Oral disorders, saliva secretion and oral health-related quality of life in patients with primary Sjögren's Syndrome

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Abstract

Chemosensory function, burning sensations in the tongue (BST), halitosis, saliva secretion and oral health-related quality of life (OHRQoL) were investigated in patients with primary Sjögren's Syndrome (pSS). In 31 pSS patients and 33 controls, olfactory and gustatory functions were evaluated. Self-reported complaints of dysgeusia, BST and halitosis were recorded. Saliva secretion rates were measured and OHRQoL was assessed using the short-form Oral Health Impact Profile (OHIP-14). Patients had significantly lower olfactory (8.8±3.5 vs 10.7±1.2) and gustatory scores (18.9±7.1 vs 25.4±4.3) than controls, and significantly more patients complained of dysgeusia (58.1% vs 0%), BST (54.8% vs 6.1%), and halitosis (41.9% vs 0%). A significantly greater proportion of pSS patients had ageusia (19% vs 0%), hypogeusia (32% vs 12%), anosmia (13% vs 0%) or hyposmia (29% vs 9%). Significantly lower saliva secretion was observed in pSS patients for stimulated (0.62±0.40 vs 1.57±0.71) and unstimulated (0.08±0.07 vs 0.29±0.17) saliva. The mean OHIP-14 score was significantly higher in pSS patients (16.2±10.8 vs 2.7±3.1) and was positively correlated with dysgeusia, BST and halitosis. In conclusion, patients with pSS reported higher occurrence of dysgeusia, BST, and halitosis, and demonstrated relatively impaired chemosensory and salivary functions. The patients' poorer OHRQoL was associated with dysgeusia, BST and halitosis.

Keywords: Chemosensory disorders, burning sensations, saliva, oral health-related quality of life, primary Sjögren's Syndrome

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Sjögren's Syndrome (SS) is an autoimmune disease that affects mainly women. The prevalence of SS has been shown to range between 0.05% and 1% in European populations (1, 2). Sjögren's syndrome can be divided into primary (pSS) and secondary Sjögren's Syndrome (sSS) (3). The main manifestations of pSS are fatigue and dryness of the mouth and eyes, along with muscle and joint pain (4). For a pSS diagnosis, patients have to fulfill at least 4 out of the following 6 classification criteria: dry mouth, dry eyes, reduced tear secretion, reduced saliva secretion, histopathology of minor salivary glands showing infiltrates of lymphocytes, and positive autoantibodies to Ro/SSA and/or La/SSB (5). The presence of any 4 of the 6 items indicates pSS, as long as either histopathology or serology is positive. Moreover, the presence of 3 of 4 of the objective criteria also justifies classifying patients as having pSS. On the other hand, the sSS diagnosis is used for patients with underlying autoimmune diseases (such as rheumatoid arthritis, systemic lupus erythematosus, or scleroderma) diagnosed prior to developing their sicca symptoms (6).

The lower saliva secretion observed in patients with pSS can have a major negative impact on their oral health and may contribute to mucosal infection and dental caries, in addition to difficulties in speaking, eating and swallowing (7). Oral complaints are shown to play an important role in the oral health-related quality of life (OHRQoL) in these patients (6, 8, 9). Fatigue, pain and systemic manifestations may also have an impact on general health-related quality of life (4, 10).

Several studies on the oral aspects of pSS have focused on factors related to lower salivary secretion (11, 12, 13). A few studies have reported on taste and smell impairments in pSS patients (14, 15, 16), but little is known about chemosensory disorders and other oral complaints, such as dysgeusia, burning sensations in the tongue (BST) and halitosis. Chemosensory disorders include gustatory and olfactory dysfunctions, in which the senses of taste or smell can either be reduced, distorted or totally absent. Olfactory disorders are classified into anosmia (complete loss of smell), hyposmia (reduced ability to smell), and dysosmia (distorted smell perception) (17). Classification of gustatory disorders follows a similar scheme, namely ageusia (complete loss of taste), hypogeusia (partial loss of taste), and dysgeusia (distorted taste perception in the presence of normal stimuli) (18). Many patients with chemosensory disorders experience burning sensations or numbness in the mouth, especially in or on the tongue. These may originate in the gustatory nerve fibres (19). Patients are diagnosed with burning mouth syndrome (BMS) if they experience intense BST, or in other mucosal membranes, lasting for at least 4 to 6 months, which may or may not be associated with normal clinical and laboratory findings (20). BMS may be classified into two clinical forms: primary, in which the organic local/systemic causes cannot be identified, and neuropathological pathways are involved and secondary, caused by local, systemic or psychological factors (21). Halitosis (or oral malodour, defined as an unpleasant breath odour of oral or extra-oral origin), is another common oral complaint that can be associated with low salivary secretion (22) or chemosensory disorders (23).

