ORAL FLUID CHANGES IN XEROSTOMIA PATIENTS ON MEDICATIONS: CLINICAL AND LABORATORY CHARACTERISTICS

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Drug-induced xerostomia is common among elderly patients taking multiple medications. The condition significantly affects dental health and quality of life. This study aimed to evaluate the clinical and laboratory characteristics of oral fluid (OF) in xerostomia patients taking xerogenic medications, and to assess associations between total xerogenic load, salivary flow rates, and OF composition. The study included 60 people aged 45–75 years. The treatment group consisted of 40 patients with at least 3 months of dry mouth history and routine intake of two or more medications with known xerogenic potential. The control group included 20 healthy individuals exhibiting no signs of xerostomia and not taking medications routinely. We used the Xerostomia Inventory questionnaire to collect data from the participants; they also underwent clinical dental examination and sialometry for unstimulated and stimulated oral fluid (OF). The fluid samples were examined in the laboratory to determine pH, buffer capacity, total protein content, alpha-amylase activity, glucose and lactate levels. Compared to the control group, patients in the treatment group showed marked hyposalivation, decreased OF pH and buffer capacity, increased total protein content and alpha-amylase activity, and tended more often to have multiple caries lesions, candidal stomatitis, and atrophic changes in the oral mucosa. Thus, drug-induced xerostomia is accompanied by pronounced quantitative and qualitative changes in OF as well dental health and quality of life deterioration. A comprehensive clinical and laboratory assessment of OF provides an objective measure of xerostomia severity and enables compilation of tailored prevention and treatment programs.

Keywords: xerostomia, hyposalivation, oral fluid, saliva, medications, sialometry, dental health status

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Compliance with ethical standards: the study was approved by the local Ethics Committee of North Ossetian State Medical Academy of the Ministry of Health of the Russian Federation (Minutes No. 5 of September 20, 2025). All participants have voluntarily signed informed consent forms. The study did not involve animal experiments.

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КЛИНИКО-ЛАБОРАТОРНАЯ ХАРАКТЕРИСТИКА ИЗМЕНЕНИЙ РОТОВОЙ ЖИДКОСТИ У ПАЦИЕНТОВ С КСЕРОСТОМИЕЙ НА ФОНЕ ПРИЕМА ЛЕКАРСТВЕННЫХ ПРЕПАРАТОВ

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Медикаментозная ксеростомия широко распространена на фоне полипрагмазии у пациентов старших возрастных групп и существенно влияет на стоматологический статус и качество жизни. Целью исследования было оценить клинико-лабораторные характеристики ротовой жидкости (РЖ) у пациентов с ксеростомией, развившейся на фоне приема лекарственных препаратов (ЛП) с ксерогенным эффектом, и определить связь между суммарной ксерогенной нагрузкой, показателями слюноотделения и изменениями состава РЖ. В исследование включено 60 человек 45–75 лет. Основная группа — 40 пациентов с жалобами на сухость во рту продолжительностью не менее 3 месяцев при одновременном приеме двух и более ЛП с известным ксерогенным потенциалом. Контрольная группа — 20 здоровых лиц без признаков ксеростомии и без регулярного приема ЛП. Проводили анкетирование (опросник Xerostomia Inventory), клиническое стоматологическое обследование, сиалометрию нестимулированной и стимулированной РЖ, а также лабораторное исследование РЖ с определением pH, буферной емкости, общего содержания белка, активности альфа-амилазы, уровней глюкозы и лактата. У пациентов основной группы выявлены выраженная гипосаливация, снижение pH и буферной емкости РЖ, повышение общего содержания белка и активности альфа-амилазы, а также более высокая частота множественного кариеса, кандидозного стоматита и атрофических изменений слизистой оболочки полости рта по сравнению с контрольной группой. Таким образом, медикаментозная ксеростомия сопровождается выраженными количественными и качественными изменениями РЖ, ухудшением стоматологического статуса и снижением качества жизни. Комплексная клинико-лабораторная оценка РЖ позволяет объективизировать тяжесть ксеростомии и обосновать индивидуализированные программы профилактики и лечения.

Ключевые слова: ксеростомия, гипосаливация, ротовая жидкость, слюна, лекарственные препараты, сиалометрия, стоматологический статус

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The physiology of salivation and the composition of oral fluid are fundamentally important for dental health. Normally, saliva moisturizes the mucous membranes, helps form the food bolus, supports remineralization of hard tooth tissues, regulates acid-base balance, and performs protective functions via its enzymes, mucins, and immune proteins [1, 2].

Xerostomia is a subjective feeling of dryness in the oral cavity; it can be concomitant with decreased salivation, qualitative changes in secretions, or impaired saliva distribution on the surface of the mucous membrane [3–5]. Dry mouth is a common complaint among adults, particularly older patients [6, 7].

