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Maxillary dental anomalies in children with cleft lip and palate: a controlled study

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Objective. To evaluate the prevalence of dental abnormalities of the primary and permanent maxillary dentitions in children affected by unilateral (UCLP) and bilateral (BCLP) cleft of the lip and palate.

Methods. One hundred and fifty-six Caucasian patients (64 females and 92 males) affected by non-syndromic UCLP or BLCP were selected. A control sample of 1000 subjects (482 males and 518 females) without CLP was selected. All comparisons were carried out by means of *z*-tests on proportions.

Results. The prevalence rate for missing primary lateral incisors in UCLP subjects was 8.1% and it was 27.9% for the permanent lateral incisors. In BLCP subjects, the prevalence rates were 17% for the primary lateral incisors and 60% for the permanent lateral incisors. The second premolar was absent in 5.4% of UCLP subjects and in 8.8% in the BCLP sample. The statistical analysis revealed significant differences for the prevalence rates of all dental anomalies compared with the control group except for second premolar agenesis.

Conclusions. In both UCLP and BCLP subjects the most prevalent missing teeth were the lateral incisors. The dental anomalies occurred predominantly in the cleft area, thus suggesting that the effect of the cleft disturbance is more local than general on the dentition.

Introduction

Tooth anomalies represent an interesting chapter of orofacial pathology, for both their aetiological background and clinical implications. Several studies[1–9] have demonstrated that dental anomalies in number, size, shape, timing of formation, eruption and enamel dysplasia are more frequent in children affected by cleft lip, cleft palate or both (CLP) than in the general population. These studies showed that both primary and permanent dentitions can be affected, and that the dental anomalies are more frequent on the cleft side of the maxilla. Missing or supernumerary teeth, and delayed dental development are the most common types of dental anomalies observed. In CLP subjects, the lateral incisor in the region of the alveolar cleft is very sensitive to developmental disorders[1,3–5]. Some authors[1,4,6–9] claim that teeth outside the cleft area are also affected more frequently than in children without CLP.

In CLP patients, multidisciplinary approach is needed, and the paediatric dentist represents an important member of the interdisciplinary cleft team. The knowledge of developmental dental disorders in CLP children can provide valuable information for treatment planning at an early age.

No previous studies in the literature analysed the relationships between CLP and tooth anomalies of both primary and permanent dentitions in a large sample of Caucasian subjects with the use of unaffected controls. The purpose of this study is to evaluate the prevalence of dental abnormalities in number, size and shape of the primary and permanent maxillary dentitions in children affected by

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unilateral (UCLP) or bilateral (BCLP) cleft of the lip and palate, and to compare it with the prevalence of dental anomalies in a control group without cleft (NCLP).

Materials and methods

One hundred fifty-six Caucasian subjects affected by UCLP or BLCP non-syndromic were observed consecutively at the Department of Orthodontics and Paediatric Dentistry of the University of Florence. The sample consisted of 64 females and 92 males (Table 1), with age ranging from 4 years 2 months to 16 years 3 months (mean age of 10 years 4 months). All subjects had received the same surgical treatment (early secondary gingivoalveoloplasty, ESGAP) at an early developmental stage (at the mean age of 30 months).

The NCLP control sample comprised 1000 subjects (482 males and 518 females), and it was selected randomly from the files of the same department. None of the control subjects had received any orthodontic treatment. Subjects with inadequate dental records, craniofacial syndromes, or other medical disorders, were not included in the NCLP sample.

Clinical examination, dental casts, intraoral photographs, and radiographic material (panoramic X-rays, occlusal and/or periapical radiographs) of all subjects were examined for the diagnosis of dental abnormalities. All available dental radiographs were of acceptable quality, and they were examined in a darkened room using an illuminated viewing box. If several panoramic radiographs were available for the same subject, then the one taken after the age of 8 years was used to avoid the possibility that the tooth germs of the second premolars had not developed yet. Moreover, the absence of the germs for the second premolars was confirmed by longitudinal records. In addition, medical, dental, and social histories, as well as the past dental treatment records, were checked for treatment procedures such as tooth extraction.

In the panoramic radiographs, the following dental anomalies in the maxillary arch were recorded:

- aplasia of primary and permanent lateral incisors;
- aplasia of premolars;
- anomaly in shape: peg or conoid shape associated with reduced size;
- supernumerary teeth; and
- enamel hypoplasia of permanent incisors (lack of enamel areas on the tooth crown surface).

