

ORIGINAL ARTICLE

Sleep quality in patients with xerostomia: a prospective and randomized case-control study

Pia Lopez -Jornet^a, Maira Lucero Berdugo^a, Alba Fernandez-Pujante^a, Castillo Felipe C^a, Zamora Lavella C^a, Pons-Fuster A^a, Silvestre Rangil J^b and Francisco Javier Silvestre^b

^aOral Medicine University, Murcia, Spain; ^bUnidad De Estomatología, Hospital Universitario Dr Peset Valencia, Spain

ABSTRACT

Objectives To investigate sleep quality, anxiety/depression and quality-of-life in patients with xerostomia. **Materials and methods** This prospective, observational, cross-sectional study was conducted among a group of xerostomia patients ($n = 30$) compared with 30 matched control subjects. The following evaluation scales were used to assess the psychological profile of each patient: the Hospital Anxiety and Depression Scale, the Oral Health Impact Profile-14 (OHIP-14), the Xerostomia Inventory, the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS). **Results** The PSQI obtained 5.3 ± 1.78 for patients with xerostomia compared with 4.26 ± 1.01 for control subjects ($p = 0.006$); ESS obtained 5.7 ± 2.1 for test patients vs 4.4 ± 1 for control subjects ($p = 0.010$). Statistical regression analysis showed that xerostomia was significantly associated with depression ($p = 0.027$). **Conclusions** Patients with xerostomia exhibited significant decreases in sleep quality compared with control subjects.

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Introduction

Sleep is an active process that occupies approximately a third of human life; it is a critical factor in maintaining mental equilibrium and physical health.[1] However, few studies have looked into sleep disorders among xerostomia patients.[2] Interrupted sleep among xerostomia sufferers can exert a considerable negative impact on their quality-of-life and, in some situations, may exacerbate other medical conditions.[2–4]

The main effects of sleep privation are physical outcomes such as daytime sleepiness, chronic fatigue syndrome, high blood pressure, and impaired immune system. It also decreases the capacity to think clearly, manage stress and can lead to cognitive disorders (decreased attention span and concentration).[1–6]

Xerostomia is a term used for the subjective feeling of dry mouth, while objectively measured reduced saliva production is denoted hyposalivation

Saliva is an essential bodily fluid for maintaining health and oral function and, when unstimulated saliva flow drops to below 0.1–0.2 ml/min, this is an objective manifestation of what is called *hyposialia* or *salivary hyposecretion*. [7,8] In general population surveys, the prevalence of xerostomia is seen to be ~20%, dry mouth being more common among women than men, and in polymedicated individuals.[8–13] Medication is the most common cause of xerostomia. Some 80% of the most commonly prescribed medicines provoke decreases in salivary excretion. In addition to medication, other

causes of xerostomia include Sjögren's syndrome, radiotherapy, HIV, dehydration and emotional upsets.[12,13]

As saliva flow and quantities of saliva decrease, a range of clinical manifestations may appear: organic manifestations mainly determined by the increase in accumulated microorganisms on the oral surfaces, which can provoke dental caries, periodontal disease (gingivitis and periodontitis), mucosal disorders (atrophy, fissures, soft tissue ulceration) and a predisposition to oral infections. This can also produce functional manifestations that make speech, chewing and swallowing difficult, as well as halitosis, irritability or depression.[13–15]

Sleep disorders add to the pathological gravity of any illness and diminish general wellbeing.[16–21] The relation between xerostomia and sleep disorders is a potentially important point that has not been researched in any depth. The mechanisms of protection that saliva provides during the day should continue to function during sleep. The prevalence of self-reported dry mouth complaints during sleep in a survey of Swedish pensioners was estimated to be 13.7% for men and 24.1% for women.[22] Another study of a Northern population showed that the prevalence of self-reported complaints of dry mouth during sleep (associated with waking up and drinking water) was 23% of the total population.[14] Meanwhile, Oksenberg et al. [16] report a prevalence of only 3.2% of their study population who reported dry mouth on awakening.

The study hypothesis was that xerostomia influences sleep quality. In spite of the importance of sleep to general health

and well-being, research into sleep quality among xerostomia patients has been scarce and contradictory. The aim of this study was to assess sleep quality, anxiety/depression and quality-of-life among patients with xerostomia in comparison with control subjects.

