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ABSTRACT

of the dissertation for the degree of Doctor of Science

**CLINICAL AND FUNCTIONAL CONDITION OF SALIVARY
GLANDS DURING SIALOSIS AND SIALADENITIS,
TREATMENTS AND WAYS OF PREVENTION**

Speciality: 3226.01 – Dentistry

Field of science: Medicine

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GENERAL REVIEW OF THE WORK

Relevance of the topic. Among the problems of the modern Stomatology the issue of the clinical course, epidemiology, diagnostics and treatment of non-tumor diseases of salivary glands accompanied by functional distortions holds one of the central positions. This is explained with the fact that first a number of accidental observations, followed by a planned experiments showed that the function of salivary glands by far is not limited to participation in digestion and their biological value is far beyond what was supposed until very recently. The tissue of salivary glands itself as understood from many researches, containing a number of biologically active substances significantly influence the normal development of human and formation of individual systems of regulation. The tight connection of both structure and function of salivary glands with functions of up internal secretion glands, especially thyroid, pancreas and sexual, was determined ^{1,2}.

Being closely connected with other systems of body, salivary glands are sensitive to changes, leading to sialosis ^{3,4}

Currently there is a constant trend of increasing (up to 5-8% a year) number of patients with kidney diseases⁵. The main problem of

¹ Alonso de Rena V., Dis Dios R. et all. A standardized protocol for the quantification of lactate dehydrogenase activity in saliva //Arch. Oral. Biol.- 2004. V. 49, №1.-P.33-37.

² Асиятилов Г.А. Заболевания слюнных желез при поражении щитовидной железы автореферат диссертации на соискание ученой степени кандидата медицинских наук Москва-2009

³ Лобейко, В.В., Иорданишвили, А.К., Заборовский К.А. Лечение заболеваний слюнных желез у пациентов старших возрастных групп// Российский стоматологический журнал, 2017.-N 1.- с.21-25.

⁴Коваленко В.А., Копчак А.В., Коваленко А.Е. Постлучевые сиалозоадениты у пациентов с папиллярными карциномами щитовидной железы // Вестник хирургии им. И.И.Грекова. 2015.-N 1, - с.75-77.

⁵ Бибков Б.Т., Томилина Н.А. Состояние заместительной терапии больных с хронической почечной недостаточностью в Российской Федерации в 1998-2009 гг. (отчет по данным российского регистра заместительной почечной терапии). Часть первая. Нефрология и диализ. Москва, 2014, т.16, №1, с. 11-127.

patients with CRI is anuria and, consequently, impossibility of excretion of catabolism products, such as urea, creatinine, etc. Hemodialysis allows eliminating hypernitrogenemia, correct electrolyte balance and acid-bas balance. At that long term treatment of such patients leads to anemia, disorders of cardio-vascular, nervous, and endocrine systems. Evolving changes are accompanied with secondary manifestation in oral cavity and that is why patients with CRI are managed by a multi-disciplinary team, including stomatologists. Authors note that such patients have less volume and speed of salivation, developed xerostomia, and had salivary pH changed. A lot of works were dedicated to description of diagnostics of clinical course and treatment of sialosis and sialadenitis.^{6,7,8} Nevertheless, there is not enough attention towards early diagnosing of salivary glands' lesions both among healthy population and those suffering from chronic renal insufficiency. There are only few statements on the condition of salivary glands of patients with CRI. Some pathogenic mechanisms of oral cavity changes remain to be unclear making treatment and prevention more difficult. Clinical data state the dependency between salivary gland function reduction and different diseases of endocrine genesis. Similar mechanisms of exocrine secretion determine the tight connection between salivary and endocrine glands.⁹ Oral cavity

⁶ Коваленко В.А., Копчак А.В., Коваленко А.Е. Постлучевые сиалозадениты у пациентов с папиллярными карциномами щитовидной железы // Вестник хирургии им.И.И.Грекова, Россия, 2015.-N 1.-С.75-77.

⁷ Афанасьев В.В., Винокурова О.Ю., Ордашев Х.А. Анализ заболеваний слюнных желез по данным клиники хирургической стоматологии челюстно-лицевого госпиталя ветеранов войны г. Москвы// Российский стоматологический журнал 2015.том 19,№3,с 27-29

⁸ Колесов В.С. Хронические сиаладениты, сиалозы, синдромы с поражением слюнных желез: патогенез, клиника, дифференциальная диагностика и лечение: Автореф. дис.... д-ра мед. наук. - Киев. - 1987. - 44 с.