The etiological factors of xerostomia are diverse and include autoimmune diseases, endocrine and metabolic disorders, chronic somatic pathology, radiation therapy in the head and neck area, as well as long-term drug therapy [5, 8–13]. Among medications, the most pronounced xerogenic potential has been described for antidepressants, anxiolytics, neuroleptics, antihypertensive agents, diuretics, antiarrhythmic drugs, and antihistamines [6, 11–13].

Clinical manifestations of drug-induced xerostomia include a constant feeling of dry mouth, thirst, difficulty swallowing dry food, speech disorders, changes in taste, burning of the mucous membranes and tongue, and reduced tolerance for removable dentures [4, 7, 12]. Prolonged hyposalivation increases the risk of multiple carious lesions, root caries, candidal mucosal lesions, and atrophic glossitis [4, 7, 12].

Diagnosis of xerostomia is based on a combination of clinical assessment and objective research methods. Standardized questionnaires, including the Xerostomia Inventory, are widely used to quantify subjective symptoms, while objective assessments of secretory function are performed using sialometry for unstimulated and stimulated oral fluid [14–16].

Laboratory examination of oral fluid enables measurement of saliva's pH, buffering capacity, protein composition, and enzymatic activity; this expands the possibilities for objectively assessing the degree of hyposalivation and the risk of dental complications [1, 2, 17]. In the context of polypharmacy, combined clinical and laboratory analysis of oral fluid appears to be the most informative [5, 6, 11–13, 18].

However, the relationship between total xerogenic drug load and specific oral fluid changes (detected via clinical and laboratory analysis) in xerostomia patients remains poorly understood.

This study aimed to evaluate the clinical and laboratory characteristics of oral fluid in xerostomia patients taking xerogenic medications, and to assess associations between total drug-related xerogenic load, salivary flow rates, and changes of the oral fluid composition.

METHODS

This was a single-stage, comparative observational study conducted at a dental clinic and the therapeutic department of a multidisciplinary hospital.

The study included 60 patients of both sexes aged 45–75 years. The treatment group consisted of 40 patients who had complained of dry mouth for at least 3 months and had routinely taken two or more potentially xerogenic medications for 6 months or longer. The control group included 20 practically healthy people of comparable age who did not complain of dry mouth, routinely take medications, or use anything beyond occasional non-narcotic analgesics and nonsteroidal anti-inflammatory drugs.

Based on the literature, the considered xerogenic drugs were antidepressants, anxiolytics, neuroleptics, the main groups of antihypertensive drugs, diuretics, antiarrhythmic medications, and antihistamines [8, 9, 11–13, 18]. Exclusion criteria: Sjogren's syndrome and other autoimmune diseases, decompensated diabetes mellitus, chronic renal or liver failure, previous radiation therapy of the head and neck, alcohol abuse, acute infectious and inflammatory diseases at the time of examination, pregnancy and lactation.

All patients underwent a standard dental examination. We evaluated their complaints, medical and life histories, drug therapy (including structure and duration), and examined the oral cavity, assessing the condition of the mucous membrane, tongue, lips, and gums, and noting any atrophy, erythema, cracks, erosions, plaques, or signs of candidal lesions. Dental health was described using the DMFT index calculated according to a generally accepted method.

The subjective severity of xerostomia was assessed using a modified Xerostomia Inventory (XI) [14, 15]. The patient filled out the questionnaire independently and asked for the doctor's help if necessary. A higher total score indicated more severe dry mouth syndrome, as perceived by the patient.

Unstimulated whole-saliva flow was quantitatively assessed using Navazesh sialometry [16]. The oral fluid was collected in the morning, no earlier than 2 hours after eating, drinking, smoking and hygiene procedures. The patient was seated, breathing through the nose, and spitting the generated saliva into a graduated tube every 30 seconds over a 5-minute period. The salivation rate was calculated in mL/min.

Stimulated salivation was measured after chewing a standard paraffin pellet (weight 1.0 g) for 5 minutes. The collected saliva was measured in a graduated cylinder to calculate stimulated flow rate. The accepted hyposalivation thresholds were 0.1 mL/min (unstimulated) and 0.5 ml/min (stimulated).

After collection, samples were centrifuged at 3000 rpm for 10 min; the supernatant was subjected to biochemical analysis no later than 2 h after sampling. Table gives the key analytical modes, reagents, and equipment used for the purpose.

To asses the drug load, we analyzed the prescribed therapy. Each xerogenic medication was assigned a conditional score depending on the severity of the effect on salivation according to literature data [11–13, 18]. The total score for each patient was considered as an integral indicator of the xerogenic load.