The aim of this study was to compare olfactory and gustatory function, salivary flow, BST, dysgeusia, halitosis, and oral health-related quality of life (OHRQoL) in pSS patients and age- and gender-matched controls.

Material and methods

The study was performed at the Dry Mouth Clinic at the Faculty of Dentistry, University of Oslo (UiO), Norway. The protocol was approved by the Norwegian Regional Committee for Research Ethics (REK 2015/363). Thirty one female patients with pSS and 33 female controls participated in the study with written informed consent obtained from all participants. The patients with pSS had been referred from the Department of Rheumatology at the Oslo University Hospital, where they had been classified according to the American-European Consensus Group criteria (5). The controls were recruited from UiO staff. Participants' medical history, chronic diseases, use of medications, social status, occupational status, and lifestyle habits (such as smoking) were recorded. Both controls and pSS patients were required to be between the age of 30 and 80 years and were continuously recruited to the study. The exclusion criteria for the controls were as follows: subjective mouth and eye dryness, presence of chronic diseases.

The participants were instructed not to eat, drink or smoke one hour prior to their appointment at the Dry Mouth Clinic. They completed oral health-related quality of life questionnaires, and a detailed patient medical history was recorded. A questionnaire was used to assess participants' experience of dysgeusia, BST and halitosis (Table 1). Open-ended questions were also asked for participants to describe their experience of dysgeusia, BST and halitosis. Participants were examined by both specialists in Oral Surgery and Oral Medicine and general dentists. The sialometry, olfactory and gustatory assessments were carried out as described below.

Using a standardized protocol, unstimulated (UWS) and chewing-stimulated whole saliva (SWS) were collected from all participants to determine salivary secretory rates. Saliva collection was performed in pre-weighed plastic cups placed on ice, and UWS was collected first for 15 min. Participants then each chewed a paraffin wax tablet (Ivoclar Vivadent, Shaen, Lichtenstein) for approximately 30 s, swallowed any saliva in the mouth, and then continued chewing for another 5 min, expectorating the SWS

regularly. Saliva samples were weighed and secretion rates were calculated for UWS and SWS (g/ml = ml/min).

Prior to olfactory testing, participants were asked to score their own general subjective smell perception on a visual analogue scale (VAS) from 0 to 10, where 0 = no smell perception, and 10 = very good smell perception. An identification test using twelve odour pens (Sniffin` Sticks-Screening, Burghart Messtechnik, Germany) was used for the cognitive evaluation of olfactory function. The pens were positioned in front of the participant's nose approximately 2 cm from both nostrils for a maximum of 3-4 s. The participants were instructed to choose from 4 possible answers on a multiple choice scoring card. The answers chosen by each participant were recorded on a protocol sheet, and the data were summarized for each participant. A normative classification (24) was used to define anosmic (score 0-5), hyposmic (score 6-9) and normosmic (score 10-12) participants.

Prior to gustatory testing, participants were asked to score their subjective taste perception (VAS, 0 to 10, score 0 = no taste perception, score 10 = very good taste perception). A gustatory assessment was conducted after a thorough explanation of the testing procedure to the participants. Gustatory function was evaluated using taste strips (25, 26) with 4 basic taste qualities; sweet, sour, salty and bitter, each tested in 4 different concentrations. Taste strips (length 8 cm, tip area 2 cm^2; Burghart Messtechnik, Germany) were gently rubbed on both sides of the anterior tip of the extended tongue, starting with the weakest concentration. The taste qualities were presented in a random manner. This protocol resulted in a total of 32 values for each participant. A chart with names of the four taste qualities was placed in front of the participants during testing so that the participants chose the taste quality with forced choice. The participants were allowed to rinse their mouths with water during the gustatory testing. A normative classification (25) was followed to distinguish between aguesic (score 0-12), hypogeusic (score 13-18) and normogeusic (score 19-32) participants.

