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Clinical orodental anomalies of Taiwanese children under age six

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Abstract

The purpose of this investigation was to collect data on several selected congenital oral and paraoral anomalies in Taiwanese children under age six. Twenty-five cities and townships were randomly sampled in different areas of the Republic of China using the stratified method. A total of 1016 Taiwanese children under age six were examined with dental mirror and explorer as part of the national dental survey. The result of this survey indicated an 11% prevalence of geographic tongue. This figure is higher than previous studies done in different countries. The occurrence of fusion in the primary dentition was found to be 2%. Ankyloglossia had a frequency of 1.18% and primary talon cusp was found to be 0.59%. Seven (0.69%) children demonstrated fissured tongue. Thirteen (1.28%) cases of congenital missing teeth were found. These prevalence values were different from those revealed in several countries which may be attributed to differences in ethnic and racial composition of the population studied.

Methods and Materials

Sample Design

Taiwan has 309 cities, villages and townships. According to their socioeconomic development and degree of urbanization, these geographic locations were divided into ten strata: 1. developing area; 2. mountainous area; 3. industrial area; 4. hilly area; 5. remote area; 6. service business area; 7. combination area; 8. Taipei city; 9. Kaohsiung city and five cities administrated directly by Taiwan province

The sample design in this study is based on the principle of stratification, multi-stage and unequal sample probability. The population of interest for this investigation are Taiwanese children under age six, excluding children in the orphanages.

Order of Interviews

We randomly selected the order of interviews for 25 sampled districts. All sample house units were interviewed and a specially designed survey questionnaire was used. If there were children under age 6 in the interviewed house unit, the child would be scheduled for an oral/dental examination.

A total of 1016 young children were examined using mouth mirrors, explorers, disposable tongue depressors and natural and/or artificial light. Specially designed charts were used for record the personal data and oral conditions. Dental radiographs were not taken. Oral examinations were performed by 3 pediatric dentists. Before the survey, the diagnostic criteria and calibration were thoroughly discussed.

The data collected was processed and analyzed by SAS software.

The following criteria for a positive finding was used to diagnose the selected conditions being investigated.

Results

In this study, 3852 families were interviewed. 1750 children in these families were aged 0 to 6 years. A total of 1016 children were available for oral/dental examination: 546 (53.74%) were boys and 470 (46.26%) were girls. The gender ratio of 1.16 boys per girl is within the accepted range. The results of this oral/dental inspection of children are shown in Table 1.

• Congenital missing teeth (hypodontia) appeared to be more common in females than in males (p=0.01).

Table 2 shows the teeth that were presented with fusion, talon cusp, supernumerary and congenital absence.

- Fusion: 7 of the 22 cases occurred between the mandibular right cuspid and lateral incisor. The second most frequent incidence of fusion occurred at the mandibular left central and lateral incisor.
- Talon cusps: 3 out of 6 occurred on the left maxillary central incisors.
- There was only one child that had a supernumerary tooth, who was seen without radiography.
- The most common congenitally absent primary tooth was the left mandibular lateral incisor.
- None of the following anomalies and conditions was found: medium rhomboid glossitis, Fordyce granule, torus palatinus and torus mandibularis.
- There was one child who was reported to have a natal tooth.

Table 3 Comparison of present prevalence values with previously reported figures from literature for the condition listed

Condition	Author	Population/ age group (year)	% with anomaly				
Ankyloglossia	Sawyer	Nigeria/ 0-15	0.2	Fusion	Jorgenson	USA/ 2258 neonates	64.8
	Sedano	Argentina/ 6-15	0.1		This study	Taiwan/ 113 infants	1.7
	This study	Mexico/ 5-15	0.83		Clayton	USA/ 3-5	0.77
Fissured tongue	Kulhar, Willemson	Finland/ 3-8	1.2	Talon cusp	Magnusson	Iceland/ 0-7	0.7
	Sedano	Mexico/ 5-15	15.7		Moller	Iceland/ 2-7	0.5
	This study	Nigeria/ 10-19	0.8		This study	Taiwan/ 0-6	2.07
Geographic tongue	Sawyer	Taiwan/ 0-6	0.69	Hypodontia	Sedano	Mexico/ 5-15	0.06
	Sedano	Argentina/ 6-15	1.71		This study	Taiwan/ 0-6	0.59
	Sawyer	Nigeria/ 10-19	0.3		Clayton	USA/ 3-5	6.01
Clefting	Wei and Chen/1992	Taiwan/ Hospital birth	0.142	Hyperdontia	Magnusson	Iceland/ 0-7	0.5
	Stevenson et al (1966)	Hong Kong/ Hospital birth	0.162		This study	Iceland/ 2-7	0.3
	Emmanuel et al (1972)	Taiwan/ Hospital birth	0.2		This study	Taiwan/ 0-6	1.28
				Peg lateral incisors	Clayton	USA/ 3-5	1.90
					Moller	Iceland/ 2-7	0.8
					This study	Taiwan/ 0-6	0.1
					Clayton	USA/ 3-5	0.33
					This study	Taiwan/ 0-6	0.3