Statistical processing was performed using standard application software packages. The normality of distribution was assessed using the Shapiro-Wilk test. The results were presented as M ± SD for normally distributed data and as Me (Q_1; Q_3) for non-normal distributions. The Student's *t*-test or Mann–Whitney *U* test was used for quantitative variables between groups; for categorical variables, the chi-square test or Fisher's exact test. Correlation analysis was performed using the Pearson or Spearman correlation, depending on the nature of the distribution. The differences were considered statistically significant at $p < 0.05$.

RESULTS

The mean age of patients in the treatment group was 62.3 ± 7.4 years, in the control group — 60.8 ± 6.9 years; the differences were not statistically significant. Female participants were the dominant cohort in both groups. The average number of concomitant medications was 4.8 ± 1.6 in the treatment group and 0.9 ± 0.4 in the control group, indicating a significantly higher drug load in patients with xerostomia.

All patients in the treatment group complained of dry mouth of varying severity. The Xerostomia Inventory mean score was 37.8 ± 6.1, which corresponded to severe xerostomia. The

Table. Key analytical modes, reagents, and equipment used in the study

Indicator/stage	Method, reagents, and equipment
Preanalytical stage	The samples were collected in graduated tubes and centrifuged at 3000 rpm for 10 minutes in a CM-6M laboratory centrifuge (ELMI Ltd., Latvia). The resulting supernatant was analyzed in the next stage
Oral fluid pH	The pH was determined immediately after centrifugation using a SevenCompact S220 desktop pH meter (Mettler Toledo, Switzerland) equipped with an InLab Expert Pro-ISM glass electrode. Three-point calibration was performed with standard buffer solutions (pH 4.01, 6.86, and 9.18)
Buffer capacity	To 1.0 mL of oral fluid, we sequentially added 0.1 mL of 0.01 mol/L HCl and 0.01 mol/L NaOH using single-channel pipettes (Research plus, Eppendorf AG, Germany) until the pH shifted by 1.0 unit. The volumes of titrant used were recorded
Total protein content	Biuret method: 1.0 mL of biuret reagent was added to 20 µL of oral fluid, and the mixture was incubated for 10 minutes at 37 °C. Optical density was measured at 540 nm using a Stat Fax 1904 Plus semi-automatic biochemical analyzer (Awareness Technology, USA)
Alpha-amylase activity	Kinetic colorimetric assay using a chromogenic substrate: mixed 20 µL of sample with 1.0 mL of reagent, and measured absorbance at 405 nm on a semi-automatic biochemical analyzer (Stat Fax 1904 Plus, Awareness Technology, USA)
Glucose	Glucose oxidase peroxidase method (GOD-PAP): mixed 10 µL of sample with 1.0 mL of reagent, then incubated for 10 minutes at 37 °C, and performed photometry at 505 nm using a semi-automatic biochemical analyzer (Stat Fax 1904 Plus, Awareness Technology, USA)
Lactate	Enzymatic colorimetric method: 20 µL of sample was mixed with 1.0 mL of reagent, incubated for 10 minutes at 37 °C, and absorbance was measured at 540 nm using a semi-automatic biochemical analyzer (Stat Fax 1904 Plus, Awareness Technology, USA)
Microscopy of sediment	Native oral fluid sediment preparations were studied at magnification ×100 and ×400 on a Primo Star light microscope (Carl Zeiss Microscope GmbH, Germany); the number of epithelial cells, leukocytes, and the presence of yeast-like fungi were evaluated

most typical complaints were a constant feeling of dryness, the need to keep water nearby, difficulty swallowing dry food, and sleep disturbances due to needing to drink water at night. In the control group, the total score of XI was 16.3 ± 3.2; the complaints were episodic and did not affect the quality of life.

In the treatment group, the mucous membrane was often pale or moderately hyperemic, thinned, with a matte surface and pronounced stickiness Papillary atrophy, flattening of the surface, and individual fissures were often observed on the tongue. The DMFT index in xerostomia patients was significantly higher and amounted to 21.4 ± 5.2, while in the control group it was 15.8 ± 4.1 ($p < 0.01$). Moreover, in the treatment group, we registered significantly more cases of multiple carious lesions, including root caries, and non-carious lesions.

Candidal stomatitis (mainly erythematous and pseudomembranous forms) was diagnosed in 32.5% of treatment group participants. These patients reported burning and soreness of the oral mucous membrane, which worsened when consuming spicy or hot food. In the control group, only one patient (5%) showed signs of candidal lesions. Atrophic glossitis was found in about a quarter of patients in the treatment group, while in the control group this condition was very rare.

Sialometry revealed severe hyposalivation in the treatment group. The rate of unstimulated salivation averaged at 0.08 ± 0.03 mL/min and was significantly lower than that in the control group (0.32 ± 0.09 mL/min) ($p < 0.001$). The stimulated salivation rate in xerostomia patients equaled 0.32 ± 0.11 mL/min, whereas in the control group it was 0.86 ± 0.21 mL/min ($p < 0.001$). Both unstimulated and stimulated saliva flow rates indicated pronounced hyposalivation in most treatment group patients.