Information about oral health-related quality of life (OHRQoL) was gathered using the 14-item short form of the Oral Health Impact Profile (OHIP-14) (27, 28, 29). The total OHIP-14 sum score ranges from 0 to 56, giving an overall indication of the patient's OHRQoL. A high OHIP-14 score indicates a poor OHRQoL.

Statistical Analyses

Statistical analyses were performed using SPSS version 12.0. An independent samples t-test was used for comparing normally distributed continuous variables in the patient and control groups. A chi-square test was used to compare dichotomous variables, and Pearson's correlations were used to measure the strength and direction of linear relationships between pairs of continuous variables. A multivariate linear regression analysis was used to adjust for characteristics such as age and smoking. All differences were considered significant at $p < 0.05$.

Results

Participant characteristics and demographic variables are presented in Table 2. The participants in the control and pSS groups had a comparable mean age, with age ranging from 32 to 70 years in the control group and from 32 to 79 years in the pSS group. The two groups did not differ significantly in their social status and smoking habits. Only seven of the pSS patients used drugs related to pSS, and on average they used significantly more medications unrelated to pSS than controls. Significantly lower saliva secretion rates were found in pSS patients than in controls for both stimulated and unstimulated saliva.

The measured mean olfactory and gustatory scores were lower in the patient group than controls (Table 3). The two groups were further divided into two subgroups based on participants' age: subgroup 1 (30-50 years old) and subgroup 2 (51-80 years old). Olfactory and gustatory testing showed that the pSS patient group had significantly lower mean olfactory and gustatory scores (Table 3) than the controls in

both age groups. The differences in mean olfactory and gustatory scores between pSS patients and controls were greater in subgroup 2 than subgroup 1.

The pSS group had a significantly lower mean self-reported smell score (6.7 ± 3.0 vs 8.3 ± 1.3, p=0.01) and taste score (6.6 ± 2.7 vs 8.3 ± 1.3, p=0.003) than the control group. In the pSS group, significant positive correlations were found between the measured and self-reported olfactory scores (r=0.69), and between the measured and self-reported gustatory scores (r=0.41). The mean olfactory and gustatory scores were also positively correlated with each other in the pSS patient group (r=0.511).

Gustatory testing categorized significantly more pSS patients as ageusic and hypogeusic and significantly fewer with normal sense of taste than in the control group (Table 4). Similarly, olfactory testing showed that there were significantly more anosmic and hyposmic pSS patients and fewer normosmic pSS patients than controls (Table 4). In the pSS group, no correlation was found between their olfactory/gustatory scores and saliva secretion rates. Similarly, no correlations were found between the olfactory/gustatory scores and the number of medications taken or disease duration.

Complaints of dysgeusia, BST, and halitosis in the two groups are shown in Table 5. While none of the controls complained of dysgeusia or halitosis, more than half of pSS patients reported dysgeusia and about 40% complained of halitosis. Patients with pSS reported a significantly higher frequency of BST than controls (54.8% vs 6.1%). Crosstabulations showed significant differences between pSS patients and controls in self-reported complaints of dysgeusia (χ^2=26.7, p<0.0001), BST (χ^2=18.2, p<0.0001), and halitosis (χ^2=17.4, p<0.0001). Eighteen pSS patients who complained of dysgeusia described the taste as metallic, sour, bitter, harsh, or rotten. These patients reported the dysgeusia as a persisting problem that disappeared temporarily during meals. Among seventeen pSS patients who complained of BST, 42% of them stated that this sensation accompanied food intake, especially sharp/spicy and sour food items.

