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Frequency of occurrence of dry mouth in women with high risk of cardiovascular diseases during the menopause

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Abstract: Among the risk factors for dry mouth, or xerostomia, are both estrogen deficiency in women during menopause and the use of medications with xerogenic properties. Until now, it has not been clearly determined, whether dryness in the oral cavity in women during menopause is only associated with subjective sensations or is accompanied by qualitative and quantitative changes in mixed saliva. To determine the frequency and nature of xerostomia syndrome in women during menopause with high and extremely high risk of cardiovascular diseases. The study involved 35 patients (with subjective sensations of dryness in the oral cavity) and 20 apparently healthy women. All study participants were questioned for any dental complaints, and the quantitative indicators of the oral fluid were assessed. An individualized oral hygiene complex and a moisturizing gel were prescribed as correction of the subjective signs of xerostomia. The follow-up visit was carried out after 1 month. The patients in natural menopause felt slight subjective manifestations of dry mouth confirmed by objective decrease in salivary secretion; whereas in most cases subjective dryness in the oral cavity is accompanied by normal secretion. The prescribed complex for correction of dental complaints ensures decrease in the subjective signs of dryness, decrease in taste distortion and halitosis.

Keywords: menopause; xerostomia; moisturizing gel; salivation rate; high risk of cardiovascular diseases

1. Introduction

Today, dryness of the oral cavity (or xerostomia) is fairly considered to be one of the urgent problems of modern medicine, in particular dentistry, due to its widespread occurrence among the population, little study, diagnostics complexity and duration of therapy measures [1–3]. Subjective signs of dryness are accompanied with difficulties in chewing and swallowing food, cause changes in taste sensations, bad breath, thus significantly impairing quality of life [4,5]. The number of patients complaining of dry mouth is steadily growing – according to various authors, the incidence of xerostomia reaches 25%–70% of the population and depends on age, hormonal levels, presence of any somatic pathologies and medications intake, etc. [6,7]. Xerostomia can be accompanied only by subjective sensations, or it can be associated with changes in qualitative and quantitative indicators of mixed saliva (true xerostomia), which entail violation of the oral mucosa moisturizing and protection, excessive plaque formation, the risk of developing teeth and periodontal tissues pathologies [8,9].

According to the available data, occurrence of xerostomia in many cases is associated with both the pathology of internal organs and the xerogenic properties of medicines that affect the salivary glands and lead to decreased salivation [10,11]. Besides, the results of the studies proved that the secretory activity of the small

salivary glands decreases with age, especially in women during menopause and postmenopause.

The prevalence of menopausal symptoms in Europe is 74% and depends on many factors: general health, social status, lifestyle, and psychological status. Women with moderate to severe menopausal symptoms often experience fatigue, sleep problems, anxiety, vasomotor symptoms that affect quality of life [12]. Dry mouth is one of the manifestations of menopause. This fact is explained by the presence of sex hormone receptors (estrogen) in the salivary glands, fluctuations in the level of which cause changes in salivation [13–15]. However, it still stays completely unclear whether dryness in the oral cavity in women during menopause is only associated with subjective sensations or is accompanied by qualitative and quantitative changes in mixed saliva.

To restore subjective comfort in the oral cavity and mitigate the manifestations of xerostomia, the range of symptomatic therapy means available on sale include moisturizers in the form of solutions, gels, pastes [16]. Also, the complex of preventive measures is to be added with hygienic care of the oral cavity individually developed for each patient and aimed at preventing further changes and improving the patient's well-being.

The aim of this study was to determine the frequency and nature of the xerostomal syndrome in menopausal women with high and extremely high risk of cardiovascular diseases.

2. Material and methods

As part of the research and development activities implemented by the Department of Complex Reduction of Risks of Chronic Noncontagious Disease on the basis of the State Institution “L.T. Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine”, female patients, both being on inpatient or outpatient treatment, were examined.

A total of 54 women with high and extremely high risk of cardiovascular diseases were questioned, of which 35 patients (with subjective sensations of dryness in the mouth) were included into the study. The average age of the patients was 50.31 years (45–55 years).