Materials and methods

Study design

This descriptive, observational, cross-sectional study was conducted at the Department of Oral Medicine, Faculty of Medicine and Dentistry, University of Murcia, Spain. The study conformed to STROBE Guidelines.[23]

Participants

The study sample consisted of patients diagnosed with xerostomia who were attending the Department of Oral Medicine (Faculty of Medicine and Dentistry, University of Murcia, Spain). The study protocol followed principles established in the Declaration of Helsinki and was approved by the Ethics Committee of the University of Murcia. All patients were volunteers, provided informed consent to take part and received no remuneration

The inclusion criteria for xerostomia group patients were as follows: patients over the age of 18 years; unstimulated whole saliva flow (evaluated using the 'draining method') of under <0.2 ml/min; and willingness to sign the informed consent form. Exclusion criteria were: patients with Sjogren's syndrome; patients with unstable medical conditions or debilitating pathologies, cancer or autoimmune diseases; and patients receiving radiotherapy or chemotherapy.

The control group consisted of a randomized group of healthy patients attending the clinic during the study period that matched for age and gender against the study group. Inclusion criteria for control subjects were as follows: (a) older than 18 years; (b) no history of psychiatric disorders; and (c) attending the clinic exclusively for dental diseases.

Data collection

A total of 42 patients with xerostomia who fulfilled the inclusion criteria were invited to take part consecutively. However, 12 were unwilling to participate for various reasons

(mainly lack of time or interest), leaving a total of 30 patients who underwent analysis. Participants in both groups (xerostomia and control) had not been screened for sleep disorders before. Data were collected by means of a standardized clinical interview. Demographic characteristics were registered: age, sex, smoking (yes/no) and alcohol consumption (yes/no).

Sialometry

Whole unstimulated saliva samples were collected using the drainage method, as recommended by Navazesh et al. [24] Patients were instructed not to eat, drink, smoke, chew or carry out oral hygiene practices for 60 min before saliva collection. Any whole saliva flow rate of less than <0.2 ml/min was considered pathological.

Xerostomia severity test

The xerostomia Inventory (XI) (Thomson et al. 1999) was used to assess the severity of xerostomia symptoms.[25] The XI is the total sum of Likert-type scale scores for 11 items. Patients choose one of five responses to each question: Never (1); hardly ever (2); occasionally (3); quite often (4); and very often (5). The inventory has a 4-week reference period and a maximum score of 55 (Table 1).

Hospital Anxiety-Depression Scale (HAD)

Patients' psychological profiles were assessed using the Hospital Anxiety-Depression scale (HAD).[26] This instrument consists of two sub-scales relating to anxiety and depression. Each sub-scale contains seven items pertaining to mood disorder. For interpreting HAD scale scores, >10 indicates the probable presence of anxiety or depression, scores <7 or less indicate no significant anxiety or depression and scores of 8–10 are of borderline significance.

Oral Health Impact Profile (OHIP-14)

This questionnaire, in its short version, was applied to evaluate oral quality-of-life. The instrument consists of 14 items that explore different aspects of oral function and quality-of-life. The patients were questioned about problems relating to

Table 1. Xerostomia inventory XI.

Complaint	Never 1	Hardly ever 2	Occasionally 3	Quite often 4	Often 5
1. I sip liquids to help swallow food.					
2. My mouth feels dry when eating a meal.					
3. I get up at night to drink.					
4. My mouth feels dry.					
5. I have difficulty in eating dry foods.					
6. I suck sweets or cough lollies to relieve dry mouth.					
7. I have difficulties swallowing certain foods.					
8. The skin of my face feels dry.					
9. My eyes feel dry.					
10. My lips feel dry.					
11. The inside of my nose feels dry.					

speaking, taste perception, eating discomfort and problems with dentures. The score ranges from 0–70, with higher scores corresponding to poorer oral quality-of-life.[27]

Sleep quality

Self-reported sleep quality was measured with the Pittsburgh Sleep Quality Index (PSQI).[28] The PSQI is a self-administered questionnaire consisting of 19 questions correlating to seven domains: subjective sleep quality, sleep latency and sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication and daytime dysfunction. Each domain is awarded a direct score of 0–3. A score of 0 indicates no problem in this domain, while 3 indicates a serious problem. The sum of the seven scores gives an overall score of 0–21.

Epworth sleepiness scale

The Epworth daytime sleepiness scale (EES) [29] is a Likert-type questionnaire that aims to determine or measure daytime sleepiness by means of eight items. The subject is questioned as to the frequency (or probability) of falling asleep on a scale of 1–3 in eight different situations that most people experience in daily life. The eight items are totaled to give an overall score of 0–24, with higher scores indicating greater sleepiness during common daily activities. A score of 0–9 is considered normal. A score of 11–15 indicates the possibility of slight-to-moderate sleep apnea, while a score of over 16 indicates severe sleep apnea or narcolepsy.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) for Windows (release 19.0; SPSS Inc., Chicago, IL). All variables were tested with the Kolmogorov-Smirnov test to determine whether their distributions were normal. A descriptive study was made for each variable as mean and standard deviation (SD). Patients and control subjects were compared applying Student's *t*-test for samples and the chi-square test. Multiple linear regression was used to identify significant predictors of xerostomia; residual analysis confirmed the suppositions. Statistical significance was established as $p < 0.05$.