Thirteen pSS patients complained of halitosis as a persisting daily problem, although they mentioned that they could manage their daily halitosis problem by the frequent use of chewing gums, zinc tablets and other saliva stimulating tablets. In the pSS group, no correlations were found between saliva secretion rate and dysgeusia/BST/ halitosis. Similarly, no correlations were found between patients' age, number of medications (unrelated to pSS), disease duration and dysgeusia/BST/halitosis.

The pSS group had a significantly higher mean OHIP-14 sum score than the control group (16.2 ± 10.8 vs 2.7 ± 3.1, $p<0.001$). Scores in all domains of OHIP-14 (functional limitation, physical limitation, psychological limitation, and social limitation) were higher in pSS patients than in controls. In the pSS group, the mean OHIP-14 sum score was moderately and positively correlated with dysgeusia ($r= 0.40$) BST ($r=0.39$) and halitosis ($r=0.33$). The mean OHIP-14 sum score was not correlated with gustatory score or olfactory score. The mean OHIP-14 sum score was not correlated with age or saliva secretion rate.

Discussion

The principal findings of this study were that the pSS patients (i) had poorer olfactory and gustatory function, (ii) more often reported experiencing dysguesia, BST and halitosis, (iii) had lower salivary secretion rates, and iv) had poorer OHRQoL than the control group. However, within the groups, no significant correlations were found between saliva secretion rates and the presence of dysgeusia, BST, halitosis or olfactory and gustatory scores. The OHRQoL was found to be associated with dysgeusia, BST and halitosis. Moreover, no associations were found between the OHRQoL and age/gustatory function/olfactory function or saliva secretion rates.

To our knowledge, this is the first study reporting on the presence and possible associations between chemosensory disturbances, BST, halitosis, salivary gland function, and OHRQoL in Sjögren's patients.

Dysgeusia, BST and halitosis were found to be common complaints among pSS patients. The findings are consistent with other studies where the impairment of taste and smell function in SS patients has been reported (14, 15, 16). However, in the literature there are no comparable studies regarding the occurrence of dysgeusia, BST and halitosis among pSS patients. In the present study, gustatory dysfunction was found to be more pronounced than the olfactory dysfunction which is consistent with some studies (14, 15) and contradictory to one (16). A possible reason behind the contradiction may be related to the difference in methods of testing smell function. An attempt was made to detect the cognitive smell function using smell identification test in the present study, whereas chemosensory threshold (which reflects peripheral sensory impairment) was assessed by Kamel and co-workers (16). An ideal way of testing smell function would involve assessing threshold, detection and identification tests but due to time limitations only identification testing was performed in the present study.

Some studies indicate that hyposalivation may cause smell and taste impairments (14, 16), as well as a burning sensation in the mouth (30). Meanwhile, contradictory results rejecting salivary factors to be responsible for taste performance have also been reported (31). In the present study, the pSS patients had significantly lower salivary secretion rates than controls. However, within the groups, no correlations were found between salivary secretion rates and the presence of oral disorders, suggesting low salivary flow was not directly responsible for the oral disorders examined in this study. An interesting finding in the present study was the relatively high percentage of ageusic and hypogeusic pSS patients. While ageusia is a rare condition, reported to account for less than 1% of chemosensory patients (32, 33, 34), 19.3 % of the pSS patients in the present study were categorized as ageusic in the pSS group. On the other hand, anosmia is one of the most common complaints of patients needing treatment for chemosensory disorders (32, 33, 34); this was also reflected in the present study, where 12.9% of the pSS patients were categorized as anosmic. Previous studies indicate that about half of the patients with complaints of anosmia and hyposmia experience a shift in food preferences and report an increased consumption of sugar and seasonings (32, 34). Similarly, in another study, patients with

gustatory dysfunction stated that their inability to taste also affected their eating habits (35). Both an increase in food intake, in order to compensate for the missing sensory experience, and a reduction in food intake, due to unpleasant sensation and lack of appetite, can be observed in patients with chemosensory disorders (34). This could be expected to further result in either an increase or decrease in body weight.