Discussion

- **Geographic tongue:** Prevalence reports for this condition have varied in the literature from 0.27% to 4.25%, depending on the population studied. Redman stated that geographic tongue is more common in females. Our observations found this condition to be equally frequent in both sexes with overall prevalence values at 11%. Prinz and Greenbaum stated that children between the age of 1 to 5 are especially favorable to its appearance. Redman suggested that the peak age for this condition was 2 to 3 years. This may explain a higher prevalence value of this condition in our study since the populations studied were children aged 0 to 6.
- **Fissured tongue:** In the present study, we found 7 children (0.69%) with this condition. Chosack et al and Halperin and coworkers reported a steady rise in the prevalence of fissured tongue increasing with age. Our figure is lower than those previously reported (Table 3), which is possibly attributed to age and ethnic factors. There was one child with a combination of both fissured tongue and geographic tongue observed.
- **Clefting:** Two cases, one boy and one girl, of cleft lip with cleft palate were observed. The two cases among 1016 children represent an incidence level in accordance with previously reported incidence of orofacial clefts.
- **Gingival cyst:** Two infants, one one-month old boy and one 10-month old girl, were identified. Usually, the cysts are transient and degenerate early in infancy. In this survey, there were 113 children under age one. Therefore, gingival cyst represents 2 out of 113 infants (1.8%).
- **Fusion of teeth:** Fusion was seen in nine (1.65%) boys and in twelve (2.55%) girls, giving an average of 2.07% for both sexes combined. The gender difference was statistically insignificant. Our findings show a higher prevalence for fusion than those in previous reports. Ethnic and genetic composition may account for this disparity. This study and previous reports in the literature all indicate that fusion were usually observed in the incisor-canine area of either jaw.
- **Talon cusp:** Talon cusp had been reported in both permanent and primary dentition. This anomaly in the permanent dentition occurred three times more often than primary dentition. Less than 15 cases of primary talon cusp have been reported in the literature. Our present study found 6 children (3 boys and 3 girls) with total of 8 talon cusps.
- **Hypodontia:** The frequency of missing teeth in our study is 1.28%. The present study shows a higher prevalence with greater predilection towards females (p=0.01). Most of the missing teeth involved lateral incisors. Our study confirms that the most frequent missing teeth were mandibular lateral incisors.
- **Supernumerary teeth and peg lateral incisors:** In the present study, both conditions had low prevalence values. However, since dental radiographs of this population were not taken, some unerupted supernumerary teeth may have been undiscovered. Two peg lateral incisors occurred on mandible. The 0.2% prevalence for primary peg lateral incisors is similar to the frequency reported by Clayton (Table 3).

Table 1 Prevalence values of orodental anomalies in children of Taiwan

Anomaly	Male		Female		Total	
	no.	%	no.	%	no.	%
Ankyloglossia	7	1.28	5	1.06	12	1.18
Fissured tongue	5	0.29	2	0.43	7	0.69
Geographic tongue	59	10.81	52	11.06	111	10.93
Fusion/ Geniunition	9	1.65	12	2.55	21	2.07
Talon cusp	3	0.55	3	0.64	6	0.59
Hypodontia	1	0.18	0	0	1	0.10
Hyperdontia	2	0.55	10	2.13	12	1.28
Cleft palate/ lip	1	0.18	1	0.2	2	0.2
Peg lateral incisors	1	0.18	1	0.2	2	0.2
Gingival cyst	1	0.18	1	0.2	2	0.2

Table 2 Distribution of teeth affected by fusion, talon cusp, supernumerary and congenital absence

tooth	Fusion		Talon cusp		Supernumerary		Congenital absence	
	no.	%	no.	%	no.	%	no.	%
61-62	3	51	2	72	1	52	3	
71-72	5	53	1					
72-73	4	61	3					
81-82	3	62	1					
82-83	7	67	2					
Total	22		9		1		20	

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CRANIOFACIAL AND AIRWAY MORPHOLOGY CHANGE AFTER WEARING ORAL APPLIANCE DURING SLEEP FOR SIX MONTHS ON A COHORT OF OBSTRUCTIVE SLEEP APNEA CHILDREN

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**Background:** Myofunctional therapy (MFT) for obstructive sleep apnea (OSA) could improve breathing during sleep, and decrease Apnea-Hypopnea Index (AHI) by about 50% in adults and 62% in children. MFT can improve the tongue muscle, particularly in hypotonic premature infants. But the level of compliance for MFT has often been low in children. The oral device with a tongue bead could be a passive MFT appliance and improve clinical respiratory symptom in the OSA children during sleep. The device is designed on the basis that intrusion of a foreign object close to the tip of the tongue stimulates tongue activity at least during light stages of sleep.