The inclusion criteria for the study were: climacteric age (menopause and postmenopause); signed informed consent; dry mouth sensation according to subjective symptoms; desire and ability to use prescribed means for the oral cavity moisturizing; high level of adherence to the ongoing research or treatment. The criteria for exclusion from the study were: no complaints of dry mouth; acute or aggravated diseases in the oral cavity; burdened allergic anamnesis; Sjogren's syndrome and rheumatoid conditions; taking hormone replacement therapy; insulin-dependent diabetes mellitus (DM); heart failure of III-IV functional class (FC).

3 patients had a history of combined arterial hypertension, coronary heart disease, and type 2 diabetes mellitus. In 2 patients, diabetes mellitus was combined with hypertension. The rest of the patients did not suffer from diabetes, but took therapy for coronary heart disease and hypertension, recommended by international and domestic standards [17,18]. Among the medicines, those that can cause xerostomia (angiotensin

converting enzyme inhibitors (I-ACE), beta-blockers (β -blockers), acetylsalicylic acid (ASA) were taken into account.

The control group was represented by 20 somatically healthy women who did not take any medications at the time of the survey, representative in age with the main group.

Before individual consultations with patients, various specialists (cardiologist, nutritionist, endocrinologist, physiotherapy specialist, dentist) conducted group sessions in order to increase knowledge of risk factors for somatic pathology.

The patients were given modified questionnaires for making the xerostomia diagnosis. The questionnaire was focused on the nature of food, attitude to oral hygiene, the presence of bad habits (smoking). Subjective assessment of health status was carried out on the visual analog scale, where “0” meant the worst, and “100”—the best health condition.

The nature of dryness and other complaints in the oral cavity, their duration during the day, occurrence of the first complaint manifestations were determined. The combination of complaints was defined, all possible causes that could contribute to their occurrence were ascertained. Dental examination was carried following the existing standards, palpation determined the state of tissues in the area of large and small salivary glands, light finger massage was done paying attention to possible characteristic changes in the secretion.

The study of the unstimulated rate of salivation was carried out by the standard method on an empty stomach in the morning hours by free flowing into a graduated test tube with evaluation of the volume obtained per unit of time [19]. Before this procedure was started, the patients were advised to refrain from eating and drinking, smoking, and performing hygiene procedures. The salivation rate was expressed as the ratio of the volume of saliva obtained (mL) to the time (10 min). The viscosity was calculated using the standart method. To determine pH of saliva, an indicator pH-test strip with the gradation from 4.5 to 9.0 was used.

All patients who, after the questionnaire were selected for participation in the study by the random sampling method, were subdivided into the main group (18 patients) and the comparison group (17 persons). In addition to group sessions, the patients of the main group were given recommendations on oral care, selected items and means of hygienic care, and, if necessary, carried out professional oral hygiene. Besides, the examined women of the main group were additionally prescribed means for moisturizing the oral cavity (gel) containing betaine, taurine, sodium hyaluronate, xanthan gum, caragenan, xylitol, hydrogenated castor oil, hyaluronic acid, stevia rebodiana extract, CI 19140, CI 42090 flavore. The follow-up examination was carried out after 1 month according to the data of subjective sensations (questionnaire survey) and salivation studies. The research protocol was approved by the ethics commission of the State Institution “L.T. Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine”, in compliance with the principles of the Declaration of Helsinki.

Statistical processing of the obtained data was carried out using the statistical software package “SPSS 17” and Microsoft Office Excel. Normal distribution data are presented as mean values and mean errors. Data that do not meet the normal distribution criteria are given as median, 25% and 75% quartiles.

3. Results

35 patients were selected based on the inclusion criteria out of 54 women with high and extremely high risk of cardiovascular diseases. After filling out the questionnaires and collecting dental complaints, statistically significant differences from the group of somatically healthy women were recorded (**Table 1**). Thus, it was found out that 100% of patients with high and extremely high risk of cardiovascular diseases complained of dryness in the oral cavity of different severity and duration, and 25 patients reported of constant dryness, regardless of the time of the day and food intake, while 10 patients noticed dry mouth primarily on evenings and nights. It should also be mentioned that each of the interviewed patients drank a sufficient amount of fluids throughout the day, and associated dryness with some medication intake and age.