Laboratory examination of the oral fluid revealed significant qualitative changes. The average pH in the treatment group was 6.47 ± 0.21, significantly lower than in the controls (6.86 ± 0.18) ($p < 0.01$). Xerostomia patients had reduced buffering capacity, which made titrant-induced pH changes occur more rapidly. The oral fluid total protein content in the treatment group was higher than in the control group, potentially indicating compensatory restructuring of the salivary glands' secretory function.

Alpha-amylase activity in the treatment group was also significantly higher than in the control group. At the same time, we registered a moderate growth of the levels of glucose and lactate. Microscopic examination revealed increased numbers of exfoliated epithelial cells and leukocytes, along with more frequent yeast-like Candida fungi. These findings aligned with the clinical signs of candidal stomatitis.

The analysis of drug therapy confirmed the significant role of xerogenic drugs in the development of hyposalivation. Most treatment group patients took antidepressants and antihypertensive drugs in various combinations. The mean integrated xerogenic load index was 7.1±2.4 (arbitrary units). Correlation analysis revealed a statistically significant negative relationship between the total xerogenic score and the rate of unstimulated as well as stimulated salivation, whereas a positive correlation was observed with the Xerostomia Inventory total score.

Thus, patients who take xerogenic medications for a long time develop persistent hyposalivation with pronounced clinical manifestations of xerostomia and a complex of quantitative and qualitative changes in oral fluid that adversely affect dental health.

DISCUSSION

The results of our study confirm previously reported findings that drug-induced xerostomia and hyposalivation are especially common in senior patients receiving combination therapy for chronic somatic diseases [5–7, 11–13, 18]. The registered unstimulated and stimulated salivation rates indicate pronounced hypofunction of the salivary glands, consistent with values reported in clinical recommendations and review papers [5, 7, 16].

High Xerostomia Inventory scores in the treatment group confirm dry mouth's significant impact on the daily activities and quality of life of the patients. The revealed relationship between the total xerogenic load and the severity of subjective complaints corresponds to data on the role of polypragmasia in the pathogenesis of xerostomia [6, 13–15, 18].

Clinical manifestations, including multiple caries, non-carious lesions, candidal stomatitis, and atrophic glossitis are consistent with prolonged saliva deficiency and changes in its composition. A decrease in salivary pH and buffering capacity

favors cariogenic bacteria growth and enamel demineralization, explaining the higher DMFT index in the treatment group [1, 2, 7, 12, 17].

An increase in total protein content and alpha-amylase activity reflects compensatory adaptation in salivary gland secretion as overall secretion volume declines. The more frequent detection of Candida yeasts and the increased incidence of clinically evident candidal stomatitis suggest impaired local immunity and disruption of the oral microbiota [2, 7, 12].

The findings emphasize the need for an interdisciplinary approach to the management of patients with xerostomia. Correcting drug therapy — taking into account the xerogenic properties of the drugs — by a general practitioner, cardiologist, psychiatrist, or other specialists can help reduce symptoms and partially restore normal salivation [5, 11–13]. When therapy cannot be adjusted, local symptomatic measures become more important, including salivation stimulation, use of salivary substitutes, optimization of oral hygiene, prevention of caries and candidiasis [5, 13].

It is clinically important to include not only sialometry but also an extended oral fluid analysis (assessing pH, buffer capacity, protein profile, and enzymatic activity) in protocols for examining patients with dry mouth complaints. This approach enables more accurate quantification of the severity of drug-induced xerostomia, allowing use of the resulting indicators to monitor the effectiveness of preventive and therapeutic measures.

The limitations of this study include a relatively small sample size, the simultaneous nature of the observations, and a lack of stratified analysis for individual classes of xerogenic drugs. In the future, it is advisable to conduct prospective studies involving a larger number of patients and comparing different schemes for the prevention and treatment of drug-induced xerostomia.

CONCLUSIONS

Patients with medication-induced xerostomia develop hyposalivation, characterized by a significant reduction in unstimulated and stimulated saliva flow rates, decreased pH and buffering capacity of oral fluid, and increased total protein content and alpha-amylase activity. Medication-induced xerostomia is accompanied by a high incidence of multiple caries, non-carious lesions, candidal stomatitis, and atrophic changes in the oral mucosa, leading to deteriorated dental status and reduced quality of life. A comprehensive assessment of the clinical and laboratory characteristics of oral fluid enables objective evaluation of drug-induced xerostomia severity, links xerogenic drug load to the degree of hyposalivation, and provides a basis for individualized prevention and treatment programs.

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