti[11] (1998)	0.42 (<.518)	0.75	(0.31–1.80)

values in the general population[1,11,15,16] (Table 1). The most commonly absent tooth was the maxillary lateral incisor (Figure 1), with an eightfold-increased prevalence of agenesis compared to the general population (Table 1). The prevalence of third molar agenesis was also significantly increased (OR = 3.5) in the sample (Table 1). In contrast, the prevalence of supernumerary teeth was not different from reference values observed for the general population (Table 1).

The prevalence of dental anomalies for the sizes and positions evaluated in the sample are presented in Table 2. Compared to the general population,[11,17–20] patients with agenesis of second premolars presented significantly higher prevalence of microdontia of maxillary lateral incisors (OR = 5.2), palatally displaced maxillary canines (OR = 5.0), distal angulation of mandibular second premolars (OR = 43.1), mesial angulation of mandibular second molars (OR = 16.5), and infraocclusion of deciduous molars (OR = 3.3).

DISCUSSION

In the group of patients characterized by agenesis of second premolars, the prevalence of agenesis of other permanent teeth was significantly increased (Table 1). Previous analysis of tooth agenesis across racial and ethnic lines would suggest that the results of this study would be materially unchanged regardless of the race or ethnicity of the subjects or comparative samples.[21]

Only one previous study in the literature addressed the association of tooth agenesis occurrence. In the 1960s, Garn and Lewis[5] observed that patients with third-molar agenesis presented an increased prevalence of other missing permanent teeth. The prevalence of agenesis of permanent teeth in the group with third-molar agenesis was 13 times higher compared to the prevalence of agenesis in the control group. Even developmentally stable teeth such as central incisors, canines, and first premolars were missing in the sample with agenesis of third molars. Specifically, concerning the second premolars, the prevalence of agenesis observed within the study group corresponded to 11%, compared to 1.5% in the control group.

The present study confirmed the results of Garn and Lewis[5] showing other physical dental traits associated with the occurrence of tooth agenesis. It contributes to mounting evidence that agenesis and its associated abnormalities are under genetic control. The possible explanation is that a single genetic defect may give rise to different anomalies, so that two or more dental anomalies in the same patient may present a common genetic origin. Studies of families,[2,3,22–24] as well as in-

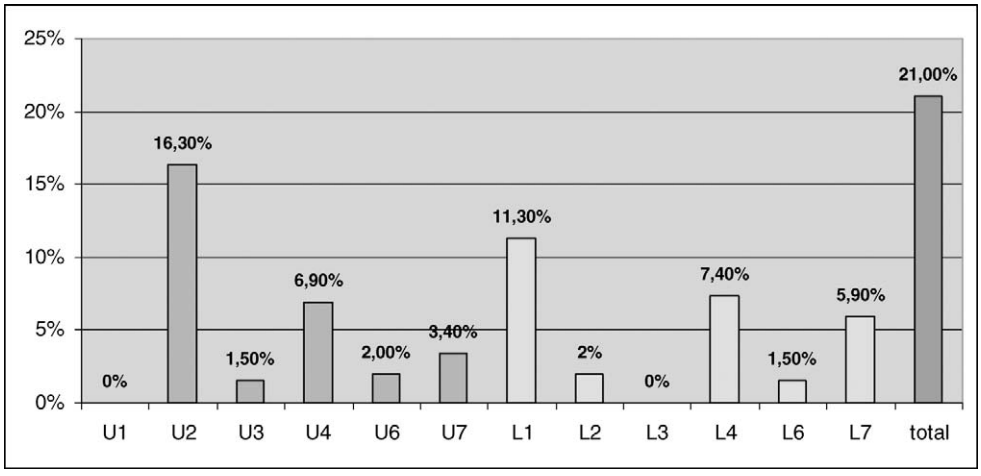

Figure 1. Prevalence of agenesis of permanent teeth in the sample with second premolar agenesis.