Table 1. Comparison of the frequency and nature of the main dental complaints (%).

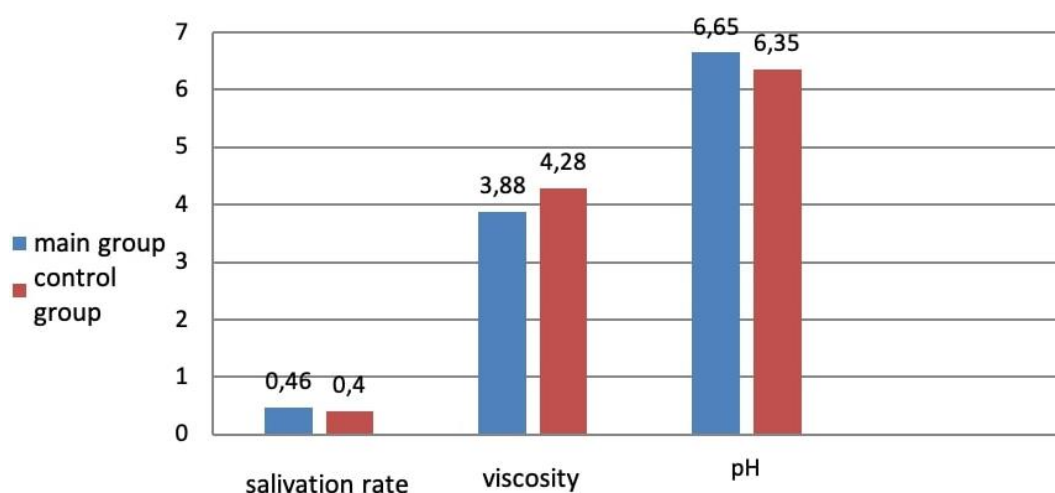
Sign		Main group	Control group	$\chi^2 p$
Dry mouth	Total	100 ± 0.0	40 ± 11.0	26.860 $p = 0.001$
	Constant	71.4 ± 7.6	0	
	Periodic	28.6 ± 7.6	40 ± 11.0	
	No	0	60 ± 11.0	
Taste distortion		54.3 ± 8.4	15 ± 9.7	8.185 $p = 0.005$
Burning tongue and lips		68.6 ± 7.8	0	
Sticky plaque		71.4 ± 7.6	0	
Halitosis	Total	86.0 ± 5.9	20 ± 8.9	7.139 $p = 0.008$
	Constant	48.6 ± 8.4	0	
	Periodic	37.3 ± 8.2	20 ± 8.9	
	No sign	14.3 ± 5.9	80 ± 8.9	

It is worth saying that 8 patients in the control group also experienced periodic dryness in the oral cavity, but this fact did not cause them significant discomfort. Also, 3 patients in the control group noted periodic changes in taste sensations, and 4—bad breath. A distinctive feature of complaints coming from patients with high and extremely high risk of cardiovascular diseases was the emphasis on periodic and constant burning of the tongue and the mucous membrane of the lips, presence of the soft sticky plaque on the teeth, which was found after waking up in the morning, frequent changes in taste sensations, bad breath.

To assess effectiveness of the prescribed measures for correction of xerostomia, the group of patients with high and extremely high risk of cardiovascular-vascular diseases by the method of blind sampling were subdivided into two groups – the main group and the control group. It should be noted that the main group and the control group at the time of the first visit did not have statistically significant differences in most of the features, which made it possible to consider them equivalent (**Table 2**, **Figure 1**). The patients completed subjective assessment of their health status against a visual analog scale, the resulting mean values in the groups also did not differ statistically (56.6 ± 2.76 and 58.82 ± 2.88).

