Acta Odontologica Scandinavica, 2011; 69: 310–315

informa
healthcare

ORIGINAL ARTICLE

Orofacial dysfunction in individuals with Prader-Willi syndrome assessed with NOT-S

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Abstract

Objective. The objective of the study was to evaluate orofacial dysfunction in individuals with Prader-Willi syndrome (PWS) and compare it with a healthy reference group. ***Methods and materials.*** The Nordic Orofacial Test-Screening (NOT-S) protocol was used for evaluation of orofacial function in 45 (23 Male, 22 Female) individuals with PWS, aged 19.8 ± 9.5 years, and a reference group of 40 (18 M, 22 F) healthy individuals, aged 24.0 ± 16.3 years. ***Results.*** The NOT-S score was markedly higher for the individuals with PWS than for the healthy reference group (3.9 ± 2.1 vs 0.3 ± 0.5, $p < 0.001$). The most common domains of dysfunction in individuals with PWS were Oral motor function (60.0%), Habits (55.6%), Face at rest (53.3%), Speech (44.4%), Drooling (44.4%) and Breathing (42.2%). ***Conclusions.*** Eighty-seven per cent of the participants with PWS demonstrated dysfunction in two or more domains, particularly in the domains *Oral motor function, Habits* and *Face at rest.*

Key Words: *NOT-S, oral dysfunction, Prader-Willi syndrome*

Introduction

Prader-Willi syndrome (PWS) is a complex medical condition affecting multiple organ systems. The prevalence of the genetic disorder has been estimated to be 1/8000–1/52,000 [1–6]. Symptoms associated with PWS are muscular hypotonia and feeding problems in infancy followed by obesity and hyperphagia from preschool age, developmental delay and mental retardation [5]. Orofacial complications present in PWS are: characteristic facial features with a small mouth in infancy, imprecise articulation of speech [7], dental abnormalities and thick viscous saliva with decreased salivary flow rate [8–10]. Decreased salivary secretion rate and increased viscosity of saliva impairs the ability to chew and swallow and alters the perception of taste. It may also influence clarity of speech and quality-of-life [11–13].

Previous studies have dealt with specific areas of orofacial function in individuals with PWS, but a comprehensive evaluation, including areas such as eating and drinking, oral habits, drooling, respiration and speech, has not previously been presented. The Nordic Orofacial Test-Screening (NOT-S) score has recently been developed for orofacial assessments in research and clinical use [14].

The aim of the study was to assess orofacial function in a group of individuals with PWS and compare it to a healthy reference group, using the NOT-S protocol [14]. The hypothesis was that individuals with PWS present a higher total NOT-S score than a reference group of healthy individuals.

Materials and methods

The participants in the present study were recruited by the Norwegian Prader-Willi syndrome Association. The minimal age of the participants was set to 5 years. Fifty-three (26 Male, 27 Female) of the invited people, who were clinically diagnosed with PWS, initially agreed to participate in the study. Due

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(Received 14 September 2010; accepted 6 February 2011)

ISSN 0001-6357 print/ISSN 1502-3850 online
DOI: 10.3109/00016357.2011.568961

to long travelling distance to the clinic, two (2 F) of these withdrew before the study began. A further four (2 M, 2 F) persons were excluded from the study due to lack of cooperation and another two (1 M, 1 F) were excluded as the diagnosis of PWS could not be verified by a genetic test (MLPA). Forty-five individuals with a confirmed genetic diagnosis of PWS were included in the study. The reference group incorporated an available sample of healthy individuals from a previous study [14], after exclusion of individuals below the age of 5 and above the age of 49 years. Characteristics of the 45 individuals with PWS in the study group and the 40 healthy individuals in the reference group are presented in Table I.