Table 2. Prevalence Rate of Dental Anomalies of Size and Position in Subjects with Second Premolar (P2) Agenesis, Compared with Reference Values

Dental Anomaly	Prevalence Rate in Study Sample	Reference Values		Difference Chi-Square (*P*-value)	Odds Ratio	95% Confidence Interval
		Prevalence Rate	Study (Year)			
Small maxillary lateral incisor	20.6% (42/203)	4.7% (47/1000)	Baccetti[11] (1998)	62.97 (<.001)	5.29	(3.38–8.28)
Palatally displaced canines	8.1% (15/185)	1.7% (25/1450)	Dachi and Howell[17] (1961)	28.02 (<.001)	5.03	(2.60–9.73)
Mandibular second premolar distoangulation	7.8% (16/203)	0.20% (52/26,264)	Matteson et al[18] (1982)	464.1 (<.001)	43.13	(24.18–76.92)
Mandibular second molar mesioangulation	1.0% (2/203)	0.06% (3/5000)	Grover and Lorton[19] (1985)	17.39 (<.001)	16.50	(2.75–99.74)
Deciduous molar infraocclusion	24.6% (50/203)	8.9% (94/1059)	Kurol[20] (1981)	41.83 (<.001)	3.35	(2.29–4.92)

vestigations of the association of agenesis and other types of dental anomalies,[6,8,10,11] previously highlighted the role played by genetic mechanisms in the etiology of various dental anomalies.

The prevalence of supernumerary teeth in the analyzed sample was not statistically different from the prevalence observed for the general population (Table 1). This suggests that these anomalies present different or independent etiologic factors. This fact is coherent, considering that tooth agenesis is a hypoplastic dental anomaly, whereas supernumerary teeth represent hyperplastic anomalies. No previous study reported an association between tooth agenesis and supernumerary teeth. Baccetti[11] investigated this association and also did not find any statistically significant difference in the prevalence of supernumerary teeth between a sample with agenesis of second premolars and a control group.

Compared to the general population, patients with agenesis of second premolars presented significantly higher prevalence of microdontia of maxillary lateral incisors (Table 2). The results showed that 20% of patients with second premolar agenesis also presented reduced size of lateral incisors. These results corroborate previous studies and suggest that agenesis and microdontia are different expressions of the same genetic defect, since these phenotypes are frequently associated. Garn and Lewis[6] observed that patients with agenesis of third molars presented a general and significant reduction in tooth size, more significantly in patients with multiple agenesis. Brook[23] analyzed families of patients with dental anomalies and observed that agenesis and microdontia often occur concomitantly. Baccetti[11] observed results similar to the present study, demonstrating that 18% of patients with agenesis of second premolars presented microdontia of maxillary lateral incisors, and nearly half of patients with small maxillary lateral incisors (42%) presented agenesis of second premolars. The practical implications of these findings are related to the fact that orthodontists will rarely observe crowding in patients with agenesis, while spacing is the common picture. Therefore, difficulty in mechanical space closure in these patients can be expected.

Distoangulation of mandibular second premolars was also evaluated in this study. The results revealed that 7.9% of patients in the sample presented this ectopia, representing a 40-fold increase in occurrence compared to the general population (Table 2). The occurrence of distoangulation in the general population is rare, with a prevalence of 0.20%.[18] Shalish et al[12] investigated a sample with unilateral agenesis of mandibular second premolars and observed that the contralateral tooth bud presented a mean 10° increase in distal angulation compared to a control group without agenesis. They concluded that distal angulation of mandibular second premolars represents a different phenotype of the same genetic defect causing the agenesis. This type of association is similar to the classical clinical situation of microdontia of maxillary lateral incisors in patients with unilateral agenesis of this tooth. Symons and Taverne[24] observed distal angulation of the tooth buds of mandibular second premolars as well as delayed tooth development in individuals of the same family presenting multiple agenesis, including mandibular second premolars.