Table 2. Comparison of the frequency and nature of the main dental complaints after subdivision into the main group and the control group (%).

Sign	Main group (n = 18)	Control group (n = 17)	χ^2 p
Dry mouth	100 ± 0.0	100 ± 0.0	-
Distortion of taste	66.66 ± 11.1	76.4 ± 10.3	2.289 p = 0.131
Burning tongue and lips	61.11 ± 11.5	76.4 ± 10.3	0.957 p = 0.328
Sticky plaque	61.11 ± 11.5	82.3 ± 9.3	1.933 p = 0.165
Halitosis	72.22 ± 10.6	100 ± 0.0	0.509 p = 0.019

**Figure 1.** Difference in quantitative parameters of the oral fluid between the main group and the control group.

During the initial study of the oral fluid parameters, differences were recorded only in pH level ($p = 0.042$). It should be noted that despite the subjective sensations of dryness in the oral cavity, the average salivation rates for the group were within the normative values (0.3–0.6 mL/min were taken as the norm). Likewise, the values of the oral fluid viscosity (ranging of the norm—from 1.8 to 4.2 relative units) and pH value (6.5–7.2) were located within the normal range.

Comparative assessment of complaints after using the prescribed prophylactic complex showed that the patients of the main group noticed improvement in the oral cavity condition, as well as significant reduction in discomfort, which improved the quality of life both in physical and psychological aspects. They also noted facilitation of food intake and swallowing, reduced frequency of drinking water when eating. Some patients reported that the use of the recommended gel felt like stimulating increased saliva production, which greatly improved the condition of the patients. It should be noted that in the main group, persistent dryness remained in 2 out of 14 patients, while 8 patients practically did not notice the dry mouth sensation ($\chi^2 = 10.2286$, $p = 0.002$) (**Figure 2**).

Besides, dysgeusia ($\chi^2 = 1.029$, $p = 0.34$), tongue and lips burning ($\chi^2 = 4.050$, $p = 0.045$) significantly decreased, while the frequency of halitosis and complaints of sticky plaque on the teeth and tongue remained unchanged. Repeated interviewing of patients in the control group showed increase in distortions of taste perception, while the frequency of other complaints remained unchanged.

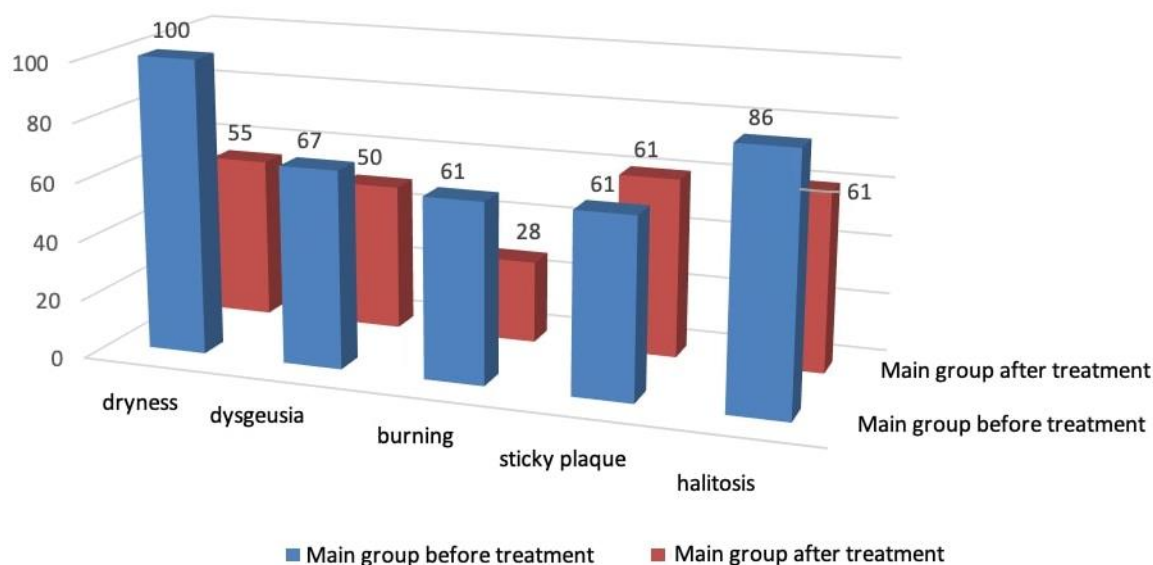


Figure 2. Difference in the complaint frequency in the main group at the beginning and the end of the study.