**Aim:** The aim of the present investigation was to evaluate the treatment effect of the passive myofunctional therapy through an oral appliance with a tongue bead and to compare the differences in craniofacial and airway morphology before and after wearing the oral appliance for preterm with full term obstructive sleep apnea children.

**Design:** Twenty-nine children with OSA problem were included and divided into the full-term (n=18) and preterm (n=11) group, and all participants were wearing the oral device during sleep for six months. The lateral cephalometric radiograph was taken to compare lateral craniofacial and airway morphology before (T0) and after (T6m) the oral device treatment.

**Results:** The full-term group (n=18) had significantly decreased AHI in sleep, hypopnea index (HI), and awake % after oral appliance wearing for six months. The preterm group (n=11) had significantly decreased AHI in rapid eye movement period (REM) and mean heart rate after treatment. The total finding had significantly decreased AHI in sleep, AHI in REM, HI, awake % and mean heart rate after treatment. The skeletal and airway morphology had significantly grown in length of the mandible, posterior face height and upper airway in the full-term group, no significant growth in the preterm group.

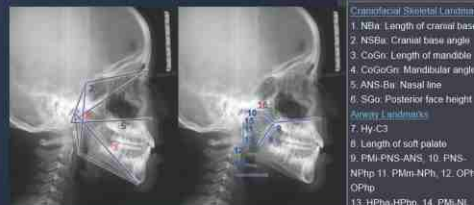
**Conclusions:** The oral device could significantly improve the breath during sleep in both groups with OSA children. But the preterm group did not show significantly craniofacial and airway growth development after the oral device treatment.



Oral device design: mandible advancement device (with tongue bead) for passive myofunctional therapy

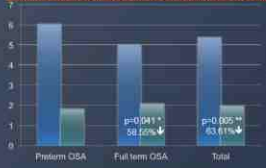


Facial characteristics of preterm children: Hypotonic muscle, long face, narrow arch, and mouth breath



- Craniofacial Skeletal Landmarks**
1. NbB: Length of cranial base
  2. NSSt: Cranial base angle
  3. CoGn: Length of mandible
  4. CoGoGn: Mandibular angle
  5. ANS-Ba: Nasal line
  6. SGo: Posterior face height
- Airway Landmarks**
7. Hy-C3
  8. Length of soft palate
  9. PMS-PNS-ANS
  10. PNS-NPtp
  11. PMS-NPh
  12. OPha-CPtp
  13. HPha-HPtp
  14. PMS-NI
  15. PNS-AD1
  16. PNS-AD2

Apnea-Hypopnea Index (AHI) in sleep

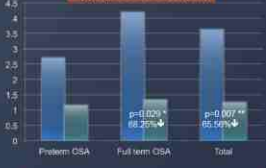


AHI in rapid eye movement (REM)

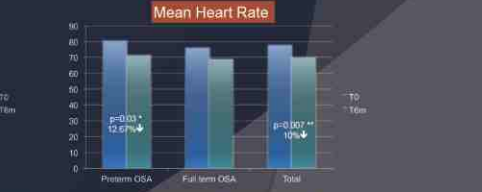
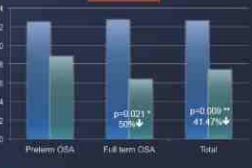


Result summary			
	Preterm	Full-term	Total
Sleep Breathing	BW and BHA	BW and BHA	BW and BHA
	AHI in REM: 43.75%	AHI in sleep: 58.55%	AHI in sleep: 63.61%
	Mean H.R.: 12.67%	HI: 68.25%	AHI in REM: 41.94%
Skeletal	X	Mandible counterclockwise growth	Mandible counterclockwise growth
		Airway width	Airway width
Airway	X	Airway width	Airway width

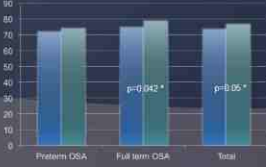
Hypopnea Index (HI)



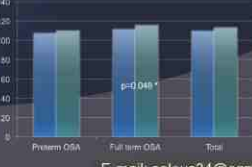
Awake %



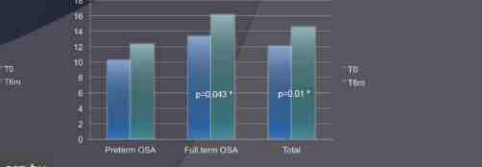
Posterior Facial Height: S-Go (mm)



Sagittal Mandible Growth: Co-Gn (mm)



Airway Width: PNS-AD2 (mm)



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學術專題

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Intraoral scanning and setting up virtual occlusion in 3D planning of orthognathic surgery: a comparison with the conventional dental model approach



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Introduction

Determination of ideal dental occlusion is an important step in the planning of orthognathic surgery (OGS). Conventional 2D planning and dental model approach are time consuming and have some errors, such as image distortion, incorrect facebow transfer and reposition of the lower jaw. In order to overcome the problems inherited with the conventional manual procedures, virtual occlusion used from the 3D system has been reported. As most studies still used the dental model imaging for virtual occlusion, and the experience of intraoral scanning for final virtual occlusion setting and OGS planning was rarely reported. The study was to propose a novel and standard protocol for determination of virtual final occlusion using intraoral scanning and computer-aided technique, as well as to compare the accuracy with the conventional method.