An additional finding provided by the present study was that distoangulation of mandibular second premolars is observed not only in individuals with unilateral agenesis of mandibular second premolars but also in patients with agenesis of maxillary second premolars. Nearly 25% of individuals with distal angulation had agenesis of maxillary premolars only, whereas the remaining 75% of patients with this ectopia presented unilateral agenesis of second premolars in the mandible. Therefore, clinicians should not be surprised when observing this anomaly of tooth position in patients with tooth agenesis. This ectopia usually self-corrects and does not require intervention[12,25] unless it is very severe.[26]

The present sample included two cases of mesial angulation and impaction of mandibular second molars, a rare irregularity of eruption affecting 0.06% of the population.[19] The occurrence of two cases in 203

patients represents a prevalence rate of 1%, which is significantly higher compared to the prevalence for the general population (Table 2). Impaction of mesially angulated permanent mandibular second molars is an eruption disturbance which the etiology is frequently assigned to local factors, such as deficient dental arch perimeter.[27] There is a lack of previous studies investigating the occurrence of ectopic eruption of mandibular second molars associated with other dental anomalies, even though this association was mentioned in some case reports.[27,28] Not all cases of retention of mandibular second molars may be assigned to local causes, such as deficient dental arch space and mechanics involving distalization of mandibular first molars. In some cases, a normally developing tooth bud of a mandibular second molar may, in a short time and without apparent causes, change its angulation to a significant mesial inclination, thus remaining impacted on the distal aspect of the mandibular first molar.[27] According to the present study's results, this event may represent another genetically programmed dental anomaly.

This study also investigated PDC. The prevalence rate (8.1%) of this anomaly in the study sample was nearly five times higher compared to that in the general population (Table 2). These data corroborate previous results that the PDC presents an occurrence pattern that suggests an essentially genetic origin.[9,29,30] Peck et al[9,30] observed that patients with PDC presented a significantly increased prevalence of agenesis of second premolars and third molars. They further observed that PDC is significantly associated with microdontia of one or both maxillary lateral incisors but not to agenesis of these teeth, the prevalence of which was not different compared to the general population. These data present important clinical relevance for the possibility of early diagnosis of PDC, since patients with second premolar agenesis have a considerable chance of developing ectopic eruption of maxillary canines during the late mixed dentition period. Thus, based on a ''red flag'' presented by second-premolar agenesis, early detection of associated anomalies could permit early intervention and, in most of the cases, avoid canine impaction as well as the possible sequelae of resorption of the roots of neighboring teeth.[31]

Among patients with agenesis of second premolars, 24.6% presented infraocclusion of deciduous molars (Table 2). This prevalence rate was significantly larger than the value representing occurrence in the general population (8.9%). The present results suggest that genetic factors are involved in the etiology of infraocclusion, in agreement with other studies.[7,11,20] Kurol[20] earlier observed that the prevalence of infraocclusion is increased in siblings of affected subjects and noted significantly associated increases in occurrence of ectopic eruption of permanent maxillary first molars, ectopic eruption of maxillary canines, and agenesis of second premolars.[7]

In summary, the clinical implications of patterns of associated dental anomalies are important, since early detection of a single dental anomaly (such as the emergence of a conical maxillary lateral incisor or radiographic evidence of second premolar agenesis) may call the attention of professionals to the possible development of other associated anomalies in the same patient or in the family, allowing timely orthodontic intervention.

CONCLUSIONS

- There was strong association between agenesis of second premolars and agenesis of other permanent teeth, as well as significantly increased occurrence of microdontia of maxillary lateral incisors and of clinically important anomalies of tooth position, such as palatal displacement of canines. Thus, these results justified rejection of the null hypothesis that subjects with agenesis of at least one second premolar do not demonstrate a significantly increased prevalence of other dental anomalies.
- The findings of this study provide additional evidence that tooth agenesis, microdontia, and certain discrete tooth ectopia are related in occurrence through shared genetic mechanisms.

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