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CLINICAL RESEARCH

Received: 2017.08.11 Accepted: 2017.11.22 Published: 2018.01.10		Xerostomia Among the N	Non-Sjögren Adult				
Authors' Contribution: Study Design A Data Collection B Statistical Analysis C Data Interpretation D Manuscript Preparation E Literature Search F Funds Collection G	CDE 2	artmental sources and mouth dryness are the most common symptoms reported during ophthalmological and dental exam- tions, and their frequency increases with age. In connection with population aging and the huge variety of tors and conditions that can induce this condition, it is becoming a serious and growing problem. The pur- se of the present study was to determine whether ocular dryness and concomitant xerostomia is associat- with particular systemic diseases. enrolled 642 non-Sjögren patients referred for examination to the ophthalmology or dental clinic of Lublin ion, Poland. The research was conducted using a standardized interview: The Interview and Examination estionnaire. All patients responded to the survey questions, which concerned systemic diseases, lifestyle, h special emphasis on computer work, spending time in polluted and air-conditioned rooms, and subse- ent questions about the subjective symptoms of ocular and mouth dryness. ere were 424 patients who presented signs and symptoms of both ocular and mouth dryness. Our study wed a statistically significant association between this condition and the age and sex of the patients and temic diseases such as hypertension (p=0.0000), cardiovascular disease (p=0.057), and stress (p=0.036), d time spent at the computer (p=0.00015). ular dryness and concomitant xerostomia may occur in apparently healthy individuals, but is more frequent batients with systemic disorders. The lack of dry eye and dry mouth symptoms does not exclude insuffi- nt tearing and salivation; thus, the disorders are usually underestimated. Our study indicates that ocular d mouth dryness are the most common conditions seen in out-patients, due to increased use of medica- tors, computers, and air conditioning. alt • Dry Eye Syndromes • Xerostomia ps://www.medscimonit.com/abstract/index/idArt/906618					
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MEDICAL SCIENCE MONITOR

Background

Dry eye and xerostomia are the most frequent symptoms that lead patients to seek medical help. According to the International Dry Eye Workshop (DEWS II) "dry eye syndrome is a multifactorial ocular disease characterized by the absence of tear film homeostasis, which results in visual disturbances, discomfort and other ocular symptoms. The syndrome is accompanied by increased osmolarity of the tear film and inflammation of the eye surface" [1]. Therefore, this is one of the most common disease recognized in patients during oph-thalmic examination. Dry eye is estimated to occur in 10–35% of the population over 50 years of age [2].

Dry eye and mouth can result from many factors, both external and internal. The most common and most difficult to avoid are environmental factors associated with living conditions (e.g., low humidity and wind), working conditions (e.g., night work and long hours spent watching a TV screen or computer monitor), and lifestyle (e.g., smoking and long hours spent in air-conditioned, smoke-filled, or dry places).

The problem of dry eye and mouth increases with age and the coexistence of particular systemic diseases such as hypertension, cardiovascular disorders, diabetes mellitus, hyperthyroidism, osteoporosis, rheumatic diseases, allergies, skin diseases, and connective tissue diseases. Most of the drugs used in systemic diseases significantly affect hydration of the ocular and mouth surfaces. The long list of these drugs includes betablockers, diuretics, antiarrhythmic drugs, steroids, contraceptive preparations, cytostatics, antidepressants and neuroleptics, antihistamines, anticholinergic, antispasmodic, analgesic, anti-migraine, statins, and the commonly-used aspirin [3–5].

Tear film disorders also occur via direct damage to the ocular surface or lacrimal ducts as a result of injuries, burns, rolling up the eyelids, abnormal growth of eyelashes, disorders of blinking, cosmetic procedures, and inflammations or diseases such as trachoma, cicatricial pemphigoid, and erythema multiforme [3].

