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Prader Willi Syndrome: Saliva quantification and culture in 10 patients

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Abstract

Prader Willi Syndrome (PWS) is a relatively rare neurogenetic illness. It is of interest to dentists for its clinical characteristics. The aim of this study was to evaluate the amount of saliva and the presence of *Streptococcus mutans* (*S mutans*) in patients with this syndrome. We measured saliva stimulated by chewing paraffin tablets for 5 minutes, and cultured saliva samples in order to determine the colony-forming units (CFUs) of *S mutans*. The study was conducted in a group of 10 children with PWS at the Hospital Sant Joan de Déu, Barcelona. Results showed that patients with PWS had lower saliva secretion than considered normal for a standard population and most cultures presented a high number of colony-forming units. We conclude that these patients are likely to present caries, and stress the need to place special emphasis on prevention.

Key words: *Prader Willi, culture, saliva, Streptococcus mutans.*

Introduction

Prader Willi Syndrome (PWS) is a complex, multi-systemic neurogenetic illness reported for the first time in 1956 by Prader, Labhart and Willi (1). Its incidence is estimated to be 1:10 000 to 15 000 in live newborns. It is caused by the deletion of chromosome 15 in loci 11 and 13 and is transmitted by the father (2,3).

The main clinical characteristics are neonatal hypotonia and feeding difficulties due to poor sucking reflex, and later, during childhood, hyperphagia and obesity, low stature, hypogonadism, and learning and behavioural problems (4). The consensus diagnostic criteria described by Holm in 1993 are widely accepted today (5) (table 1). Recently, the American Pediatric Association proposed that the age factor should be taken into account for the application of these criteria, in order to speed up genetic diagnosis (6). The syndrome is of interest to dentists because of its oral clinical features. The hypotonia reduces the mouth's normal cleaning mechanisms, hindering sucking, swallowing and chewing, and making a soft diet mandatory. The abnormal appetite increases carbohydrate intake, which, together with the alteration in the quality and quantity of saliva, raises the risk of caries. The mental retardation adds to the difficulty of achieving optimal oral hygiene (7,8).

This study aimed to quantify the amount of saliva produced by pediatric patients with PWS and to culture the colonies of *S mutans* found in the oral cavity.

Material and Method

This cross-sectional, observational, descriptive and comparative study of pediatric PWS patients seen at the endocrinology service of the Hospital Sant Joan de Déu was carried out between 2004 and 2006. Saliva volume and

Table 1. Diagnostic criteria for Prader-Willi syndrome.

Major criteria	• Neonatal and infantile central hyptonia gradually improving with age
	• Feeding problems in infancy with need for special feeding techniques and poor weight gain/failure to thrive
	• Rapid weight gain between 1 and 6 years of age causing central obesity
	• Hyperphagia
	• Facial features: narrow bifrontal diameter, almond-shaped eyes, down-turned corners of the mouth
	• Hypogonadism
Minor criteria	• Decreased fetal movement and infantile lethargy improving with age
	• Characteristic behavior problems, temper tantrums, obsessive/compulsive behavior; rigid, manipulative, steal and lie
	• Sleep disturbance or sleep apnea
	• Short stature for genetic background
	• Hypopigmentation
	• Small hands with straight ulnar border
	• Esotropia, myopia
	• Thick, viscous saliva
Supportive findings	• High pain threshold
	• Decreased vomiting
	• Scoliosis and or kyphosis
	• Early adrenarche
	• Osteoporosis
	• Unusual skill with jigsaw puzzles
	• Normal neuromuscular studies
Scoring: major criteria are weighted at 1 point each. Minor criteria are weighted at 0,5 point. Requirements for diagnosic are	• Children 3 years of age or younger: 5 points (minimum 4 major criteria)
	• Children older than 3 years of age: 8 points (minimum 5 major criteria)

the number of CFUs of S *mutans* were evaluated.

The study group comprised 10 patients with PWS, out of the 23 seen at the endocrinology service between 1994 and 2004: seven girls and three boys aged between 4 and 13 (mean age: 8.6). The 13 other patients were not included in the study group because they could not be located or because they were now over 18 years of age. All had been genetically diagnosed. The endocrinology service provided a list of the patients with the syndrome, whom we then contacted by telephone. The nature and objectives of the study were explained to the parents or tutors. Patients were instructed not to eat, smoke, brush their teeth, or use antimicrobial mouthwash in the two hours prior to collecting the samples; fluoride varnishes were not allowed in the two weeks prior to the test, nor antibiotic treatment in the previous month. Written, informed consent was obtained from the parents or tutors prior to the start of the procedure and the study was approved by the hospital's ethics committee. We decided to study stimulated saliva because the amount obtained without stimulation would have been insufficient to perform and quantify the culture.