Results

A total of 60 subjects took part in the study (30 xerostomia patients and 30 control subjects), of who (15%) were men and (85%) women. Subject ages ranged from 35–86 years, with a mean age of 61.47 ± 11.2 . Study and control groups were matched for age and gender distribution. Three participants (5%) were smokers and 57% (95%) were non-smokers. When alcohol consumption was assessed, (11.7%) were drinkers and 55 (88.3%) were not.

The OHIP14 identified significant differences between xerostomia patients and control subjects, with a poorer oral quality-of-life among xerostomia sufferers ($p = 0.001$). In the same way, when psychological profiles were assessed using

Table 2. Clinical characteristics of study population.

	Healthy subjects (n = 30)	Xerostomia (n = 30)	p Value
Demographic characteristics			
Age	58.17 ± 11.19	64.77 ± 10.37	0.021
Sex			0.718
Male	5 (16.7%)	4 (13.3%)	
Female	25 (83.3%)	26 (86.7%)	
Alcohol use			0.688
No	3 (10%)	4 (13.3%)	
Yes	27 (90.0%)	26 (86.7%)	
Smoking			0.554
No	2 (6.7%)	1 (3.33%)	
Yes	28 (93.3%)	29 (96.7%)	
Epworth Sleepiness Scale (ESS)	4.40 ± 1.7	5.7 ± 2.1	0.010
PSQI	4.26 ± 1.01	5.33 ± 1.78	0.006
Xerostomia Inventory	11.8 ± 0.7	23 ± 4.7	< 0.001
OHIP 14	9.26 ± 3.4	20.3 ± 5.5	< 0.001
HAD-A	4.2 ± 1.8	5.6 ± 1.6	< 0.001
HAD-D	4.1 ± 2.6	7.9 ± 4.0	0.003

OHIP 14: Oral Health Impact Profile; HAD-A: Hospital Anxiety and Depression–Anxiety; HAD-D: Hospital Anxiety and Depression–Depression; PSQI: Pittsburgh Sleep Quality Index; ESS: Epworth Sleepiness Scale.

HDD and HAD, xerostomia patients presented higher scores for anxiety and depression. As for sleep quality and daytime sleepiness, xerostomia patients presented average scores of 5.5 ± 1.7 in the PSQI and 5.7 ± 2.1 in the *Epworth Sleepiness Scale*, with statistically significant differences in comparison with control subjects (Table 2).

Table 3. Multiple factor linear regression analysis influencing patients with xerostomia.

Predictors	Beta (SE)	p
Gender	−1.89 (2.2)	0.391
Age	0.19 (0.1)	0.063
Smoking	3.87 (3.2)	0.239
Alcohol	0.59 (2.9)	0.839
OHIP	0.03 (0.1)	0.839
HAD- A	1.18 (0.6)	0.059
HAD-D n	1.18 (0.5)	0.027*
PSQ I	0.51 (0.6)	0.427
EPWORTH	0.14 (0.6)	0.798
R ² (%)	59.9	
Model	F(9.20) = 3.32**	

* $p < 0.05$. OHIP 14: Oral Health Impact Profile; HAD-A: Hospital Anxiety and Depression–A anxiety; HAD-D: Hospital Anxiety and Depression; PSQI: Pittsburgh Sleep Quality Index; EPWORTH: Epworth Sleepiness Scale.

A regression model for the xerostomia variable showed an association between xerostomia and depression ($p = 0.027$) and tendencies towards association with anxiety and age, although these did not reach statistical significance.

Discussion

Numerous articles of research have indicated that saliva flow follows circadian rhythms and decreases during sleep.[7,12,15] However, few studies have looked into sleep disorders among xerostomia sufferers. The present study observed a disordering of the structure and architecture of the sleep cycle among xerostomia patients associated with poor sleep quality, showing statistically significant differences between the study

and control groups—PSQI ($p = 0.006$)—and increased daytime sleepiness—ESS ($p = 0.010$).

Patients with nocturnal xerostomia find they have to drink liquids at intervals through the night; this need can cause frequent sleep interruptions and they must then get up to urinate and thereafter may find it difficult to get back to sleep again.[13,15,22] Of course, sleep is a crucial and essential factor of general well-being and health-related quality-of-life.