Similar to dry eye syndrome, the development of dry mouth is influenced by immunological processes that lead to an inflammatory reaction in the oral mucosa [6]. Xerostomia is defined as the phenomenon of subjective sensation of dry mouth [7]. It can be caused by a decrease in salivary glands activity (the so-called true xerostomia). It is not unusual that in spite of normal salivary secretion, hydration of the oral cavity is not sufficient. This phenomenon is called false xerostomia, which is caused by excessive evaporation and absorption through the mucous membrane, or swallowing of saliva. The secretion rate of saliva is strongly connected with the composition of the final saliva secreted into the oral cavity. The relationships between low salivary flow rates and increased *Lactobacillus* counts have been observed in patients with hyposalivation of different origins [8]. At low flow rates, the bicarbonate concentration, pH, and buffer capacity, as well as the clearance of micro-organisms and dietary sugars in the oral cavity, generally decrease, while with low flow rates the saliva contains higher sodium and chloride concentrations [9].

Any situation in which the balance between the secretion of saliva or tears and demand for it is disturbed can be both a clinical problem and a source of discomfort for the patient, and can reduce quality of life.

In this report, we assessed the prevalence of ocular dryness and xerostomia and subjective symptoms in 642 non-Sjögren patients of the Lublin region of Poland. The aim of the study was to explore the relationships between various risk factors and dry eye and mouth.

Material and Methods

Formal and legal issues

Informed consent was obtained from all participants. Personal data of patients have not been disclosed in this study. Research was conducted in accordance with the tenets of the Declaration of Helsinki. The study was approved by the Bioethics Committee of the Medical University of Lublin (No. KE-0254/227/2014).

Inclusion and exclusion criteria

Inclusion criteria

The study was carried out over a period of 4 years (2011–2015) in 686 adult patients living in Lublin district area referred for examination to ophthalmology or dental clinics (some of the healthy patients were examined due to preventive care or taking a driving license test, to obtain reading glasses, or were referred from another specialist). The participants underwent a comprehensive ophthalmological biomicroscopy (clinical assessment of tears meniscus and state of cornea and conjunctival folds) and dental examination (clinical assessment of oral mucosa), and work-up with use of a standardized interview: The Interview and Examination Questionnaire. All patients responded to the survey questions, which concerned systemic diseases, lifestyle (with special emphasis on computer work), staying in polluted and air-conditioned rooms, and addictions, as well as subsequent questions about the subjective symptoms of ocular and mouth dryness (such as foreign-body sensation of "sand" under the eyelids, itching, burning eyes, and in the mouth there are those accompanying the patient during the day and/or night dryness, burning sensation, the need for moisturizing the lips or eating sweets and chewing gum to stimulate saliva production), systemic diseases, and medications used. The questionnaire uses closed single-choice questions.

Patients were divided into 2 groups depending on the presence of systemic disorders and dryness subjective symptoms:

- 1. Generally healthy with or without ailments and clinical symptoms of dryness;
- 2. Systemic diseases, participants with declared systemic disease with or without ailments and clinical symptoms of dryness.

Terms used in the names of groups mean:

- generally healthy the patient did not report any diseases that may affect hydration of the mouth or the conjunctiva and did not take medications with such side effects;
- systemic diseases there were diseases such as hypertension, diabetes, hyperthyroidism, cardiovascular disease, and depression;
- ailments the patient reported subjective problems associated with dryness.

Exclusion criteria

The exclusion criteria included: Sjögren's syndrome confirmed in patient medical records, history of treatments or injuries in the craniofacial region, history of radiotherapy, high refractive errors (over 6 D spherical and/or cylindrical over 2 D: those with such a condition are prone to frequent eye-rubbing, squinting, or strong contracting of the eyelids, thus mechanically interfering with tear film), contact lens use, smoking, acute inflammation in the oral cavity or the eye, history of allergic conjunctivitis, gross lid abnormalities, life-threatening systemic disease, acute ocular infections, extra- and intraocular surgery within the last 6 months, and patients taking systemic medication known to cause dry eyes such as antihistaminics and anticholinergics.

Statistical analyses

Statistical evaluation of the data was performed using Statistica 10. The results are reported mainly as percentage values. A pvalue of less than 0.05 was considered statistically significant. Normal distribution was checked with the Shapiro-Wilk test. Quantitative variables with normal distribution were analyzed with the *t* test for 2 independent means. Proportions were analyzed by chi-square test, with Yates correction when needed.