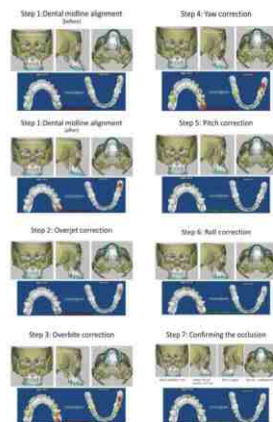
Methods

**Patients:** 30 consecutive patients undergoing two-jaw OGS for treatment of mandibular prognathism and asymmetry were included. There were 18 women and 12 men aged 18 to 30 years (mean 23.5 years).

**Study design:** Three-dimensional (3-D) images were acquired two weeks before surgery using i-CAT CBCT scanner. Dental casts (control group) and intraoral scanning (study group) were simultaneously collected for the design of final dental occlusion. The study procedure was outlined to the right.

**Setting up the digital final occlusion:** The 3D simulation was carried out by Dolphin Imaging® software on the composite skull model for setting up the digital final occlusion. The standard procedures for setting an intraoral-scanning-based virtual occlusion were determined (to the right). The setup of occlusion is based on normal overjet, overbite and arch coordination (occlusal symmetry) which was same as control group. The occlusalgram with color map reflected the contact points, contact depth and bilateral symmetry. (At least 3 contact points is required in occlusion as a tripod showing the green color, preferably one in front teeth, and two in bilateral mid or posterior teeth.)

**Comparison of the manual and virtual occlusions:** The 3D images of dental-model-based digital final occlusion (conventional occlusion) and intraoral-scanning-based virtual occlusion were superimposed to quantify the shell-to-shell difference of occlusal relationship. The precision of the surface superimposition was calculated in terms of the root-mean-square deviation (RMSD) of distance between the superimposed models, with RMSD ≤0.5 mm considered acceptable.



**Assessment of intraobserver and interobserver variability:** The virtual occlusion procedures were performed by two orthodontists and for two times to investigate the intraobserver reproducibility and interobserver reliability of setting up the digital final occlusion by comparing RMSD value.

**Comparison of the fitness of splint fabricated from the conventional occlusion and the virtual occlusion methods:** Evaluation of the printed splint fitness was performed by fitting trials on patients. The inter-occlusal fit of the splint was judged as fitness or not. (below)



Results

- 1) Average root-mean-square difference of the final occlusion images between the two groups was 0.45mm (< 0.5 mm) indicating comparable occlusal relationship. (Table 1 below)
- 2) The intraobserver reproducibility and interobserver reliability for setting up the virtual occlusion were satisfactory with no statistically significant difference. (Table 2 below)
- 3) There was no significant difference in the splint fitness test between the two groups. (Table 3 below)

Table 1. Root-mean-square distance (RMSD) value for comparison of the occlusal relationship between the conventional model approach and virtual method in the mandibular dentition. The maxillary dentition was used for registration of the two image sets.

RMSD	maxillary dentition (mm)	mandibular dentition (mm)
Mean	0.19	0.45
SD	0.04	0.11

Table 2. Statistical results of the intraobserver and interobserver setting up virtual occlusion by comparison of superimposition RMSD value.

Intraobserver (Operator A)	Mean±SD	Minimum	Maximum	Pearson Correlation coefficient (r)
1 <sup>st</sup> operation	0.45±0.09	0.19	0.62	0.987
2 <sup>nd</sup> operation	0.47±0.11	0.18	0.64	
Interobserver	Mean±SD	Minimum	Maximum	Cronbach's alpha
1 <sup>st</sup> operation	0.45±0.09	0.19	0.62	0.736
Operator B	0.48±0.10	0.29	0.64	
2 <sup>nd</sup> operation	0.47±0.11	0.18	0.67	0.726
Operator B	0.49±0.12	0.27	0.65	

Table 3. Comparison of splint fitness between the conventional model occlusion and 3D virtual occlusion fabricated by 3D printing.

	Fitness	Unfitness	p value*
Conventional method	28	2	0.153
Virtual method	30	0	

\*Chi-square test (χ<sup>2</sup>), the difference was considered statistically significant if p< 0.05.