⁹ Киченко СМ., Барер Г.М., Оболенский Ю.А., Игнатова М.В., Петрова Л.Г., Сергеева Г.С. Некоторые особенности состава смешанной слюны и десневой жидкости у больных сахарным диабетом 1 и 2 типов // Сб. тр. Всеросс. научн.-практ. конф. «Образование, наука и практика в стоматологии». - М. - 2004. -С.137-139.Ибрагимов Т.И., Лебеденко И.Ю. Прогнозирование эффективности лечения пародонтита на фоне сахарного диабета // Интернет: Терра Медика. - 2001. - №3. - 3 с.

tissue and organ lesion prevalence during diabetes mellitus is 52% - 90%¹⁰, salivary gland diseases - 3% to 34%¹¹, of which sialosis - 12% to 22%.

Sialolithiasis is the most prevalent condition among salivary gland diseases. It accounts for, according to different authors, 20,5% to 78% of cases. This is explained by the emergence of new diagnostics methods and elaboration of knowledge on etiology and pathogenesis of sialolithiasis. The prevalence of sialolithiasis is at the rate of 12 per 1000. It is noted that it happens 3 times more among urban population, than rural. Clinicians determined that submandibular salivary glands are involved more (90-95%) than parotid gland (5-8%).¹²

The issue of etiology and pathogenesis of sialolithiasis is not finally resolved yet. All theories have polyetiological character, including the delay and thickening of saliva, invasion of microorganisms into salivary duct, disturbance of mineral balance in the body. We haven't seen any work, determining optimal treatment options for different forms of stages of the condition. Low efficiency of previously proposed treatment methods and possible complications force to search for new treatment approaches with regards to patients with inflammatory and dystrophic salivary gland conditions. Given the above, the topical problem of the modern stomatology is the detection of early signs and development of adequate treatment methods for sialosis and sialolithiasis management.

¹⁰ Ибрагимов Т.И., Лебеденко И.Ю. Прогнозирование эффективности лечения пародонтита на фоне сахарного диабета // Интернет: Терра Медика. - 2001. - №3. - Зс. Черкасова И.И. Радионуклидные методы исследования больших слюнных желез при неопухолевых и опухолевых заболеваниях: Автореф. дис. ...канд. мед. наук. - М. - 1997. - 20с.

¹¹ Черкасова И.И. Радионуклидные методы исследования больших слюнных желез при неопухолевых и опухолевых заболеваниях: Автореф. дис. ...канд. мед. наук. - М. - 1997. - 20с.

¹² Иорданишвили А.К., Лобейко В.В., Желудь М.В. некоторые аспекты диагностики сиаолитиаза в стоматологических лечебно-профилактических учреждениях // Биомед. Журнал. Медлайн.ру.2013,Т.13,- с.726-734

Object of the study. The study included patients with chronic sialadenitis, sialolithiasis, as well as sialosis associated with chronic kidney disease and type 2 diabetes mellitus.

The aim of this study. Based on complex study, pathogenesis and differential diagnostics elaborate new methods of treatment, improve outcomes of sialosis and sialolithiasis, reduce temporary loss of working capacity and ensure the prevention of sialadenitis.

Objectives of the research:

1. To perform an integrated research and assess clinical and functional status of salivary glands in patients with sialolithiasis, sialosis and sialadenitis.
2. On the basis of a comprehensive laboratory examination using biochemical, physicochemical, cytomorphological and immunological methods in patients with sialosis and sialadenitis, to study the direction of shifts in these indicators.
3. To perform an integrated laboratory examination of local immune correction, stimulated by autoleucocytes. Determine the comparative efficiency of the elaborated method of integrated treatment.
4. To study the endotoxemia products urea and creatinine in OC and determine the efficiency of sorbent therapy combined with hemodialysis in patients with CRI.
5. To develop and ground the systemic enzyme therapy for Diabetes mellitus 2 type patients with sialosis.
6. Based on outcomes obtained, develop practical recommendations on treatment and prevention procedures for oral cavity and salivary glands in patients with sialadenitis and sialosis.
7. To study the mineral structure of salivary stones using diffractometry and infrared spectroscopy in patients with sialolithiasis and to develop integrated treatment methods and methods of prevention.

Methods of research: During the research clinical studies, using biochemical, cytomorphology, visuographic and spectral methods of diagnostics, as well statistical processing of outcomes will be performed.

The main provisions for the defense:

- In patients with chronic sialadenitis during exacerbation the inflammation in oral cavity is manifested by the elevation of the endogenous intoxication in oral fluid
- In patients with chronic sialadenitis the level of local immunity substantially changes with the reduced salivation on the background
- Enzyme therapy during the integrated treatment of sialosis patients with Diabetes mellitus 2 type on the background manifested anti-inflammatory effect.
- The study of oral liquid endotoxemia products showed that following the sorbent therapy by natural zeolite, patients with sialosis and CRI manifest the reduction of short-wave fraction of substance with low and middle molecular weight, containing uremic toxin - urea.
- Sialotripsy is a perspective alternative and palliative treatment method for patients with sialolithiasis.