In UCLP subjects the prevalence of dental anomalies was also recorded for the cleft side and for the non-cleft side, separately.

The authors have not considered separately males and females because previous studies[6,10,11] found that there are no statistically significant differences between the two genders with respect to the dental anomalies in the cleft area.

All radiographs and dental casts were examined by two trained operators (MC and TB) and were re-analysed at a 3-month interval. Reproducibility of the diagnosis was complete for all dental anomalies except for small size of upper lateral incisor (94.2%) and enamel hypoplasia (94.8%).

Surgical protocol

The surgical protocol used included ESGAP performed at 18–36 months of age during the stage of hard palate repair, while lip, nose, and soft palate were repaired at 4–6 months of age[12].

Table 1. Details of the analysed sample: cleft type, gender and mean age.

	UCLP		BCLP		
	Cleft right side	Cleft left side			
	Subjects	Subjects	Subjects	Total subjects	Mean age
Females	20	18	26	64	9 Years 11 months
Males	36	37	19	92	10 Years 9 months
Total	56	55	45	156	10 Years 4 months

Statistical analysis

The prevalence rates for the various dental anomalies were calculated in UCLP, BCLP, and total CLP groups, and they were contrasted to those in the NCLP group. The prevalence rates for dental anomalies in this study refer to 'subjects' who presented with dental anomalies. The use of single dental anomalies as statistical units is not recommended[13], since general aetiologic factors may affect the appearance of the dental anomaly in more than one tooth within the same subject. Therefore subjects were used as statistical units in this study.

All comparisons were carried out by means of *z*-test for proportions (SigmaStat 3.1, Systat Software, Inc., Point Richmond, CA, USA). Statistical significance was set at $P < 0.05$.

Results

Tables 2–6 report the prevalence rates of the dental anomalies in the different groups. The statistical results of the comparisons are reported in Table 7. The statistical analysis revealed significant differences for the prevalence rates of all dental anomalies compared with the control group with the exception of the aplasia of the second premolars.

Discussion

Tooth development is a complex process that involves signalling interplay between the embryonic stomodeal epithelium facing the oral cavity and the underlying neural-crest-derived mesenchyme[14]. Both the cleft lip/palate condition and the dental anomalies examined present with a genetic component in their aetiologies[14–16].

This study focused on dental anomalies like hypodontia, supernumerary teeth, anomalies in size (microdontism) and shape (peg or conoid-shape associated with the reduced size) and enamel hypoplasia, in the maxillary arch. These traits tend to occur with high frequency in patients with CLP; previous studies showed that these anomalies were found both inside and outside the cleft area[8,9,12]. Prevalence rates for these tooth anomalies in CLP subjects were compared to a large control sample of unaffected orthodontically untreated subjects ($n = 1000$).

Congenitally missing teeth

Hypodontia is a complex phenotype, with variable penetrance and expressivity affecting various numbers of teeth in different regions[14]. In agreement with previous studies about the prevalence of congenitally missing permanent teeth on the cleft side[6,11,12,17–20], our results confirm that the permanent maxillary lateral incisor is the tooth most frequently missing in the cleft area in UCLP subjects (Table 2): 8.1% for the primary lateral incisors and 27.9% for the permanent lateral incisors. These prevalence rates are

Table 2. Prevalence of subjects with congenitally missing primary and permanent lateral incisors in children affected by UCLP or BCLP.

Congenitally missing lateral incisors	UCLP subjects ($n = 111$)				BCLP subjects ($n = 45$)		Total subjects ($n = 156$)
	Cleft side		Noncleft side				
	No. subjects	UCLP subjects (%)	No. subjects	UCLP subjects (%)	No. subjects	BCLP subjs (%)	
52 and 12	2	1.8	0	–	5	11.1	7
62 and 22	7	6.3	1	0.9	1	2.2	9
52, 62 and 12, 22	0	–	0	–	2	4.4	2
12 or 22	22	19.8	1	0.9	9	20.0	32
12 and 22	0	–	0	–	10	22.2	10
Total congenitally missing primary lateral incisors	9	8.1 Total subjects (%) 5.7	1	0.9 Total subjects (%) 0.6	8	17.0 Total subjects (%) 5.1	18
Total congenitally missing permanent lateral incisors	31	27.9 Total subjects (%) 18.9	2	1.8% Total subjects (%) 1.3	27	60.0 Total subjects (%) 17.3	60

Table 3. Prevalence of subjects with congenitally missing first and/or second premolars in children affected by UCLP or BCLP.