Conclusion

The proposed intraoral scanning and setting-up the digital final occlusion was reliable and accurate. The method can replace the dental model approach for 3D planning of OGS. (References on request)

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Maxillary Anterior Caries of Taiwanese Preschool Children



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BACKGROUNDS

Children with caries of maxillary primary anterior teeth is considered to be associated with early childhood caries. Studies reviewing the etiologies, microbiologic nature, epidemiology, prevention and contributing social and biopsychological factors have been assessed in most Western-type countries<sup>1,2</sup>. However, prevalence of this caries pattern and related background factors have not been explored extensively in some Asian countries.

AIM

1. To determine the prevalence of caries of maxillary primary incisors among 3 to 6 year-old Taiwanese preschoolers
2. To assess the related background information reported by their parents and contrast them to other caries pattern's of the children.

METHODS

**Patients:**  
In this cross-section study, the subjects of this study were 959 preschool children aged 3 to 6 enrolled in four private preschool in northern part of Taiwan. Children's information form and questionnaire were given to parents of all 959 preschoolers. A total of 851 (89%) children returned information forms and questionnaires were included in study.

Measurements

1. Students were randomly assigned to two different pediatric dentists, and dmfs data was recorded according to WHO guidelines.
2. Information and questionnaires were obtained regarding child's demographic information, brushing and flossing behavior, snacking habits, baby bottle usage and fluoride usage and dental visits.

Statistical analysis

1. All data collected were processed by SAS 6.04 computer software.
2. Statistical differences between parental reported informations were assessed by chi-square test.

DISCUSSION

1. This study found that only 4.3% of children with the maxillary anterior pattern did not have a posterior pattern, an indication that once the factors necessary for the initiation of caries process, they are difficult to reverse<sup>3</sup>.
2. 32% of children with upper anterior caries in present study were reported not have taken a bottle to bed after age one. Perhaps the carious lesions might have initiated before and deteriorated.
3. The children with maxillary anterior caries were more likely to have seen the dentists before and had irregular dental visits indicated that these group of children in this study did not have regular dental visit, they only seek dental help when problems occur.
4. The mean dmfs in those children with both patterns is 7 times and 3 times greater than those with posterior pattern only and anterior pattern only. This indicates that for children with both patterns, they might need more intensive care in order to prevent the current situation from further deterioration.

Reference

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RESULTS

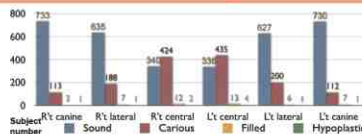
A total of 851 children were enrolled in the study. The response rate was 89% of all children

Comparison of carious pattern and dmfs

Carious pattern	N(% of subjects affected)	dmfs
Anterior caries only	37(4.3%)	3.32
Posterior caries only	208(24.4%)	7.22
Both anterior and posterior caries	472(55.4%)	21.80
Caries free	131(15.4%)	

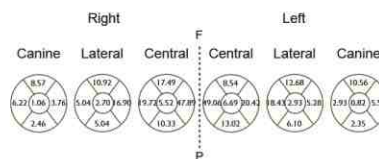
1. Only 15% of the children were caries free.
2. Maxillary anterior caries were found in 60% of children, in which 4.3% of children had maxillary anterior caries only and 55.4% of children had both anterior and posterior caries.
3. The mean dmfs of children with both anterior and posterior caries was seven

Incidence of caries of maxillary anterior teeth



1. Caries of contra-lateral sides were nearly identical
2. Maxillary central incisors were carious in more than 50% of the children.

Percentage of affected surfaces in children with maxillary anterior teeth



1. The mesial surfaces of the central incisors appeared to be the most vulnerable sites for caries
2. The facial surfaces, especially lateral incisors, were affected more than the lingual surfaces
3. The facial surfaces of canine seemed to be affected as much as lateral or central incisors. Most of them were found around the gingival third of the facial surface

Percentage of affected surfaces in children with maxillary anterior teeth

Questionnaire	Patterns with maxillary anterior caries N (%)	All other patterns N (%)	P value
Nursing bottle habits	341(67%)	214(64%)	N.S
Frequent snacking habits	367(73%)	212(63%)	<0.05
Had seen dentist before	345(69%)	174(52%)	0.000
Never had dental visit	160(32%)	169(51%)	<0.05
Dental visit every 6 month	51(10%)	40(12%)	<0.05
Irregular dental visit	283(58%)	120(37%)	<0.05
Mother had dental prosthesis	238(100%)	128(99%)	<0.05

1. No significant differences were found with regard to nursing bottle habits and maxillary caries.
2. Children with frequent snacking habits, irregular dental visit habits, whose mother having dental prosthesis tend to have maxillary anterior caries than other caries.