Scientific novelty of the research:

- For the first time the efficiency of local immune correction was studied and the use of stimulated autoleucocytes at the 2nd stage of treatment of patients with chronic sialadenitis was grounded.
- Clinical, immunological, biochemical, cytomorphological changes in process in patients with sialosis and diabetes mellitus 2 type were studied.
- In patients with sialosis and CKD under GD treatment against the background of elevated levels of urea, creatine and products of endotoxemia in RL sorbentotherapy was carried out. The treatment showed higher efficacy compared with standard methods of treatment.
- A study of the biochemical parameters of saliva in patients with chronic renal insufficiency was carried out, the results of which make it possible to scientifically substantiate the conduct of joint stomatological and urological examination and treatment of patients suffering from sialadenitis developed against the background of chronic renal insufficiency.
- The mineral structure of salivary calculi using diffractometry

and infrared spectroscopy in patients with calculous sialodentitis was studied, which will make it possible to develop complex methods of treatment and prevention of patients with sialolithiasis.

The practical significance of the obtained results:

- On the basis of laboratory and clinical tests (sialometry, sialography, biochemical tests of saliva and blood, cytological examination of saliva, ultrasound examination of SG) the character of changes in salivary glands in chronic renal failure, diabetes mellitus type 2 will be established, on the basis of which the complex of medical measures for patients with sialosis, developing against the background of renal pathology and endocrine system will be justified.
- The proposed new methods of treatment as well as the developed practical recommendations will help to reduce temporary disability of patients, prolong remission periods, improve salivary gland function in sialodentitis and sialolithiasis.

Approbation of the results of the research work. The main results and provisions of the dissertation work were presented and discussed at: scientific-practical conference dedicated to the birthday of scientist and public figure Aziz Aliyev (Baku, 2012, 2017), scientific-practical conference dedicated to the 120th anniversary of the Azerbaijan Institute of Advanced Medical Training named after A. Aliyev (Baku, 2017), scientific and practical conference of the international forum of military surgeons named after Ambroise Pare (APIMSF 2018) , all-Ukrainian scientific and practical conference "Actual problems of dentistry, maxillofacial surgery, plastic and reconstructive surgery of head and neck". (Poltava, 2014), scientific-practical conference "Topical issues of dentistry" (Ganja, 2014), IV International Scientific Practical Conference "Topical Problems of science" (Kyiv, 2021).

The materials of the dissertation were discussed at a joint meeting of the departments of dentistry and maxillofacial surgery, otolaryngology and Central Research Laboratory of A. Aliyev AzSIATD (Protocol No. 5 of 26.05.2021); at the scientific seminar at the Dissertation Council ED 2.05 of the AMU (Protocol No. 11 of 28.10.2021).

Introduction of research outcomes. The results of the study are being implemented in the clinics of the Mirkasimov Republican Hospital, the M. Javad-zade Urological Hospital, the N. Tusi Clinic and in the educational process of the Azerbaijan State Doctors Improvement Institute named after A. Aliyev.

Name of the facility where the research was implemented: Department of Stomatology and Maxillo-Facial Surgery of the Azerbaijan State Institution for Advanced Training for Doctors named after A. Aliyev, Central Research Laboratory of A. Aliyev AzSIATD, in the Republican Clinical Hospital named after M. Mirkasimov, in the clinic named after N. Tusi, in the Institute of Geology and Geophysics of ANAS, Baku.

Publications The main content of the work was published in 33 scientific works, including 18 articles (10 in republic, 8 in foreign editions), 11 theses, 2 manuals, 1 methodical recommendation and 1 Eurasian patent.

The volume and structure of the dissertation. The thesis is on 346 pages (399423 symbols), includes 67 tables, 35 figures and 24 charts. The work consists of introduction" (6 pages), literature review (51 pages), material and methods of research (24 pages), 4 chapters of own studies (179 pages), conclusion (26 pages), findings (2 pages), practical recommendations (2 pages), also the list of references (48 pages) which includes 436 sources including 15 in Azerbaijani, 209 in Russian, 212 in English.

MATERIAL AND METHODS OF RESEARCH

To fulfill the goal and objectives of the study we examined 318 patients with sialodenitis and sialosis against including the background of chronic kidney disease and diabetes mellitus. There were 81 patients with chronic sialodenitis, 137 patients with sialolithiasis, 40 patients with sialosis against the background of diabetes mellitus, 60 patients with sialosis against the background of chronic kidney disease (table 1).