	UCLP subjects (*n* = 111)						BCLP subjects (n = 45)			
	Cleft side			Noncleft side						
Congenitally missing premolars	14 or 24	15 or 25	14 and 15 Or 24 and 25	14 or 24	15 or 25	14 and 15 Or 24 and 25	14 or 24	15 or 25	14 and 15 and 24 and 25	Total subjects (*n* = 156)
	–	5	1	–	–	–		3	1	10
Total congenitally missing first premolars	1		UCLP subjects 0.9% Total subjects 0.6%	–	–	% UCLP subjects– Total subjects–	1		BCLP subjects 4.4% Total subjects 1.3%	2
Total congenitally missing second premolars	6		UCLP subjects 5.4% Total subjects 3.8%	–	–	UCLP subjects – Total subjects –	4		BCLP subjects 8.8% Total subjects 2.6%	10

Table 4. Prevalence of subjects with primary and permanent supernumerary teeth in the region of the upper incisors in children affected by UCLP or BCLP.

	UCLP subjects (*n* = 111)				BCLP subjects (*n* = 45)		
	Cleft side		Noncleft side				
Supernumerary incisors	No. subjects	UCLP subjects (%)	No. subjects	UCLP subjects (%)	No. subjects	BCLP subjects (%)	Total subjects (*n* = 156)
52 or 62	14	12.6	1	0.9	7	15.5%	22
52 and 62	0	–	0	–	5	11.1%	5
52 and 12	3	2.7	0	–	2	4.4%	5
62 and 22	1	0.9	0	–	1	2.2%	2
52,62 and 12,22	0	–	0	–	1	2.2%	1
12 or 22	22	19.8	0	–	6	13.3%	28
11 or 21	2	1.8	0	–	1	2.2%	3
Total primary supernumerary incisors	18	16.2 Total subjects 11.5	1	0.9 Total subjects 0.6%	10	22.2% Total subjects 6.4%	28
Total permanent supernumerary incisors	28	25.2 Total subjects 17.9	0	- Total subjects –	6	13.3 Total subjects 3.8	34

Table 5. Prevalence of subjects with anomalies in size and shape in permanent central and lateral incisors in children affected by UCLP or BCLP.

Anomalies in size (and shape)	UCLP subjects (n = 111)				BCLP subjects (n = 45)				Total subjects (n = 156)
	Cleft side		Noncleft side						
	12 or 22	11 or 21	12 or 22	11 or 21	12 and 22	11 and 21	12 or 22	11 or 21	
Microdontism	30	3	7	–	3	–	7	1	51
Dysmorphism*	5	2	–	2	2	–	1	–	12
Total small size permanent central incisors	5	UCLP subjects (%) 4.5 Total subjects (%) 3.2%	2	UCLP subjects (%) 1.8 Total subjects (%) 1.3	1			BCLP subjects (%) 2.2 Total subjects (%) 0.6	6
Total small size permanent lateral incisors	35	UCLP subjects (%) 31.5 Total subjects (%) 22.4%	7	UCLP subjects (%) 6.3 Total subjects (%) 4.5	13			BCLP subjects (%) 28.8 Total subjects (%) 8.3	48

*Anomaly in shape: peg- or conoid-shape associated with the reduced size.

Table 6. Prevalence of subjects with enamel hypoplasia in permanent central and lateral incisors in children affected by UCLP or BCLP.

	UCLP subjects (n = 111)						BCLP subjects (n = 45)				Total subjects (n = 156)
	Cleft side			Noncleft side							
	52 or 62	12 or 22	11 or 21	52 or 62	12 or 22	11 or 21	12 and 22	11 and 21	12 or 22	11 or 21	
Enamel hypoplasia	–	2	23	–	–	–	–	6	2	8	41
Total permanent central incisors with enamel hypoplasia	23		UCLP subjects (%) 20.7 Total subjects (%) 14.7	–	–	UCLP subjects (%) - Total subjects (%) –	14			BCLP subjects (%) 31.1 Total subjects (%) 8.9	37
Total permanent lateral incisors with enamel hypoplasia	2		UCLP subjects (%) 1.8 Total subjects (%) 1.3	–		UCLP subjects (%) – Total subjects (%) –	2			BCLP subjects (%) 4.4 Total subjects (%) 1.3	4

Table 7. Statistical analysis. All comparisons were carried out by means of *z*-test for proportions.