CONCLUSION

1. Maxillary anterior caries of Taiwanese preschool children were found in 60% of children with mesial surface of maxillary central incisors being the most vulnerable surface.
2. Nursing bottle habits after age of one may be a necessary but not a sufficient factor for maxillary anterior caries to occur.
3. Children with frequent snacking habits, irregular dental visits, whose mother had dental prosthesis tends to be more prone to maxillary anterior caries.
4. For children with both patterns of caries, more intensive care should be provided.

## 壁報論文比賽 佳作作品欣賞

口腔鱗狀乳頭狀瘤: 病例報告  
Squamous Papilloma: Case Report吳維玲<sup>1</sup>、黃廷芳<sup>2</sup>、詹惠真<sup>1,2</sup><sup>1</sup>葡萄藤兒童牙科診所<sup>2</sup>衛生福利部豐原醫院

## 前言

口腔鱗狀乳頭狀瘤(oral squamous papilloma)是常見的口腔良性疾病，致病原因大多認為與人類乳突病毒(Human papillomavirus 簡稱HPV) subtypes 6, 11有關<sup>1,5,6</sup>。然現今尚無法確定皆因HPV引起。常發生於30至50歲的族群，10歲以下亦可見。此病約佔兒童口腔病變8%<sup>7</sup>。本篇病例報告是討論一名九歲女童發生口腔鱗狀乳頭狀瘤後經由手術切除治療之後的癒後與追蹤報告。

## 病例報告

患者為一位年近9歲的女童，無其他外傷史或系統性疾病。媽媽主訴孩子兩三歲時便發現其上顎處出現一塊無痛的突出物，但當時不以為意，近年來稍微變大於是求診。經口內檢查發現其硬顎中央有一個柔軟向外生長無柄的病灶，直徑接近1公分表面粉紅色呈現顆粒狀。X照射無發現其他異常。隨後安排於門診將病灶切除，經病理科檢驗診斷為口腔鱗狀乳頭狀瘤，同時作p16免疫組織化學染色(Immunohistochemistry)，檢測結果是為陰性。術後持續追蹤中目前並未發現復發。



## 討論

口腔鱗狀乳頭狀瘤之病因與HPV關係相當密切，有些甚至與造成皮膚疣的病毒一致。然而目前尚無法確定所有口腔鱗狀乳頭狀瘤皆因HPV造成<sup>1</sup>。

HPV顧名思義是能夠在人類身上引起乳突的病毒，已發現約一百多種。HPV的構造十分簡單，只有一個圓形外殼和內部一條雙股DNA，一旦感染成功，進入人體細胞，HPV馬上把DNA直接捲入人體細胞的DNA裡。因為HPV只能存活於人類細胞，所以是人傳人的疾病沒有中間宿主，主要藉由接觸感染，包括直接接觸如性行為等親密接觸；或間接接觸如先後共用同一物品，通常間接接觸的傳播力遠遠低於直接接觸<sup>8</sup>。

HPV在人體內，原則上只能感染最外部的扁平細胞(Squamous cell)，包括皮膚和粘膜，不會穿透皮下組織，因此與血液循環接觸的機會很低不容易刺激免疫系統反應。HPV更不可能進入血管，到處傳播。與大多數病毒感染不同，HPV不會殺害宿主細胞，而是造成細胞不顧一切地拼命分裂和增長，使得本來平坦的皮膚，隆起成一團一團的小贅肉，中文稱為疣。

對於兒童感染HPV的傳染途徑目前所知有限，目前只有盛行情況的調查資料<sup>9</sup>。新生兒傳染HPV主要經由母親，以後才有經唾液或其他接觸的水平傳染。母乳中從未發現有高危險群乳突病毒，表示不會經由哺乳時奶汁傳染。據美國大型調查研究，以1235名兒童(2週至20歲大)接受口腔抹片檢查，並作問卷調查<sup>8</sup>，發現兒童口腔咽喉HPV感染盛行率平均為1.9%，傳染盛行呈現高雙峰形態，其一高峰是小於1歲者盛行率2.5%，很可能與垂直傳染有關；另一高峰是16-20歲為3.3%。

在顯微鏡下可見到最外層是增生的鱗狀上皮細胞，圍繞著內部的結締組織，形成許多指狀的突出。

p16是一種腫瘤抑制蛋白，利用免疫組織化學染色法來檢測p16的強弱可以作為HPV感染的替代指標；這樣的檢測對於口腔癌患者也是不可或缺。本病例的p16染色呈現陰性，顯示出HPV的存在的可能性低。

## 在鑑別診斷方面

口腔鱗狀乳頭狀瘤要與以下疾病區分<sup>1</sup>

1. 疣狀黃瘤(verruciform xanthoma) 好發於牙齦及齒槽骨脊(alveolar ridge)。
2. 乳頭狀增生(papillary hyperplasia) 通常有刺激物的存在，如不適合的活動假牙。
3. 尖狀濕疣(condyloma acuminatum 俗稱菜花) 病灶往往較大生長迅速，病灶底部較廣，因角質化程度較低故呈現粉紅至紅色外觀。