Table 1
Distribution of patients by diagnosis, age and gender

| Age Disease | <20 | 21-30 | 31-40 | 41-50 | 51-75 | All over abs (%) | Male abs (%) | Female (%) |
|--|--------------|--------------|--------------|---------------|---------------|---------------------|-----------------|---------------|
| Chronic sialdenitis | 13 | 16 | 17 | 22 | 13 | 81 (25,5) | 35 (43,2) | 46 (56,8) |
| Sialolithiasis | 9 | 16 | 19 | 45 | 48 | 137 (43,1) | 78 (56,9) | 59 (43,1) |
| Sialosis diabetes mellitus on the back-ground | 0 | 4 | 8 | 11 | 17 | 40 (12,6) | 18 (45) | 22 (55) |
| Sialosis with chronic renal failure on the back-ground | 2 | 5 | 9 | 15 | 29 | 60 (18,8) | 34 (56,6) | 26 (43,4) |
| Total patients | 24 (7,55) | 41 (12,9) | 53 (16,7) | 93 (29,25) | 107 (33,6) | 318 (100) | 165 (51,9) | 153 (49,1) |

Depending on the pathology and stage of the disease, conservative and surgical treatment was carried out. The efficacy of treatment by groups of patients was estimated and comparative analysis of salivary gland diseases treatment efficiency was carried out. Clinical analysis of the dental status of patients included questioning and objective examination which volume was determined by the form of pathology of dental hard tissues, periodontal and oral mucous diseases. Depending on the pathology and stage of the disease, con-

servative and surgical treatment was carried out. The efficacy of treatment by groups of patients was estimated and comparative analysis of salivary gland diseases treatment efficiency was carried out. Clinical analysis of the dental status of patients included questioning and objective examination which volume was determined by the form of pathology of dental hard tissues, periodontal disease and oral mucous membrane diseases. Along with finding out the patients' complaints the reasons contributing to caries and its complications, chronic periodontal and oral mucous membrane pathologies were identified. The whole oral mucous membrane of the patients was thoroughly studied, namely color changes, edema, epithelium desquamation, lichenization, etc. When examining the lips, attention was focused on the state of integrity of the red border of the lips, the presence of cracks, ulceration.

To determine the condition of salivary glands in patients with carbohydrate imbalance, identify early signs of reactive-dystrophic diseases, and determine the risk group for the development of sialosis, we proposed a clinical examination chart, which was filled out together with the patient. During dental examination of all groups of patients we used general principles of diagnosis. The evaluation of salivary glands and oral cavity condition was started with the identification of complaints and medical history. Patient complaints were considered in chronological order. The beginning of the first manifestations and duration of the disease course were revealed. Particular attention was paid to the presence of burning, tingling, feeling of a foreign body in the oral cavity, feeling of dryness or, on the contrary, excessive saliva secretion and its nature. Indirect manifestations of xerostomia were of importance: sharp decrease of salivation during agitation, impossibility of eating without drinking water, necessity of drinking water at night because of sharp dryness of the mouth.

From the moment of the first acquaintance with the patient the color of the skin and visible mucous membranes, facial configuration, the presence of swelling in the area of one or more salivary glands were noted. We palpated the condition of tissues in the salivary glands area, consistency and mobility of the gland, its soreness and size, presence of lumps. Regional lymph nodes were examined.

The degree of mouth opening was noted. Examination of the vestibule of the mouth began with the lips, noting the color of the red border, examined the mucous membrane, its color, moisture, the condition of the orifice of the parotid salivary gland exit duct.

Examination of the oral cavity itself was carried out under good illumination with a shadowless reflector. Mucous membrane of the oral cavity, lip, cheek, molar, palatal, lingual - small salivary glands, as well as the mouth of the main duct of submandibular salivary gland were examined. Examination of these sections revealed manifestations of xerostomia in the oral cavity.

When examining the duct mouths, salivary glands were massaged, paying attention to possible characteristic changes of the secretion: the amount of secreted saliva, consistency, color, presence of flakes, clots, salivary clots in it. If stenosis, stricture or complete obliteration of the duct was suspected, the duct was probed.

The following indices were used to assess the state of oral tissues and oral hygiene: CFE, PMA papillary-marginal-alveolar index modified by Parma (1960) to assess the degree of inflammation of gingival tissues, oral hygiene index by Fedorov-Volodkina; sonographic and radiological studies were also conducted.

All the patients under study were monitored by an endocrinologist, a nephrologist, and a dentist; therefore, the necessary adjustments in the examination and treatment of the patients were made jointly. Clinical assessment of the results of treatment was based on the patients' complaints, their general condition, local signs of the course of the disease, and data from diagnostic methods.

Radiological examinations of the patients were carried out taking into account their dental status. Basically, these studies were conducted in the form of dental X-rays and panoramic-orthopantomograms performed on the apparatus "Orthopantomograph".

Ultrasound examination of large salivary glands was performed on an ultrasound scanner Logic S7 Expert (HRUS, GE Company, USA), Ultrasound scanner allowed us to examine the salivary glands with B-mode, Doppler mode (color, energy and spectral) and elastography.