After calibration with an experienced speech- and language therapist, one experienced pediatric dentist (RS) performed the assessment of the orofacial function of the individuals with PWS, using the NOT-S protocol [14]. The protocol consisted of an interview with six domains and a clinical examination, covering a further six domains (Table II). The maximum possible NOT-S score was 12, resulting from a score of 1 in each separate domain [14]. A NOT-S score of 0 indicated no oral dysfunction. If the examined person had difficulties understanding or answering the question(s) in the NOT-S interview, support and information was provided from the accompanying parent and/or guardian. Information gained in this manner was indicated in the protocol. Ethical approval was obtained from the ethical committee at Oslo University Hospital. The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration. Informed consent was obtained from each participant and/or parent/guardian prior to the study.

Table I. Characteristics of the individuals in the study group (n = 45) diagnosed with Prader-Willi syndrome (PWS) and the healthy non-medicating reference sample (n = 40).

	PWS group		Reference sample
Gender (M/F)	23/22		18/22
Age			
Mean ± SD (years)	19.8 ± 9.5		24.0 ± 16.3
Range (years)	5.6–40.9		5.0–49.0
Median (years)	19.5		19.5
	n	%	
Supplementary disease	6	13.3	
Diabetes	2	4.4	
Epilepsy	3	6.7	
Heart disease	1	2.2	
Medication	20	44.4	
Psychopharmaca	10	22.2	
Corticosteroids	4	8.8	
Antihistamines	5	11.1	
Anti-epileptics	3	6.7	
Growth hormone	39	86.7	
Other medication	8	17.8	
Body Mass Index (BMI)			
Underweight (< 20)	0	0.0	
Normal weight (20–24.9)	14	31.1	
Overweight (25–29.9)	17	37.8	
Obese (≥ 30)	14	31.1	
Tonsillectomy (before study)	18	40.0	

Statistical analyses

The Chi-square test was used to compare the PWS-group with the reference sample of categorical data (individual domains from the NOT-S protocol). The Mann-Whitney U-test was used for the analysis of differences between the samples (PWS-group vs reference sample) with respect to non-parametric data (mean total NOT-S score). The Statistical Package for the Social Sciences (SPSS©; v. 17.0, SPSS Inc., Chicago, IL) was used for the statistical analyses. The level of statistical significance was set to < 0.05.

Results

The NOT-S screening was performed between November 2006 and October 2008. The total NOT-S scores for the two groups are presented in Table II. The mean total NOT-S score was markedly higher ($p < 0.001$) for the individuals with PWS (3.9 ± 2.1) than for the healthy reference group (0.3 ± 0.5). The difference was significant in all four of the evaluated age groups (Table III).

The range of the mean total NOT-S scores varied in the different age groups (Table III) from 3.2–4.5 in the PWS group and from 0.1–0.4 in the reference group. There was no significant difference regarding mean NOT-S score between the genders in either the PWS group (M: 4.2 ± 2.0; F: 3.5 ± 2.3) or the reference sample (M: 0.3 ± 0.6; F: 0.3 ± 0.5). Two of the PWS individuals—both adults—presented with no orofacial dysfunction. Four of the individuals with PWS demonstrated dysfunction in only one of the NOT-S domains. Three of these four single positive registrations were found in the breathing domain. The remaining 87% of subjects with PWS demonstrated dysfunction in two or more NOT-S domains. As many as 13 (29%) of the 45 individuals with PWS had a total NOT-S score higher than 5, indicating extensive orofacial dysfunction.

The scores by NOT-S domain are presented in Table II. The domains of dysfunction most frequently found in individuals with PWS were Oral motor function (60.0%), Habits (55.6%), Face at rest (53.3%), Speech (44.4%), Drooling (44.4%)

Table II. Score for each domain of the NOT-S protocol among the individuals with Prader-Willi syndrome (PWS) ($n = 45$) and the reference sample ($n = 40$).