Dental anomalies (permanent dentition)		Prevalence	Prevalence rate (%)	Control group – Prevalence	Control group – Prevalence rate (%)	*z*	*p*
Aplasia lateral incisors	Total subjects with aplasia lateral incisors/total subjects	60/156	38.5	44/1000	4.4	13.68	**
	UCLP subjects with aplasia lateral incisors/UCLP subjects	33/111	29.7	44/1000	4.4	9.77	**
	BCLP subjects with aplasia lateral incisors/BCLP subjects	27/45	60.0	44/1000	4.4	14.20	**
Aplasia second premolars	Total subjects with aplasia second premolars/total subjects	10/156	6.4	58/1000	5.8	0.12	NS
	UCLP subjects with aplasia second premolars/UCLP subjects	6/111	5.4	58/1000	5.8	–0.04	NS
	BCLP subjects with aplasia second premolars/BCLP subjects	4/45	8.9	58/1000	5.8	0.54	NS
Supernumerary incisors	Total subjects with supernumerary incisors/total subjects	34/156	21.8	39/1000	3.9	8.37	**
	UCLP subjects with supernumerary incisors/UCLP subjects	28/111	25.2	39/1000	3.9	8.74	**
	BCLP subjects with supernumerary incisors/BCLP subjects	6/45	13.3	39/1000	3.9	2.67	*
Anomaly size-shape incisors	Total subjects with anomaly size-shape incisors/total subjects	55/156	35.3	38/1000	3.8	13.28	**
	UCLP subjects with anomaly size-shape incisors/UCLP subjects	42/111	37.8	38/1000	3.8	13.00	**
	BCLP subjects with anomaly size-shape incisors/BCLP subjects	13/45	28.9	38/1000	3.8	7.29	**
Enamel hypoplasia incisors	Total subjects with enamel hypoplasia incisors /total subjects	41/156	26.3	42/1000	4.2	9.77	**
	UCLP subjects with enamel hypoplasia incisors /UCLP subjects	25/111	22.5	42/1000	4.2	7.48	**
	BCLP subjects with enamel hypoplasia incisors/BCLP subjects	16/45	35.6	42/1000	4.2	8.66	**

*$P < 0.01$; **$P < < 0.001$; NS, not significant.

lower than the values ranging from 45.3 to 58.6% reported by others[6,11,12,17–19]. It should be noted that the prevalence rates for congenitally missing primary lateral incisors might have been overestimated in this study because during ESGAP surgery some primary teeth could have been extracted[12].

In BCLP, the prevalence rates for congenitally missing maxillary lateral incisors were much higher than in UCLP: 17% for the primary incisors, and 60% for the permanent incisors. Previous investigations that analysed aplasia of permanent lateral incisors in BLCP subjects reported prevalence rates ranging from 45 to 48.1%[8,9,12]. In 17 cases (10.8% of the total CLP sample) the maxillary lateral incisor was missing in both dentitions, while in 41 cases (26.8% of the total CLP sample) only the maxillary permanent incisor was missing. Statistical analysis revealed significantly greater prevalence rates for missing lateral incisors in both UCLP and BCLP groups when compared with NCLP group (Table 7).

The maxillary second premolar was absent in 5.4% of UCLP subjects (Table 3). This result is similar to the prevalence rate reported by Tortora *et al.*[12] in their UCLP sample (4.9%), while it is lower than previous reports by Ribeiro *et al.*[11] and Rose[21] that described prevalence rates ranging from 11.8 to 20.2%. In this study, the statistical analysis showed no significant differences for second premolar aplasia in the UCLP group compared with the NCLP group (Table 7).

In the BCLP sample, the congenital absence of the maxillary second premolar was found in 8.8% of the cases, with one case showing agenesis of all four second premolars (Table 3). Also for the BCLP group no significant differences for second premolar aplasia were found in comparison with the NCLP group (Table 7).

Hypodontia is, to a great degree, genetically determined and transmitted by autosomal dominant inheritance, with incomplete penetrance and variable expression[15]. Environmental factors, however, may also play a role in the aetiology of this condition[22]. A mutation in the homeobox gene, MSX1, has been suggested as a factor causing a common developmental dental anomaly, namely familial selective agenesis of the second pre-

molars and third molars[15]. Various dental abnormalities, particularly hypodontia, have a much higher prevalence in certain groups. These dental anomalies have been frequently reported in children who also have cleft lip, cleft palate, or both[6,23]. Interestingly, these anomalies were found in proportionately higher frequencies as the severity of the cleft increased[6].