Computed tomography was performed on a Presto multilayer tomograph (Hitachi, Japan) (thickness of axial scanning 3-4 mm, continuous spiral mode, and vertical size of the whole tomographic area about 10 cm).

The method of sialography was used to assess the condition of salivary glands structure. This is an additional method of X-ray examination of the glands with their preliminary contrasting.

Biochemical and immunological studies were performed in the laboratory of the Republican Clinical Urological Hospital named after Academician M.D. Javad-zade and in the Central Scientific Research Laboratory of the Azerbaijan State Institute for Advanced Training of Physicians named after A. Aliyev.

Collection of saliva for research was collected in the morning on an empty stomach after rinsing the mouth with water. 10 minutes after rinsing, the patient collected saliva in a container without stimulating salivation for 15-30 minutes. Saliva was subjected to sequential filtration through 3 layers of gauze. Then centrifuged 1500 rpm for 15 minutes. Aliquots of the supernatant were transferred into plastic Epindorf 2.0 tubes and stored at -30°C until use

The concentration of hydrogen ions (pH) in saliva was determined by the presence of acids in the oral fluid using a Universal Indicator Paper (Cobas, Germany) with a measuring range of 5.0 to 0.8 and a scale value of 0.2 pH.

Cytomorphological studies

Cytomorphological studies were performed before and after treatment. At each examination we took a smear from the surface of mucosal lesion (erosion or ulcer), which after drying were fixed in ethyl alcohol and stained by Romanovsky-Giemsa. The stained smears were studied under the microscope at magnification of $\times 1000$ with measuring the number of segmented leukocytes (SLW), lymphocytes (LM) and macrophages (MF) as well as epithelium cells of different maturity degree (basal, parabasal, thorny and superficial cells with pykemotic nuclei). The general type of the smear was determined: "non-inflammatory" in case of absence of inflammatory cells or their extremely insignificant quantity; "inflammatory" with significant SNL, Lm and MF. In the latter case the quantitative ratio

of cellular elements, in particular SNL (Lm + MF) - inflammation index (II) was also evaluated.

Determination of salivary flow rate - sialometry

Sialometry is a quantitative method to determine the secretory function of salivary glands per unit time. Saliva was collected in the morning on an empty stomach. The patients were advised: not to brush teeth, not to rinse the mouth, not to smoke, not to use chewing gum, if possible not to take medicines with water before the examination.

It is known that, as recommended by the Commission on Dental Health, Research and Epidemiology (CORE), International Federation of Dentists (FDI, 1991), the amount of oral fluid is in most cases a fairly accurate indicator of the degree of dryness of the oral cavity.

It is recommended to perform sialometry by spitting or free-flowing saliva. Depending on the sialometric findings the degree of xerostomia is determined.

Normal sialometry readings are 3.5 - 4.6 ml per 10 minutes;

Mild xerostomia - 2.4 to 3.4 ml per 10 minutes;

Moderate xerostomia - 1.1 to 2.3 ml per 10 minutes;

Severe xerostomia is 1.0 to 0.1ml per 10 minutes.

The normal salivary flow rate is 0.4-0.5ml/min.

Saliva pH tests

Saliva pH was determined using litmus tracers. It is evaluated on a 10 score scale. Saliva is considered acidic if the grade is less than 6.0, neutral at 6.0 to 7.0 and alkaline at 7.5 and above. Acid-alkaline equilibrium of mixed saliva was determined using an indicator paper (Universal Indicator Paper) from Cobas (Germaniya) with a range of change from 5.0 to 8.0 with a division price of 0.2 pH.

Determination of saliva viscosity

Viscosity of saliva was determined using a dental spatula and a slide with a drop of saliva on it (we evaluated the character of separation of the two surfaces in a moist environment). Viscosity of saliva was determined by V.V. Afanasiev's method by measuring the length of the saliva drop between the tweezers before tearing up to 5 mm - normal, 5-10 mm - I degree viscosity, more than 10 mm - II degree viscosity.

Determination of low and middle molecular weight substances (LMWSM) in saliva

LMMWS are metabolic intermediate products (uric acid, xanthine, pyrimidine, etc.) products of proteolysis and destruction of organs and tissues, incomplete protein digestion, deamination of amino acids, as well as various biological active substances, bacterial toxins, polyamines and phenol derivatives. Determination of LMMWS was performed in mixed saliva.

The principle of the method is that the wavelength at which an individual substance maximally absorbs light is a characteristic parameter of the substance and depends on its physical and chemical properties, based on which we can conduct qualitative and quantitative analysis of substances. Material to be tested: saliva - 1ml. Reagents: 15% trichloroacetic acid (TCA), 0.9% sodium chloride solution, distilled water. Instruments: centrifuge, spectrophotometer SF-26.