Sleep is not a homogenous event, but passes through different stages of greater or lesser activity, each of which has a different purpose in biological recuperation and mental function. Two types of sleep can be distinguished. The first is slow-wave sleep (also known as no rapid eye movement (NoREM) or synchronized sleep) characterized by a different degrees of gentle reduction in most physiological functions (phases 1–4, depending on greater or lesser degrees of activation). The second is paradoxical sleep (also known as rapid eye movement (REM) or desynchronized sleep), during which there is brain activity characteristic of wakefulness, at the same time as much greater hypotonia than in slow-wave sleep; this is when dreaming occurs.[3]

Instruments for measuring sleep dysfunction that use validated questionnaires compile specific information that can be useful to healthcare professionals in the medical decision-making process.[26,28] The present study measured sleep quality using a questionnaire, the Pittsburgh Sleep Quality Index (PSQI), made up of domains for sleep quality, latency, duration, efficiency, disturbances and daytime dysfunction. However, the PSQI does not include any means of registering nocturnal dry mouth, associated with waking up and drinking water, and this is true of all the main assessment systems for screening sleep quality. Dry mouth should figure as a subjective measure of sleep quality among xerostomia patients, as many are forced to keep a glass of water by the bed to alleviate the discomfort.

Alvaro et al.,[30] in a systematic review, analyzed how sleep disorders, anxiety and depression lead to neuropsychological deterioration. The present study found that patients with xerostomia showed significantly worse oral quality-of-life, and suffered from greater anxiety and depression than control subjects, a finding that concurs with other studies.[10,20,21]

Dry mouth may cause constant feelings of discomfort or distress that can lead to mood disorders, especially in aged patients, who are especially sensitive to negative feelings and feelings of helplessness. The results of the present study give evidence of the magnitude of depression among xerostomia patients as regression analysis showed that xerostomia was associated significantly with depression ($p = 0.027$) and that there is a tendency towards associations between dry mouth and anxiety and age, although these did not reach statistical significance. In this sense, the project was exploratory and the results need further evaluation to clarify the relationship between psychiatric disorders and oral diseases.

The complaint of oral dryness is very common among mouth-breathers and normally this symptom is associated with diminished salivary flow rates. And so, in the case of mouth-breathers, the cause of xerostomia may be simply

oral desiccation. Another research approach is the analysis of relations between saliva, waking up and the circadian system; Oksenberg et al. [16] found that dry mouth on waking was a significant symptom in obstructive sleep apnea (OSA) and that its frequency increased as the severity of OSA increased.

The prevalence of dry mouth increases with increasing numbers of medications used to treat one or more conditions (polypharmacy). The drugs most commonly implicated in subjective and objective dry mouth are those with sympathomimetic actions, anti-cholinergic actions, anti-psychotics, tricyclic anti-depressants, anti-hypertensive drugs, beta-blockers and diuretics, anti-histamines, decongestants, opiates, bronchodilators, sedative hypnotics, muscle relaxants, H₂ antagonists or proton pump inhibitors.[11,12] The present study did not register the number of drugs taken by subjects or their type. However, clearly, medication is predictive of probable risk of dry mouth.

Inadequate salivary lubrication (quantity and/or quality) could explain dental deterioration; specific salivary proteins maintain calcium and phosphorus, important for tooth remineralization; the teeth are also protected by the buffering capacity of saliva, whereby acids produced by oral bacteria are neutralized.[15] In this way, therapeutic interventions for dry mouth are important for maintaining general oral health (adequate diet and hydration, abstaining from toxic habits, infection prevention) and are basic to treating xerostomia.[11,20–29] Pilocarpine is the xerostomia medication of choice, although its use is often limited by patients' other medical conditions. The lubricant and protective effects of daytime saliva are just as necessary during the hours of sleep and several devices and gels are currently in development for nocturnal use, which may provide effective relief for nocturnal xerostomia.[31,32]

The results of the present study suggest an association between hyposalivation, sleep disorders, oral quality-of-life and psychiatric disorders among xerostomia patients in comparison with control subjects. The study had some methodological limitations that should be acknowledged: first, it was a cross-sectional study and, second, data registered by means of self-report questionnaires are always subjective and may be at risk of bias. Third, 85% of the subjects were women with an average age of 61.47 years and often the menopause can alter sleep patterns. Insomnia may occur either as a primary disorder, perhaps with the underlying disorders intrinsic to sleep disturbance such as obstructive sleep apnea (OSA) or restless legs syndrome (RLS) or as a secondary problem to hot flashes, mood swings, menopause-related medical conditions, psycho-social upsets and so on.

Lastly, the present study did not look into the differences between nasal and mouth breathers, a parameter that was not included when registering subject sample data.

Nevertheless, health professionals should be aware of the issues this study has identified and respond accordingly by developing strategies to educate and motivate patients and by implementing measures for evaluation, planning and care that address xerostomia. To sum up, this study detected increases in daytime sleepiness and reduced sleep quality among xerostomia patients.

Disclosure statement

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

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