## 在治療與預後方面

口腔鱗狀乳頭狀瘤的治療以切除方式為首選，一般的外科切除或以雷射均適合。預後佳，少有復發現象。

## 結語

口腔鱗狀乳頭狀瘤不算罕見，切除之後通常少有復發，然而對兒童來說早期診斷頗為重要。HPV對口腔的傳染途徑雖尚無法十分確定，但似乎與接觸傳染非常相關，將有待後續更進一步的研究。

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The impact of systemic phosphate-regulation gene Fibroblast Growth Factor 23 (*Fgf23*) ablation on dentoalveolar complex

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Introduction

Fibroblast growth factor-23 (FGF23) is a hormone that modulates circulating phosphate (P<sub>i</sub>) levels by controlling P<sub>i</sub> reabsorption from the kidneys. When FGF23 levels are deficient, as in tumoral calcinosis patients, hyperphosphatemia ensues. On the other hand, excessive FGF23 associated low P<sub>i</sub> level patients exhibit osteomalacia, expanded alveolar bone, increased predentin/dentin ratio, interglobular dentin, and enlarged pulp chambers<sup>1,2</sup>.

FGF23 production has been localized predominantly to osteocytes, with lower levels noted in osteoblasts and cementoblasts<sup>3</sup>. FGF23 is also referred to as a phosphatonin because it decreases circulating P<sub>i</sub> joining ranks with classical hormonal Pi and calcium regulators 1,25-dihydroxyvitamin D<sub>3</sub> (1,25(OH)<sub>2</sub>D<sub>3</sub>) and parathyroid hormone (PTH). FGF23 reduces Pi by decreasing renal reabsorption via sodium Pi transporters Npt2a and Npt2c, as well as inhibition of 25-hydroxyvitamin D-1- $\alpha$ -hydroxylase<sup>4</sup>. 25-hydroxyvitamin D-1- $\alpha$ -hydroxylase is necessary for 1,25(OH)<sub>2</sub>D<sub>3</sub> activation, which, when suppressed, indirectly promotes Npt2a expression as FGF23 levels are lowered and PTH levels are increased<sup>5</sup>.

Research directed at elucidating the effects of systemic P<sub>i</sub> dysregulation on mineralized tissues have been greatly aided by the use of homologous murine models associated with hypophosphatemia, (i.e.) ARHR (Dmp1-null mice), XLH (Hyp mouse), and hyperphosphatemia, that is, TC (*Fgf23*<sup>-/-</sup>, *Klotho*<sup>-/-</sup>, and *GALNT3* mutant mice<sup>6</sup>). Mutations in dentin matrix protein-1 (DMP1) and phosphate-regulating gene with homologs to endopeptidases on the X-chromosome (PheX), factors which may indirectly influence systemic P<sub>i</sub> levels, cause ARHR and XLH in humans. Corresponding to human case reports, studies of hypophosphatemic Dmp1<sup>-/-</sup> and Hyp (PheX mutant) mice have identified dental defects primarily in the dentin, with minor changes in the cementum. To investigate the effects of FGF23-mediated systemic P<sub>i</sub> regulation on the dentoalveolar complex, histology, tooth phenotype as well as immunohistochemistry methods were used in this study.

Materials and Methods

*Fgf23*<sup>-/-</sup> mouse were generated using *Fgf23* heterozygote breeding pairs. Animals were genotyped by PCR amplified DNA extracted from tail snips using a RedExtract-N-Amp For Tissue kit (Sigma). The following PCR primers were used: *Fgf23* (5' AGT GGA CGC TGG AGA ATG GCT ATG 3' and 5' CTG GGA AAG GGG CGA CAC C 3', specific to Exon 3 of the wild-type); Neo (5' AAG GTG AGA TGA CAG GAG ATC 3' and 5' GAT CGG CCA TTG AAC AAG ATG 3', specific to neomycin of the mutant allele construct. The wild-type *Fgf23* product was 397 bp, whereas the mutant product was 310 bp.

Results

Alveolar bone, pulp, and PDL are dramatically altered in *Fgf23*<sup>-/-</sup> molar teeth.

Figure 1. Mandibular molars of *Fgf23*<sup>-/-</sup> mice exhibit disruption of odontoblast layer and ectopic matrix deposition in pulp chambers.