Process for the determination of LMMWS. To 0.5ml of saliva add 0.9ml of saline solution and add 0.5ml of 15% TCU. The tubes are mixed thoroughly and allowed to stand for 10 minutes, then centrifuged at 4000d for 30-40 minutes. For further study, 0.5 ml of supernatant is taken and diluted 10-fold by adding 4-5 ml of distilled water. Then spectrophotometrically measured between 238 and 306 nm.

Calculation of the result. Every 10th result, i.e. 244 nm, 254 nm, 264nm, etc. is used for the calculation. The results obtained are summarized. The substances' content was expressed in the conventional units, for which the received data are multiplied by 10 by formula $LMMWS = \Sigma (E_{244} + E_{254} + E_{264} + E_{304}) \times 10 \text{c.units}$.

Determination of cytokines in mixed saliva

Cytokine levels of interleukin IL-1 β , IL-2 and IFN- γ were measured in mixed saliva by enzyme immunoassay (ELISA) using Vector-Best reagent kit (Novosibirsk) on a Bio Screen MS-500 analyzer.

Reagent kits are designed for enzyme immunoassay determination of IL-1 β , IL-2 and IFN- γ concentrations in human biological fluids and culture media. The tests were performed according to the manufacturer's instructions.

For IL-1 β and IL-2 the sensitivity of the method is 2pg/ml. Meas-

uring range 0-500pg/ml.

For IFN- γ the sensitivity of the method is 2pg/ml. Measuring range 0-1000pg/ml.

To determine cytokines, mixed saliva was collected in containers by spitting. Obtained oral fluid samples were filtered through 3 layers of gauze, centrifuged at 1500 rpm for 10 minutes using the supernatant. Obtained oral fluid samples were collected in Eppendorf tubes and stored in the refrigerator at -20°C until used.

Glucose determination in blood and oral fluid

Glucose in blood serum and oral fluid was measured with "Human" kit on biochemical analyzer "BioScreen MS - 2000".

Determination of glycated hemoglobin HbA_{1c} in blood

Glycated hemoglobin HbA1 in blood was determined by Human kit on biochemical analyzer "BioScreen MS - 2000".

Blood HbA1 level in the range of 4.5-7.0% was normal, and more than 8.5% of glycemia was defined as diabetes mellitus.

Statistic processing

Statistical data processing was performed using medical software Microsoft Excel 2010. The obtained numerical material was presented in the form of arithmetic mean (M), mean error (m). Probability of differences (P) was calculated on the basis of U criterion (Wilcoxon-Mann-Whitney) between the groups. Differences were considered reliable at $P \leq 0.05$, highly reliable at $P \leq 0.01$, and not reliable at $P > 0.05$. Pearson's pair correlation coefficient (r) was used to determine interrelations between different parameters. For correlation estimation (r) we considered to be expressed moderately if $r < 0.3$; significantly - at $0.3 < r < 0.7$ and strongly expressed at $r > 0.7$. Direct and positive connection was considered to be a simultaneous increase of studied parameters values (r - positive), opposite or negative connection was considered to be an increase of one parameter at another's decrease.

Methods of treatment of sialolithiasis

A total of 137 patients with sialolithiasis treated were divided into 3 groups.

Patients only treated.

Patients having sialolithotripsy along with treatment;
Patients having surgical treatment.

Sialoliths were crushed using Karl Storz Duolith SD 1 device. The procedure was performed using the following crushing parameters: 2.6-4.6 bar, 9 Hz frequency and the total number of wave impacts 2500 to 4000 per procedure. Before the lithotripsy the size of the stone, its location in relation to the dilated duct and the angle of the lower jaw were determined by ultrasound (to facilitate targeting with the scanner during the crushing procedure). After the session the attention was paid to the condition of the skin above the gland, the presence of traces of blood from its duct.

In order to increase the efficiency of shock-wave influence in the crushing of stone in the duct of parotid salivary gland, in patients with complete adentia or partial adentia in the area of upper and lower jaw molars on the side of the affected salivary gland, during the procedure a metal medical tongue spreader was placed in the oral cavity in the projection of the parotid salivary gland duct. Sessions of sialolithotripsy were performed with the frequency of 1-2 sessions per week.

Investigations of mineral composition of salivary gland stones were carried out in the laboratory of the Institute of Geology of the Academy of Sciences of the Azerbaijan Republic. For this purpose diffractometry (rigaku miniflex 600) and infrared spectroscopy (X-ray fluorescent spectrometer S8 TIGER).

Treatment method for sialosis patients with type 2 diabetes mellitus

According to the results of the complex examination we diagnosed each patient and fixed the character of sialosis, the degree of disturbance of the salivary glands functional activity, periodontal tissues diseases, the state of oral hygiene. Individual plan of complex treatment of the patient was made according to the diagnosis. Local dental therapy was necessarily conducted against the background of the basic endocrinological correction of carbohydrate metabolism. Due to high prevalence of complicated caries all diabetic patients underwent surgical sanitation of oral cavity to prevent inflammatory

complications.