Recently, non-syndromic clefts have been associated with specific allelic variants (SNPs) of the *IRF6* gene[14]. A similar association has also been reported with non-syndromic hypodontia, most preferentially in the premolar region. TGF-alpha seems to contribute significantly to oral clefts[24] as well as to isolated tooth agenesis[14].

The increased prevalence of hypodontia in CLP children might be the result not only of genetic factors directly affecting hypodontia, but especially of the factors causing the cleft itself. This suggests that the same aetiologic factors may be responsible for both the formation of the cleft and the hypodontia in affected children[7], with agenesis of incisors related to the local developmental disturbance. Prevalence rates for aplasia of second premolars are almost identical in CLP subjects and in normal subjects, and this is opposite to the tendency revealed by the incisors in this study. Due to the fact that aplasia of second premolars is a dental anomaly that does not belong spatially to the area of the cleft (more posterior in the dental arch), the lack of significant association within the cleft may suggest that the effect of the cleft disturbance is more local than general on the dentition. This limits the evidence for a strong genetic component in the aetiology of CLP.

Supernumerary teeth

The literature reports the presence of supernumerary teeth as the second most common dental anomaly in the cleft area[1,9,25]. This study confirmed this outcome, as the prevalence rate of supernumerary teeth in the region of the maxillary incisors was 21.8% in the permanent dentition and 17.9% in the primary dentition (Table 4). The frequency of supernumerary permanent teeth in the cleft area in UCLP children in the present investigation (25.2%) is in close agreement with the findings reported by Ranta[25] (20.9%), and it is higher than the prevalence rate reported by Weise and Erdmann[17] (6.7%). In 26 subjects (14 UCLP subjects and 12 BCLP subjects) the supernumerary lateral incisor was present only in the primary dentition. In eight subjects (four UCLP subjects and four BCLP subjects), supernumerary teeth were present in both dentitions. It should be noted that the prevalence rates for supernumerary primary lateral incisors might have been underestimated in this study because during ESGAP surgery some primary teeth could have been extracted[12].

Anomalies in shape and size and enamel hypoplasia of permanent teeth

It is generally accepted that agenesis of teeth is related to an overall reduction in tooth size. Consequently, hypodontia and microdontia tend to occur in the same children[16,26]. In 48 subjects (35 UCLP subjects and 13 BLCP subjects), the permanent lateral incisor presented with some degree of anomaly in size or shape. Six subjects (five UCLP subjects and one BLCP subject) presented a malformed central incisor (Table 5). Our results agree with the findings by Vichi and Franchi[10] for the analysis of enamel hypoplasia. The permanent central incisor is more frequently affected (23 UCLP subjects and 14 BLCP subjects) than the permanent lateral incisors (two UCLP subjects and two BLCP subjects; Table 6). The statistical analysis showed significantly greater prevalence rates for anomalies in size/shape and for enamel hypoplasia of permanent teeth in cleft subjects compared with the control group (Table 7). As already stated by Dixon[4], the extremely high prevalence of enamel hypoplasia in the incisors of both dentitions in CLP patients can be in part related to the surgical repair of the cleft in the lip and/or palate.

Conclusions

This study evaluated the prevalence of dental abnormalities in number, size, and shape of

the primary and permanent maxillary dentitions in a large sample of children affected by UCLP or BCLP compared with a control group of subjects without cleft.

The results showed that over one third of CLP subjects presented with aplasia of the permanent lateral incisors with important consequences in terms of aesthetic, periodontal, and restorative implications. On the contrary, the prevalence for aplasia of second premolars was almost identical in CLP subjects and in normal subjects. The prevalence rates for all other dental anomalies analysed (supernumerary teeth, anomalies in size/-shape, and enamel hypoplasia) were significantly greater in both UCLP and BCLP subjects when compared with the NCLP subjects.

What this paper adds

- The use of a large control group of unaffected children for an adequate statistical comparison of the prevalence of dental anomalies between CLP and control subjects.
- This study provides information about maxillary dental anomalies both in children with UCLP and BCLP, and both in the primary and permanent dentitions.
- This investigation supports the theory that the effect of the cleft disturbance is more local than general on the dentition. This limits the evidence for a strong genetic component in the aetiology of the CLP.

Why this paper is important for paediatric dentists

- In cleft patients, the multidisciplinary approach is needed and the paediatric dentist represents an important member of the interdisciplinary cleft team. New and important information about dental anomalies are essential for a successful interceptive treatment of potentially severe oral rehabilitation problems.

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