		PWS ($n = 45$)		Reference sample ($n = 40$)		Difference between the groups
Domain		*n*	%	*n*	%	*p*-value*
NOT-S interview						
I	Sensory function	7	15.6	0	0.0	<0.001
II	Breathing	19	42.2	2	5.0	<0.001
III	Habits	25	55.6	4	10.0	0.003
IV	Chewing & swallowing	14	31.1	2	5.0	<0.001
V	Drooling	20	44.4	0	0.0	<0.001
VI	Dryness of the mouth	1	2.2	0	0.0	<0.001
NOT-S examination						
1	The face at rest	24	53.3	3	7.5	0.001
2	Nose breathing	4	8.9	0	0.0	<0.001
3	Facial expression	11	24.4	0	0.0	<0.001
4	Masticatory muscle & jaw function	3	6.7	0	0.0	<0.001
5	Oral motor function	27	60.0	0	0.0	0.001
6	Speech	20	44.4	1	2.5	<0.001

*Chi^2 test.

and Breathing (42.2%). The difference between the PWS group and the healthy reference group was significant for all 12 domains (Table II).

Five of the seven individuals with PWS who scored in the domain *Sensory function* experienced daily difficulties with chewing, due to putting too much food into the mouth. The other two with scores for *Sensory function* experienced daily gag reflexes elicited by tooth brushing.

Snoring almost every night was reported in 18 of the 19 individuals with PWS who scored in the *Breathing* domain. The frequency of snoring (including those with breathing support) was 40% in the studied group with PWS. Of the two individuals with PWS who used breathing support, one reported that snoring was no longer a problem since the introduction of the breathing support. The other person did not use the breathing support and thus

Table III. NOT-S scores for the individuals ($n = 45$) with Prader-Willi syndrome (PWS) and the reference sample ($n = 40$).

	Gender (No. of individuals) Difference			Total NOT-S score	Difference PWS vs Reference group
Age group (years)	Male	Female	All	(mean ± SD[min–max] median)	(*p*-value)*
PWS group					
5–9	5	3	8	4.5 ± 1.2 [3–6] 4.5	
10–18	5	9	14	4.4 ± 2.5 [1–10] 4	
19–27	8	5	13	3.5 ± 2.1 [0–7] 3	
28–49	5	5	10	3.2 ± 2.3 [0–9] 3	
Total	23	22	45	3.9 ± 2.1 [0–10] 4	
Reference sample					
5–9	4	7	11	0.4 ± 0.5 [0–1] 0	<0.001
10–18	5	2	7	0.1 ± 0.4 [0–1] 0	<0.001
19–27	3	2	5	0.2 ± 0.4 [0–1] 0	0.004
28–49	6	11	17	0.4 ± 0.6 [0–2] 0	<0.001
Total	18	22	40	0.3 ± 0.5 [0–2] 0	<0.001

*Mann-Whitney U-test.

it was not effective in alleviating snoring. Only two people (5%) in the healthy reference group snored regularly.

Nineteen (42%) individuals with PWS bit their nails or sucked their fingers or other objects on a daily basis and 10 (22%) clenched their jaws or ground their teeth during the day.

Four persons with PWS found it difficult to eat particular consistencies of food. Nine of the 14 who scored positively in the *Chewing and swallowing* domain swallowed large amounts of food without chewing and three PWS patients frequently coughed during meals.

Drooling—defined as almost daily leakage of saliva in the corner of the mouth or on the chin—was present in 20 (44%) of the PWS individuals.

One person with PWS needed to drink in order to eat a cracker. The same individual also reported frequent drooling. No one had pain from the mucous membranes in the mouth or on the tongue.

A deviant lip position—defined as an open mouth or other deviations occurring more than 2/3 of the time—was found in all 25 of the individuals with PWS and also in the three participants from the healthy reference group, who scored positively for the *Face at rest* domain. Two of the PWS patients had facial asymmetry and two experienced repeated involuntary facial movements.

Only four (9%) of the PWS patients had any difficulty in breathing through the nose. Asymmetry of facial expression when closing the eyes tightly was found in eight of the 11 PWS patients. Nine were unable to pout and round the lips symmetrically and five demonstrated asymmetry in the lip and facial muscles when showing the teeth. None of the persons in the reference group presented with asymmetry in *facial expression*.