To treat sialosis during diabetes, lavage of the gland ducts was performed. Furacilin (antiseptic agent), trypsin (proteolytic enzyme) were used during lavage. Also a compress of saline with Levomecol ointment was put on the swollen parotid glands. Topically, no spa tablets twice a day, pilocarpine 6 drops three times a day, and suvas-tin preparation containing proteolytic enzymes to improve gland re-generation and repair. The following control methods were used to evaluate the results of treatment. Basic (clinical) one included: evaluation of the general state of a patient, absence of dryness complaints in the oral cavity, change of the gland sizes, its consistency, character of the gland ducts secretion. Laboratory: sialometry, examination of saliva viscosity.

The method of treatment of sialosis patients with chronic kidney disease

We examined 39 patients with sialosis and CKD who were treated with GD. All examined patients with sialosis and CKD we divided into 2 groups: control group - 16 patients whom we used conventional treatment for sialosis. Furacilin (antiseptic agent), trypsin (proteo-lytic enzyme) were used during lavage. Also a compress of saline with Luvomecol ointment was put on the swollen parotid glands. (lo-cal no spa tablets two times a day) And the main group (n=23) where we used sorbent of natural zeolite in the form of powder for 7-10 days applying it on the oral mucosa in addition to the basic treatment of sialosis.

The method of treatment of patients with chronic sialodentitis was as follows:

The patients were divided into two groups. Patients in the compar-ison group (n- 20 people) received traditional therapy, including anti-biotic therapy (ceftriaxone 1 g x 2 times a day), tablets tavegil twice a day for 5-7 days. Topical washing of parotid salivary gland duct with 3rd generation antibiotic cephalosporin (cef-triaxone), antiseptics (furacilin), enzyme (trypsin), and compress with saline and levomecol ointment. During the first days the secretion was taken for microflora examination and sensitivity to antibiotics. After sensitivi-

ty to antibiotics had been established, the antibiotic was changed for another one if necessary. On the 7th and 8th days the patients of the main group (n-25) additionally to the traditional therapy we performed local immunotherapy (3-4 times injection of stimulated autoleukocytes by immunophan into the duct of SG).

After we obtained pus-free saliva from the patients during parotid gland massage, we injected activated autoleukocytes into the duct of the parotid gland. For this purpose 5 ml of blood was taken from the ulnar vein in tubes with heparin in the morning hours. After centrifugation at 1500 rpm, two upper fractions - blood plasma and leukocyte layer - were taken from the tubes using a microdoser. Immunophan solution (0.1 ml per 5 ml of blood) was added to the samples obtained (50 µg/ml, UNOPP Bionox, Moscow) and incubated in a test tube for one hour in an incubator at 37°C. After incubation, physiological solution was added in a 1:3 ratio. The obtained stimulated leukocytes were divided into three aliquots and stored in a refrigerator until use. Patients underwent 3 sessions of applications with stimulated autoleukocytes. Injection of autoleukocytes into the parotid duct was performed three times every two days. It should be noted that the proposed method of therapy was carried out in the complex dental treatment.

RESEARCH RESULTS AND THEIR DISCUSSIONS

Clinical and laboratory findings in patients with chronic sialoadenitis

The results of the examination showed that the secretion of mixed saliva (oral fluid) in almost healthy people averaged 0.7 ± 0.03 ml/min.

The data obtained during the examination of patients indicate that the secretion of mixed saliva is statistically significantly reduced compared to practically healthy patients. ($p < 0,05$). Average value of mixed saliva amount in patients with chronic sialoadenitis was $0,3 \pm 0,01$ ml/min. Salivation in patients with chronic sialoadenitis was significantly reduced in 2,3 times ($p < 0,05$).

In addition to decreased salivation, the patients showed indirect signs of salivary gland hypofunction: no free saliva in the mouth,

frothy saliva, saliva thrusts when opening the mouth, and complaints of dry mouth.

The functional activity of the salivary glands was also assessed by the index of salivary viscosity. Before treatment, all patients in the control and main groups had grade 1 salivary viscosity. The results of the saliva viscosity test showed that after the treatment 14 (70%) patients in the control group and 15 (60%) patients in the main group had grade 1 saliva viscosity, there was no grade 2 saliva viscosity detected. After treatment, salivary viscosity decreased in the control group and was 6.25 ± 0.2 mm, which was 1.3 times higher than in healthy persons ($p < 0.05$), i.e. salivary viscosity indicators were not restored in the process of treatment with basic therapy.

Salivary viscosity in the main group before treatment averaged 7.6 ± 0.25 mm, which was statistically significantly 1.6 times higher relative to virtually healthy people. After basal treatment and local immunocorrection, salivary viscosity decreased 1.3 times compared to the pre-treatment data and was 1.1 times lower than in comparison group patients.