The correlations between self-reported smell/taste function and tested olfactory/ gustatory function showed strong associations indicating that these chemosensory disorders are somatic in nature, and consistent with the patients' own experiences. Considering that smell and taste functions are known to reduce with age (36, 37), it was of interest to examine whether impaired olfactory and gustatory function was related to age, or due to the pSS disease itself. The present findings confirmed that olfactory and gustatory functions were negatively correlated with age, both in pSS patients and controls, but the presence of pSS disease significantly impaired these chemosensory functions. In the present study, both younger and older pSS patients had significantly lower gustatory and olfactory mean scores than the corresponding control age groups.

More than half of the pSS patients complained of BST, which for many of the patients was found to be related to food intake. Burning sensation in the mouth is a common complaint among SS patients and has been considered enigmatic, since the intensity of discomfort cannot be easily correlated to clinical symptoms (20). As a result, these patients are usually not investigated thoroughly for this by health personnel (20, 23). A similar problem is anticipated for patients complaining of dysgeusia and halitosis (23). Given that a large proportion of patients with pSS in the present study experienced oral disorders on a daily basis, our findings highlight how these oral problems deserve considerably more attention.

Burning mouth syndrome usually diminishes the patients' quality of life, and 'psychological dysfunction' is common in patients with this diagnosis (38). Consistent with this, the present study showed that dysgeusia, BST and halitosis were correlated with mean OHIP-14 score. In contrast, no significant correlation was found between olfactory and gustatory scores and the mean OHIP-14 score in the present study. It may be concluded from the current findings that the pSS patients' OHRQoL was more influenced by dysgeusia, BST, and halitosis, rather than by impaired smell and taste functions. However, other studies have shown that patients with olfactory dysfunction have symptoms of depression that are greater with greater severity of smell loss (41). The OHIP-14 questionnaire is designed to examine certain aspects of oral health related quality of life. Presumably, a questionnaire better designed to detect taste and smell dysfunction is needed to gain more specific insight into the patients' chemosensory experiences and oral health-related quality of life. Accordingly, it would be valuable to design a questionnaire that is specifically aimed at evaluating chemosensory functions and oral health.

Oral malodour is a problem that has received increasing attention over the last decades. In the present study, almost half of the pSS patients complained of halitosis, while none of the controls did so. The main oral etiological factors of this disorder are understood, and effective treatment strategies have been established (39). Interestingly, clinicians have reported that one-third of the patients seeking treatment for halitosis do not actually have oral malodour, and they therefore cannot be categorised as genuine halitosis patients (23). The presence of chemosensory disorders such as smell and taste dysfunction in these patients may provide an alternative explanation for this phenomenon, rather than it being caused by the production of volatile sulphur compounds (VSC) (23). Given that saliva plays a key role in removing the malodorous VSC from the oral cavity (40), the complaints of halitosis among pSS patients may be partly explained by their markedly impaired saliva secretion. However, since levels of VSC were not measured in the present study, whether complaints of halitosis in these patients may be a result of chemosensory disorders rather than the oral production of VSC is speculative at best.

No associations were found between dysgeusia, BST, halitosis, or chemosensory dysfunction and age, the number of medications taken or the disease duration. Thus, within the limitations of this study, with a relatively low number of pSS patients, none of these factors were found to be associated. No associations were found between the mean olfactory and gustatory scores, when compared to number of medications taken, disease duration and salivary secretion rate. These findings may suggest that the olfactory and gustatory dysfunctions in pSS patients may be partly caused by other immunopathological aspects of pSS.

One explanation for the high frequency of chemosensory and other oral complaints in these pSS patients may be found in the systemic inflammatory activity associated with primary Sjögren's syndrome; that is overexpression of Interferon–inducible genes (42) and increased responses to stimulation with Interferon-α and Interferon-γ in B-cells and monocytes (43). Toll-like receptor pathways and IFN-pathways act in collaboration in mediating the inflammatory responses in taste tissue, and hence may interfere with normal taste transduction and taste bud cell turnover (44). More studies at the cellular level, investigating the inflammatory activity in pSS patients and its effect on the peripheral taste and smell organs, are necessary to understand the occurrence of these oral disorders in pSS patients.