Sialometry indices practically did not differ in patients of both groups before the study (except for pH value). Despite the positive dynamics in the patients of the main group in terms of dental complaints, no significant differences in the salivation rate between the visits were recorded (0.46 ± 0.04 mL/min and 0.492 ± 0.026 mL/min, $p = 0.077$). The same statistically unreliable data were recorded in the patients of the control group, for whom no changes in the quantitative indicators of mixed saliva were observed.

4. Discussion

Development of subjective dryness in the oral cavity does not always depend on the objective rate of salivation, just as severity of symptoms is not always proportional to the amount of saliva secreted by the glands. At the same time, the salivary glands change their structure and function with various fluctuations in hormones, including sex hormones, which leads to qualitative and quantitative changes in the composition of their secretions. Estrogens have been shown to have the direct effect on the function of the salivary glands in women with both natural and surgical menopause, receiving hormone replacement therapy [20]. Estrogen deficiency makes significant impact on the organs and tissues of the oral cavity, which is explained by the presence of specific nuclear receptors for estrogens in the basal layer of the gingival epithelium, endotheliocytes of the periodontal vessels, cells of the acini and ducts of the salivary glands, etc. Dental symptoms with lack of both estrogen and progesterone can manifest itself as dry mouth and burning sensation in the mouth, dysgeusia, halitosis, damage to hard and soft tissues, which, according to some studies, is associated with changes in the salivary film on the mucous membrane formed by the secretion of small salivary glands [21]. So, in our study, among patients in natural menopause, only a small number of women showed subjective manifestations of dryness confirmed by objective decrease in saliva secretion; and the majority of patients had subjective dryness in the oral cavity with the normal rate of secretion.

In addition, the dryness sensation is a side effect of β -blockers and ACE inhibitors,

which reduce the activity of RAAS and cause decrease in pressure in the vessels, vasodilation, and decrease in the volume of regional blood flow, including the flow in the parenchyma of the salivary glands [22]. There may also be several reasons for dysgeusia, but its occurrence can be caused by the influence of inconsistent sensory stimulation of taste receptor and distorted perception due to the action of medicines or their metabolites. Thus, occurrence of dry mouth in patients is associated with both medications and estrogen deficiency due to natural menopause. However, manifestations of xerostomia constitute a genetically determined process with smooth beginning, caused by the physiological adaptation mechanisms.

5. Conclusions

Timely diagnostics of xerostomia is an urgent problem of modern dentistry due to broad prevalence among women with high and extremely high risk of cardiovascular diseases in menopause. The complex of preventive measures should include individual hygienic care of the oral cavity. Moisturizing gel for dry mouth problem mitigation reduces the severity of subjective symptoms and improves the quality of life of patients with xerostomia

6. Prospects for the future

An individualized approach to prophylactics of xerostomia in patients with the indicated pathology will prevent occurrence and weaken the clinical manifestations of pathological changes in the organs and tissues of the oral cavity.

7. Ethical statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from every participant included in the study.

8. Limitation of the study

The study was conducted with the participation of a small number of patients and limited to one month of observation. A small number of participants was due to the selection of patients with high compliance and the opportunity to attend classes regularly.

Author contributions: Conceptualization, NE and DE; methodology, NE; software, DE; validation, NE and DE; formal analysis, DE; investigation, DE; resources, NE; data curation, NE; writing—original draft preparation, DE; writing—review and editing, NE and DE; visualization, NE; supervision, NE; project administration, NE. All authors have read and agreed to the published version of the manuscript.

Conflict of interest: The authors declare no conflict of interest.

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