Results

After verification, in accordance with the above-described exclusion criteria, 642 adult patients aged 18–82 years remained in the study. We observed a statistically significant difference in age between groups: the mean age in group 1 was 47.65 years and in group 2 it was 53.53 years (p<0.05). Females accounted for 63.08% (405) of study subjects *vs.* 36.92% (237) male (p=0.043). Data on sex and age proportions of study groups are presented in Tables 1–3.

History-taking showed that 32.5% of patients had hypertension, 8.3% had cardiovascular diseases, 7.56% had diabetes mellitus, 3.23% had hyperthyroidism, and 0.93% had depression. There were significant associations between dry eye and hypertension, cardiovascular disease, time spent at a computer, and stress (p<0.05) (Table 4).

Subjective symptoms reported by patients with ophthalmic problems were mostly a foreign-body sensation, described as a feeling of sand under the eyelids (26% of respondents), itching (16.82%), and burning (18.32%). Mouth problems included dryness during the day or night (35.82%), burning sensation (23.36%), need to moisturize the lips (31%), or eating sweets and chewing gum (6.07%) to stimulate saliva production. In the present study, the sensation described as a feeling of sand under the eyelids was by far the most frequent ocular symptom. Among the mouth symptoms, dryness and burning sensation during the day (27.72%) prevailed and, resulting from these symptoms, the need for frequent drinking. The least frequent complaint was halitosis (bad breath) (2.49%). The distribution of ocular surface and mouth symptoms in the study groups is listed in Table 5.

The prevalence of symptoms was very similar between both examined groups (generally healthy and with systemic diseases), and the only significant differences were ocular symptoms like burning sensation of the eyes and thus needing to rub or compress the eyelids, and for oral symptoms there were dryness during meals and the need to moisturize the mouth at night.

Discussion

Dryness of the exocrine glands, especially in the eyes or mouth, is referred to as "sicca syndrome" when there is no evidence of autoimmune disease present. Although sicca symptoms occur in the vast majority of Sjögren's patients, not everyone with these symptoms really has Sjögren's syndrome. In our study, 424 patients had ocular and mouth dryness. The prevalence of ocular and mouth dryness increases with age and one of the risk factors for dry eye syndrome and xerostomia is older age. This is demonstrated by clinical observations and statistical

Table 1. Age of patients in the studied groups.

		Group							t-Student			
			1					2				test
			Max	Μ	SD	N	Min	Мах	Μ	SD	t	р
Age (years)	369	23	79	47.65	11.69	273	27	82	53.53	10.08	6.67	0.000000

Table 2. Age of the study population by groups and gender.

			Gro				
Age		1			2		t-Student test
	N	Μ	SD	N	Μ	SD	
Female	245	49.60	11.29	160	53.14	10.24	p=0.18
Male	124	43.79	11.54	113	54.07	9.86	p=0.09

Table 3. Gender distribution in the studied groups.

		Gro	-	Total			
Gender	1		2			Test χ²=4.08	
	N	%	N	%	N	%	λ
Female	245	66.40%	160	58.61%	405	63.08%	m 0.042
Male	124	33.60%	113	41.39%	237	36.92%	p=0.043

Table 4. Association between systemic diseases and environmental factor in study group.

Systemic diseases		Dry	eye		Chi-squ	ıare
Systemic diseases		Yes		No	Value	р
Hypertension	179	(85.24%)	31	(14.76%)	50.83	0.0000
Diabetes mellitus	38	(79.17%)	10	(20.83%)	3.92	0.14
Cardiovascular diseases	46	(85.18%)	8	(14.82%)	5.72	0.0000
Hyperthyroidism	18	(85.71%)	3	(14.29%)	3.71	0.15
Depression	6	(100%)	0		3.09	0.21
Computer	109	(56.19%)	85	(43.81%)	12.32	0.00015
Air-condition	40	(64.52%)	22	(35.48%)	0.081	0.77
Stress	64	(76.19%)	20	(23.81%)	4.35	0.036