No marked symmetrical activity could be observed in the jaw muscles in three (7%) of the PWS patients when the patient clenched their teeth hard on the back teeth. All patients could open the mouth to the minimum criteria of a width of two fingers.

Oral motor function domain scored positively for 60% in the PWS group. Twenty-one individuals (47%) could not lick around their lips or reach the upper lip and the corners of the mouth with the tongue.

In the *Speech* domain, 17 (38%) of the PWS group had difficulty performing diadochokinesis (the performance of rapidly alternating movements) when pronouncing 'pataka' three times sequentially. Articulation and resonance were affected in 10 (22%) of the individuals with PWS.

The NOT-S interview was completed with help from a parent or guardian in 30 (14 M, 16 F) (66.7%) of the individuals with PWS. None of the individuals in the reference sample needed assistance to complete the NOT-S protocol.

Discussion

A total of 130 Norwegian individuals have been diagnosed with PWS after clinical examination or genetic analyses. Individual variations are anticipated in orofacial function, as PWS is a complex medical condition with a marked clinical variability throughout life [5]. As the reference group was sampled from a previous study, the characteristic data available for the healthy non-medicated reference group was limited (Table I).

This is the first comprehensive evaluation of orofacial function among individuals with PWS. NOT-S was developed for orofacial screening in clinical use from 3 years of age. The NOT-S has been successfully used to assess the orofacial dysfunction in patients with ectodermal dysplasia [15] and for evaluation of changes in oral motor function following different surgical procedures in the treatment of adenotonsillar hypertrophy [16]. The NOT-S score was therefore considered to be suitable for the present evaluation of individuals with PWS.

Orofacial dysfunction affecting two or more of the 12 studied domains was present in 87% of the individuals diagnosed with PWS. This high frequency of impaired oral motor function is in agreement with previous reports [7,17–19]. According to the recommendations made by Bakke et al. [14] such a result indicates that further assessment by a team of experts with experience in the field of oral motor function should be considered for individuals diagnosed with PWS. Depending on the severity of symptoms, referral to a specialist should be considered, even when symptoms from only a single NOT-S domain are identified.

The relatively low frequency of 4% triggering the gag reflex during daily tooth brushing is in accordance with a previous study which did not find any higher sensitivity to vibration in PWS [20]. The risk for death due to choking has previously been described by Stevenson et al. [21]. Ogura et al. [22], who questioned parents of individuals with PWS aged 1–42 years, found a tendency to overfill the mouth in 37–59% of the individuals with PWS. The lower frequency of 11% (five individuals) with PWS in our study who experienced daily chewing difficulties due to much food in the mouth, can be attributed to the structured care provided for PWS patients in Norway. To limit overfilling of the mouth, the patient can benefit from appropriate food preparation and possibly texture modification, as well as supervision at meals to avoid choking.

Snoring was frequent among the PWS patients. Since severe snoring may be associated with obstructive sleep apnea [23] and could be a symptom of severe respiratory problems, it is important to refer PWS patients regarding snoring to an ENT-specialist for examination and to consider appropriate treatment.

Treatment options include behavioral interventions, weight control, adenotonsillectomy and breathing support [24]. The use of medication or previous adenotonsillectomy was not evaluated in the present study.

The prevalence of oral habits was higher in our study than in a previous study by Ogura et al. [22], who used a questionnaire to parents of individuals with PWS aged 1–42 years. They found that 15–28% of the children with PWS were chewing and sucking on items [22]. The limited number of patients and cultural differences between Norway and Japan could possibly have contributed to this difference.

Decreased mastication and poor motor coordination have been noted as risk factors for choking-induced death [21]. These risk factors are clearly present in some of the PWS patients, as demonstrated by frequent coughing and swallowing of large bites in some of the patients. This should be evaluated to implement proper measures to prevent fatal complications.

Drooling is a frequent finding in PWS and was present in almost half of the individuals with PWS in our study. The consistency of the saliva in individuals with PWS is usually foamy and highly viscous. The influence of saliva consistency on drooling and on the forming of a bolus for swallowing is not known.