In conclusion, this study found that pSS patients had impaired olfactory and gustatory function, and reported a higher occurrence of oral disorders such as dysgeusia, BST and halitosis. Furthermore, the lower saliva secretion rates in the pSS patient group could not account for the oral dysfunctions observed. Finally, the patient group reported poorer oral health-related quality of life in, and this was associated with complaints of dysgeusia, BST and halitosis.

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Table 1

Questionnaire for dysgeusia, burning sensations in the tongue (BST) and halitosis

Dysgeusia					
Do you experience a bad taste on the tongue?	Yes			No	
If yes, can you describe the taste?	Metallic	Sour	Rotten	Bitter	Harsh
How often do you experience this bad taste on the tongue?	Constantly	Daily	Sometimes	In bad periods	Other
BST					
Do you experience a burning sensation in the tongue?	Yes			No	
If yes, when do you experience this burning sensation?	Constantly	Sometimes	During meals	In between meals	Other
If during meals, what kind of food items lead to burning sensation?	Sharp/ Spicy	Sweet	Sour	Salty	Bitter
How often do you experience this burning sensation?	Constantly	Daily	Sometimes	In bad periods	Other
Halitosis					
Do you have complaints of bad breath?	Yes			No	
How often do you have these complaints?	Constantly	Daily	Sometimes	In bad periods	Other

Table 2

Summary of participant characteristics

Characteristic	Patients* (n=31)	Controls (n=33)
Age, mean ± SD (y)	52.0 ± 12.4	50.1 ± 12.7[a]
Occupation, n (%)		
Working full/part time	17 (54.8%)	30 (90.9%)[b]
On sick leave/disabled	10 (32.3%)	0 (0%)[b]
Retired	5 (9.7%)	2 (6.1%)[a]
Unemployed	1 (3.2%)	1 (3%)[a]
Married/Cohabitation	20 (66.7%)	21 (63.6%)[a]
Smoking	3 (10%)	1 (3%)[a]
Saliva flow, mean ± SD (ml/min)		
Unstimulated	0.08 ± 0.07	0.29 ± 0.17[b]
Stimulated	0.62 ± 0.39	1.57 ± 0.71[b]
Number of drugs taken unrelated to pSS, mean ± SD	1.9 ± 1.6	0.6 ± 0.9[b]
Disease duration, mean ± SD (y)	8.4 ± 8.2	-

*Patients with primary Sjögren's syndrome, [a]not significant, [b]p<0.001

Table 3

Mean gustatory and olfactory scores in the two age groups for pSS patients and controls

	Age group (y)					
	All ages		**30-50**		**51-80**	
	Patients (n=31)	Controls (n=33)	Patients (n=14)	Controls (n=19)	Patients (n=17)	Controls (n=14)
Olfactory score (mean ± SD)	8.8 ± 3.5	10.7 ± 1.2[a]	9.9 ± 2.7	11.0 ± 0.7[b]	7.8 ± 3.8	10.2 ± 1.6[b]
Gustatory score (mean ± SD)	18.9 ± 7.1	25.4 ± 4.3[a]	22.6 ± 5.1	26.7 ± 2.4[b]	15.9 ± 7.2	23.6 ± 5.6[b]

[a]p<0.001, [b]p<0.0001

Table 4

Categorization of patients with primary Sjögren's syndrome and controls according to the gustatory and olfactory classification

		Patients n (%)	Controls n (%)
Gustatory function	Ageusic	6 (19.3)	0 (0)[a]
	Hypogeusic	10 (32.3)	4 (12.1)[b]
	Normogeusic	15 (48.4)	29 (87.9)[c]
Olfactory function	Anosmic	4 (12.9)	0 (0)[b]
	Hyposmic	9 (29.0)	3 (9.1)[b]
	Normosmic	18 (58.1)	30 (90.9)[c]

[a]p= 0.01, [b] p<0.05, [c]p<0.003

Table 5

Dysgeusia, burning sensations in the tongue (BST) and halitosis in patients with primary Sjögren's syndrome and controls

	Patients n (%)	Controls n (%)
Dysgeusia	18 (58.1)	0 (0)[a]
BST	17 (54.8)	2 (6.1)[a]
Halitosis	13 (41.9)	0 (0)[a]

[a]p<0.0001