data [10]. Presumably this has to do with a decrease in androgen levels, and applies to both sexes. As a result of apoptosis of interstitial cells, gland atrophy occurs [11,12]. This tendency is evident in the overall population and in particular groups, regardless of the coexistence of other diseases and reported symptoms. It is estimated that up to 1/5 of the population experiences dryness symptoms. Moreover, the number of patients has been increasing with the aging of the population and widespread use of computers, mobile devices, and air conditioning. Our analysis showed that elderly patients with systemic disease reported more subjective symptoms than healthy patients (p=0.0000). Among our participants, there were more women than men (p=0.043), indicating that females are more aware about their health. Moreover, it is scientifically proven

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		Gro				
Symptoms	1	l	2	2	Chi-square	
	-	+	-	+	Value	р
Burninig sensation of the eyes	313 84.83%	56 25.17%	211 77.29%	62 22.71%	5.93	0.014
Itching of the eyes	302 81.85%	67 18.15%	232 85%	41 15%	1.01	0.29
Sand under the eyelids	271 73.45%	98 26.55%	204 74.73%	69 25.27%	0.134	0.71
Blurred vision	309 83.74%	60 16.26%	235 86%	38 14%	0.66	0.41
Need to rub or compression of the eyelids	307 83.2%	62 16,8%	243 89%	30 11%	4.31	0.037
Dryness at night	337 91.32%	62 16.8%	235 86.09%	38 13.92%	4.44	0.034
Dryness during the day	226 72.1%	103 27.9%	198 72.53%	75 27.47%	0.015	0.90
Dryness during meal	355 96.2%	14 3.8%	245 89.75%	28 10.25%	10.71	0.001
Difficulties in swallowing	352 95.39%	17 4.61%	253 92.67%	20 7.33%	2.13	0.143
Burning in the mouth or the tongue	266 72.02%	103 27.92%	198 72.53%	75 27.47%	0.015	0.901
Halitosis	364 98.65%	5 1.35%	262 95.97%	11 4.03%	3.58	0.058
Necessity of moisturizing during the day	266 72.1%	103 27.9%	198 77.53%	75 7.47%	0.015	0.901
Necessity of moisturizing during the night	337 91.33%	32 8.67%	236 86.45%	37 13.55%	3.89	0.048
Necessity of chewing gum or candies	342 92.68%	27 7.32%	261 95.6%	12 4.4%	2.34	0.125

Table 5. The distribution of ocular surface and mouth symptoms in the study groups.

that women are more likely than men to complain about their health; thus, they more often visit the doctor [13]. The higher incidence of reported problems in women than in men has also been confirmed. This phenomenon has been described by many authors [14–16], suggesting that estrogen regulation of tears may help explain the female predilection in some ocular diseases, including dry eye syndromes, resulting in reduced antioxidative function of the eye.

The most common health problem among the patients studied was hypertension, which occurred in 32.5% of all persons reporting any systemic diseases. We observed a statistically significant association between hypertension and dry eye occurrence and symptoms (p<0.05). A possible reason for these results may be use of antihypertension drugs, especially diuretic drugs [17]; this involves dehydration of the body, disorders of water-electrolyte metabolism, and secondary dryness of all mucous membranes [18,19]. In addition to hypertension, 7.56% of the studied patients had diabetes, 8.3% had systemic diseases or cardiovascular diseases (including 4.01% with myocardial infarction), 3.23% had hyperthyroidism, and 0.03% had depression. Numerous publications indicate diabetes is causes of dry eye [6,20,21]. These disorders result firstly from abnormal metabolism, and secondly from sensory disorders on the surface of the eye in the course of diabetic neuropathy. People with normal corneal sensation feel dryness in the eyes earlier, begin to blink more often, and apply drops. Patients with reduced corneal sensation may not report symptoms for a long time and the progression of changes in the eye associated with dryness can lead to severe complications, such as trophic ulcers of the cornea. Also, the state of the oral cavity of diabetics is the focus of attention of dentists. In this group, more