Only one (2%) of the total number of individuals in the PWS group reported symptoms of dry mouth. Individuals with hypohidrotic type of ectodermal dysplasia have congenitally low salivary secretion and could possibly experience oral dryness. The questions used for the evaluation of oral dryness in our study were not sufficient to exclude objectively decreased salivary secretion rate, which is frequently found in patients with PWS [9,25]. This is in accordance with studies among other patient groups, where subjective xerostomia is not always reported by individuals with severely decreased salivary secretion rate [26]. This highlights the importance of measuring salivary flow rate, in addition to asking about the subjective experience of oral dryness, in order to evaluate salivary dysfunction.

Only a few persons were found to have difficulties breathing through the nose in the clinical NOT-S examination. However, this does not contradict previous findings that mouth-breathing is common in PWS [27], since the examination in our NOT-S assessment focused on the ability to breathe through the nose, while other studies have focused on habitual breathing patterns [27].

Asymmetry of facial expression was seen in 24% of the PWS group. The reason for these asymmetries is not clear, but is presumed to be associated with hypotonic muscles in PWS. Hypotonic muscles can also account for the reduced muscular activity observed in some PWS patients when clenching the teeth.

The finding that almost 2/3 of people with PWS had varying degrees of oral motor dysfunction according to the NOT-S evaluation is in agreement with previous studies [18,19]. Mild-to-severe oral motor dysfunction has been estimated to be present in more than 90% of individuals with PWS, with the highest prevalence among children under the age of 12 years [19].

A majority of the individuals who scored positively in the Oral motor function domain could not use the tip of the tongue to wet the lips or reach the corners of the mouth. This supports previous studies by Kleppe et al. [17] and Akefeldt et al. [18]. It is possible that hyposensitivity in individuals with PWS may contribute to these difficulties.

The speech domain in NOT-S consists of counting from one to 10 and incorporates all of the basic movements required for the production of speech sounds. The speech tasks are limited and give no opportunity to repetitive listening for confirmation of suspected misarticulation. A positive mark in the speech domain of the NOT-S score indicates unclear speech in general terms of articulation or resonance. Several authors have described speech in PWS [7,17,18]. Younger children with PWS have demonstrated phonological problems (difficulty with speech sounds). These difficulties often resolve with increasing age, but phonetic (sound articulation/production) errors—including frequent sound distortions—persist in 18–29% of the individuals with PWS [7]. Production of liquid /r/ is particularly difficult for all the individuals with PWS [7,18].

The NOT-S speech assessment gives limited information about sound articulation skills and resonance. To further explore the type of speech error identified in the NOT-S, an extended speech assessment is required. The lower prevalence of speech problems identified in this study may reflect the differing skills of a pediatric dentist and a speech-language therapist/pathologist in identifying subtle speech error. Otherwise the lower prevalence of speech problems found in our study is due to a better availability for speech and language therapy training among individuals with PWS in Norway.

Early diagnosis and thorough orofacial examination of these patients is important to optimize treatment planning and management and to minimize the risk of symptoms developing.

Conclusions

There was a higher NOT-S score in the studied group of individuals with PWS than in the healthy reference sample. Symptoms in the domains Oral motor function, Habits and Face at rest were common among the individuals with PWS. Eighty-seven per cent of the participants with PWS demonstrated dysfunction in two or more NOT-S domains.

Assessment of orofacial dysfunction in individuals diagnosed with PWS should therefore be considered in order to optimize management. We find NOT-S a useful tool in identifying oral motor dysfunction in the same areas as other more detailed examinations.

Acknowledgements

Thanks to the Norwegian Prader-Willi Syndrome Association for distributing information and invitations for participation in the study. Thanks to all patients and families who participated. The study was supported by a grant from the Norwegian Foundation of Health and Rehabilitation, through the Norwegian Prader-Willi Syndrome Association.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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