A: Low magnification of WT buccolingual section.  
 A': *Fgf23*<sup>-/-</sup>. Increase in volume of alveolar bone region vs. WT.  
 A'': *Hyp* section.  
 B: Buccal aspect of WT mandibular molar at 33dpc.  
 B': *Fgf23*<sup>-/-</sup> mice exhibited increased volume in alveolar bone region. No clear differences were noted in the odontoblasts, predentin, dentin, cementum and PDL vs. WT.  
 C: Lingual aspect of mandibular molar of WT.  
 C': Compared to WT, odontoblast layer in *Fgf23*<sup>-/-</sup> mouse lost its polarized nature (arrows). PDL width is reduced and fibers are slightly disorganized.  
 D: Coronal region.  
 D': Compared to WT, loss of polarization in the *Fgf23*<sup>-/-</sup> odontoblast layer is noted. Arrows indicate areas of ectopic matrix in pulp chamber.  
 H&E stain, 33, 45, and 61 dpc mouse teeth. P = pulp, oD = odontoblasts, D = dentin, C = cementum, PDL = periodontal ligament, B = bone.

Figure 2. SEM and TEM analysis. Mineralization defects were noted in *Fgf23*<sup>-/-</sup> mouse teeth.

A: Cross section of WT, *Fgf23*<sup>-/-</sup> and *Hyp* samples.  
 B: Higher magnifications. Note inconsistent mineralization and abnormal osteocyte (arrow) in the *Fgf23*<sup>-/-</sup> bone.  
 C: Root surface. Note lack of a clear demarcation between dentin and cementum in the *Fgf23*<sup>-/-</sup> and *Hyp* mice.  
 D: TEM analysis of root surface. Note lack of fibrillar structure in the *Fgf23*<sup>-/-</sup> mice and a lack of a clear demarcation between dentin and cementum in the *Fgf23*<sup>-/-</sup> and *Hyp* mice.

SEM: Scanning electron microscopy.  
 TEM: Transmission electron microscopy.

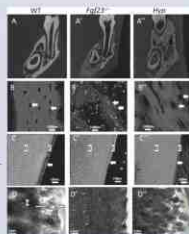


Figure 3. Mandibular incisors of mice exhibit dentin and enamel abnormalities (Cross section).

A, A': Inset shows cross-sections of the entire mandible.

Note large cyst-like structure in the *Fgf23*<sup>-/-</sup> section.

Cells embedded in the dentin of *Fgf23*<sup>-/-</sup> mouse incisors (white arrows). Absence of enamel matrix (stain pink in the WT) in the mouse suggests dysfunctional amelogenesis.

B, B': SEM analysis. *Fgf23*<sup>-/-</sup> incisor dentin was hypomineralized on the labial aspect and multiple embedded cells could be seen. Enamel rod structure is lacking (arrow).

C, C': Note almost complete obliteration of pulp chamber in the *Fgf23*<sup>-/-</sup> mouse incisor.

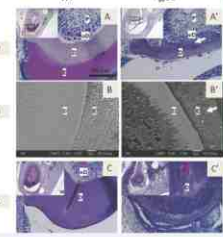


Figure 4. *Fgf23*<sup>-/-</sup> mice exhibit increased apoptotic cells in the mandible compared to WT.

A, A': TUNEL (dark brown stain).

B, B': Caspase 3 (red stain) to detect apoptotic cells.

Both stains indicated increased incidence of apoptosis in osteocytes and osteoblasts (arrows).

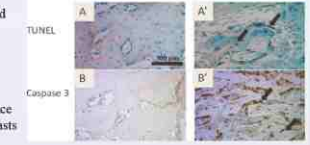


Figure 5. *Fgf23* ablation cause altered expression of extracellular matrix genes and proteins in the oral mineralized tissues.

Immunohistochemical images from the buccal of mandibular first molar.

A, A': BSP was seemingly absent in *Fgf23*<sup>-/-</sup> alveolar bone directly adjacent to PDL, but strongly localized in the region associated with open osteocyte lacunae (arrowhead), and stained weakly in cementum (arrow).

B, B': DMP1 staining was absent in cementum of WT tissues, whereas DMP1 was absent in mantle dentin, cementum (arrow), and in bone in *Fgf23*<sup>-/-</sup> mouse tissues.

C, C': DSP was detected in dentin tubules and mantle dentin of WT specimens. DSP staining in *Fgf23*<sup>-/-</sup> dentin tubules was diffuse, but intensely localized to mantle dentin (5C', arrow).

BSP: bone sialoprotein; DMP1: dentin matrix protein-1; DSP: dentin sialoprotein.

Conclusions

*Fgf23* ablation dramatically altered morphology and matrix composition of dentin, bone, and cementum. This study highlights the complexity of positive and negative feedback interactions of the homeostatic factor P<sub>i</sub> in the influence of FGF23, in addition to well-known calcium levels and PTH effects.

The significant similarities between the *Fgf23*<sup>-/-</sup> in mice and humans in terms of bone pathology, coupled with the added knowledge from this study may lead to more accurate diagnosis of phosphate metabolism disorders. Understanding the roles for FGF23 in control of the dentoalveolar complex may lead to new approaches for developing more effective treatment for disorders in phosphate metabolism than those used at present.

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