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than in healthy people, there are problems with the secretion of saliva, and ulceration and inflammation in the oral cavity. This is particularly true of patients with diagnosed peripheral neuropathy [6]. Hyperthyroidism occurs in about 2% of the adult population [22]. In our study, we observed 3.23% of participants had hyperthyroidism, but without any significant association with ocular and mouth dryness. As a result of hyperthyroidism, the development of thyroid orbitopathy with eye socket tissue damage may occur. Occupation of the muscles and fascia within the eye socket results in exophthalmos and consequently with excessive exposure of the eyeball surface to external factors. There appear typical symptoms of dry eye syndrome, and the vision problems in the form of reduced visual acuity and double vision. Chronic inflammation of autoimmune character may not only concern thyroid tissues and the eye socket, but also nervous, circulatory, and gastrointestinal systems, as well as skin. Dryness of the mouth can be one of the symptoms of the inflammation [7,23,24].

Eye and mouth dryness are significantly associated with anxiety disorders and depression. One large population-based, cross-sectional study found clear signs of depression in 13.7% of patients with dry eye disease, compared with 8.6% of the control group [25]. In our study population, only 6 patients reported depression, but many people are reluctant to admit to this illness. Drugs used to treat depression or allergy also can cause dehydration. These side effects occur when taking antidepressants (e.g., amitriptyline and imipramine), benzodiazepines, neuroleptics (e.g., chlorpromazine and haloperidol), and medications for asthma or chronic obstructive pulmonary disease (e.g., salbutamol and fenoterol) [26].

The exposure to environmental factors may lead to ocular surface disorders by inducing proinflammatory cytokines, particularly receptor activating, myofibroblast expression, and changes in extracellular stromal matrix. These process influence tear film stability, osmolarity, and conjunctival goblet cell density. Both environmental factors and systemic disease are crucial agents associated with dryness symptoms. In our study, there was no significant difference in the distribution of environmental factors between the groups, which confirms the independent influence on dry eye and xerostomia [27].

Patients with a deficiency of moisture in the eye and mouth report different ailments. In this study, the most common ocular symptom was a feeling of sand under the eyelids, which was reported by 26% of respondents with subjective symptoms. Other symptoms included burning (18.32%), itching (16.82%), periodic blurring of vision (15.26%), and discomfort, rubbing eyes, or eyelid clamping (14.33%). For comparison, authors

from Bialystok [28] indicate that 90% of patients with rheumatoid diseases reported burning of eyes, 83.3% had the feeling of sand under the eyelids, and 10% of respondents complained of itching. The occurrence of these symptoms is also confirmed by other authors [26,29].

With regard to oral cavity symptoms, the most common problem was the feeling of dryness throughout the day, which occurred in 27.72% of respondents with symptoms. For most of these people, the sensation was so unpleasant that 27.72% of subjects had to moisten their mouths regularly throughout the day. We found 15.57% of subjects had feeling of dryness at night, and 10.74% had to moisten the oral cavity during the night. Another very common symptom was a burning sensation in the mouth and on the tongue, which was reported by 27.72% of subjects, with 6.54% of all patients reporting that mouth dryness hindered them in eating their meals, and 0.057% had trouble swallowing food. Some subjects (0.02%) reported halitosis. Results of other authors confirm the occurrence of these symptoms of xerostomia [7,18], but they do not provide quantitative data regarding their occurrence.

Conclusions

Occurrences of subjective ailments related to dry mouth or dry eye syndrome are not always connected with coexistence of systemic diseases, and they can also affect healthy people. A detailed medical survey should be performed in all such patients to confirm or exclude the influence of a major disease or effect of medication on a patient's complaints. The lack of dry eye and dry mouth symptoms does not exclude insufficient tearing and salivation; thus, these disorders are usually underestimated. Dry eye and xerostomia are multifactorial diseases; therefore, a single factor such as systemic disease or an environmental factor does not usually have a profound impact on subjective symptoms among non-Sjögren patients. Our study, with some limitations, indicates that ocular and mouth dryness are the most common conditions seen in outpatients, due to increased use of medications, computers, and air conditioning. These complaints appear to be trivial, but affect everyday life and reduces quality of life.

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