Subjects chewed a paraffin tablet for five minutes in order to stimulate saliva, which they then spat out into a receptacle. After five minutes the saliva volume was measured using 1 to 5 ml syringes. To quantify the CFUs of *S mutans* we used the Dentocult® SM Strip Mutans test (Orion Diagnostica Oy, Espoo, Finland) (9) (fig. 1), which comprises a set of plastic strips on which the sa-

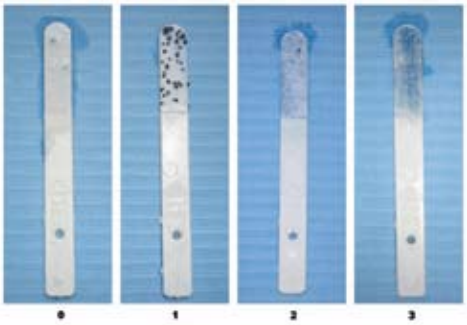

Fig. 1. Dentocult® SM Strip Mutans test.

liva sample is collected, and a liquid culture medium in which a growth inhibitor for other bacteria is deposited. Following the manufacturer's instructions, after the first minute of chewing, the sample for the *S mutans* culture was collected by passing the plastic strips over the surface of the patient's tongue. The sample was then submerged in the culture tube and incubated at 36ºC for 48 hours at the microbiology service of the Hospital Sant Joan de Déu. After this time, the samples were classified in 4 groups according to the table provided by the Dentocult® SM Strip Mutans system: 0 below 10 000 CFU, 1 below 100 000 CFU, 2 between 100 000 and 1000 000 CFU and 3 above 1000 000 CFU.

Results

Of the ten patients included, three were unable to collaborate in the evaluation of saliva volume due to their mental retardation. The results for the amount of stimulated saliva were in the range of 0.1 to 5 ml five minutes after collection, the mean value being 1.53 ml/5min.

Bacterial cultures could be performed in 10 patients: six presented CFU value 3, two CFU value 2, and two CFU value 1.

Discussion

The main clinical features of patients with PWS have been reported to be neonatal hypotonia and feeding problems due to the inability to suck well, and later, during childhood, hyperphagia and obesity, low stature, low saliva volume, hypogonadism, and learning and behavioural problems (1,3-5).

Due to the medical complexity of patients with this syndrome, we stress the importance of the participation of a multidisciplinary team to provide integral treatment (3, 11).

As in the study by Bailleul-Forestier I et al. (9), our sample of patients with the syndrome was small, since the incidence of the disease is low. In addition, the inability of some patients to collaborate fully limited the collection of samples for analysis.

Various studies have confirmed lack of saliva as a characteristic diagnostic trait of this syndrome (5,7,8,10,11). Although the methods we used to collect saliva differed from those used by Bailleul-Forestier I et al. (9), we also found that the production of saliva in patients with PWS was low. According to Sreebny (11) the normal value for stimulated saliva is 1.2 ml/min. In our study, which lasted 5 minutes, the normal score would thus be 6 ml, but the mean value in our PWS group was 1.53 ml/5min, considerably lower than normal. The limitation of this comparison is that Sreebny's study was not performed in a pediatric population. Bearing in mind the importance of saliva in the maintenance of oral and dental health, the low saliva volume recorded in these patients represents a risk factor for the development of caries.

Sixty per cent of the group studied had a CFU value > 1 000 000. This finding suggests that children with PWS have a high risk of caries, according to the ADA classification and the instructions of the manufacturers of the Dentocult® method (Orion Diagnostica Oy, Espoo, Finland), which considers CFU scores of 100 000 and above as high risk.

Conclusions

Our results stress the importance of establishing a series of preventive measures such as a first oral examination when the first temporary teeth erupt, oral hygiene supervised by parents or tutors, use of topical fluoride, periodic checkups, and dental treatment as necessary, always bearing mind the patient's capacity to collaborate.

It is also important to evaluate other factors to classify the risk of caries in this group of patients, such as the bacterial plaque index, caries index, and diet. These recommendations open up new areas for further study.

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