Other important indicators of saliva are acid-base balance - pH. Determination of oral fluid pH in patients with chronic sialoadenitis showed that this index averaged 6.3 ± 0.07 units. In the group of practically healthy people the pH was $6,9 \pm 0,06$ units.

The use of local immunotherapy in patients with chronic sialoadenitis showed that in the main group 20 out of 25 patients showed "improvement", which was 80%.

Saliva secretion in the main group before treatment averaged 0.27 ± 0.01 , which was significantly lower by 2.6 times compared to the data in virtually healthy people. After basal treatment in combination with local immunocorrection the average amount of mixed saliva was $0,43 \pm 0,01$ and was 1,2 times higher than in the comparison group ($p < 0,05$).

It should be noted that the functional state of salivary glands according to sialometry data was decreased in all patients before treatment and the 1st degree of xerostomia was determined in 24 (53,3%) patients with chronic sialoadenitis, and the 2nd degree of xerostomia was determined in 21 (46,7%) patients.

In order to study the state of local immunity, we studied the main cytokines (IL-1 β , IL-2, and IFN- λ) in the mixed saliva of patients with chronic sialo-denitis in the dynamics of basal and complex treatment. The choice of such tests was necessary to study the effect of different therapeutic regimens on the local immune status and to identify the efficacy of the therapy. The content of cytokines in saliva was studied in the dynamics of the basic (control group) and complex treatment (main group). The treatment of the main group patients was complex and included general and local measures. Local immunocorrection with the use of stimulated autoleukocytes was used in the treatment of the main group patients.

There was a high reliability of differences in the content of IL-1 β before and after treatment in the comparison group and in the main group, but more pronounced in the main group ($p < 0.002$). A significant difference ($p < 0.05$) was found between the content of IL-1 β in mixed saliva after treatment between the patient groups. The mean value of IL-2 level in saliva after treatment in the comparison group was 17.7 ± 0.5 pg/ml, in the main group 14.7 ± 0.4 pg/ml. After treatment the IL-2 level in the control group decreased by 26,6%, in the main group by 38,8% ($p < 0,05$) relative to the pre-treatment data ($p < 0,05$). We also found that there was a significant decrease in IFN- γ in saliva in comparison group patients and in the main group before treatment. After treatment according to the traditional scheme, the IFN- γ level in the control group increased up to 7.2 ± 0.2 pg/ml, increasing 1.1-fold compared to its value before treatment. At the same time when including local immunocorrection into the treatment scheme, increase of IFN- γ in the main group was more significant and averaged $8,0 \pm 0,1$ pg/ml, which was more than 1,3 times higher than the initial level ($p < 0,05$).

In the dynamics of treatment in the comparison and main groups, the local immunity was studied by estimating the cytomorphological parameters of oral mucosa. Cellular composition of smears-prints before treatment was characterized by the predominance of leukocytic cells and neutrophils appeared to be the major fraction. As is known, neutrophils play the leading role in inflammation induction. They constantly migrate from the bloodstream to the tissues and per-

form their protective functions.

Massive neutrophil infiltration constitutes the most important element of acute inflammatory reaction and is one of the nonspecific defense mechanisms. Neutrophils as phagocytic cells are able to provide a wide range of responses to activating stimuli. There is a release of metabolic products, proteolytic enzymes, cytokines, lysozyme, lactoferrin, etc. Using these indices we can conclude that from the cytomorphological point of view in the comparison group the II has only a tendency to decrease, and basal therapy does not remove the picture of inflammation and the average II in the group was $1,23 \pm 0,03$.

After treatment using local immunocorrection the clinical effect consisted in earlier normalization of temperature, increased salivation and decreased viscosity of saliva. Also local clinical signs of the arrest of inflammatory process, purification of salivary gland secret and decrease of IB down to $1,08 \pm 0,03$ were determined.

After the conducted course of treatment in patients with chronic sialadenitis we studied phagocytic activity of neutrophils in the FAN-1 test.

In the main group (traditional therapy + local immunocorrection) a statistically significant increase in phagocytic activity of neutrophils in the FAN-1 test was registered. Thus, in the main group FAN-1 initially was $5.8 \pm 0.3\%$, and after treatment increased up to $9.4 \pm 0.3\%$. There was a decrease in the percentage of FAN-2 to $5.8 \pm 0.2\%$.

FAN-1 and FAN-2 were normalized completely as a result of treatment only in some patients, but not in both indices and unequally in the study groups.

FAN-1 in the comparison group normalized in 50% of the patients, and in the main group - in 88%, which is significantly higher. FAN-2 value had positive dynamics in 36% of patients in the main group and 15% of patients in the control group.

After treatment, the neutrophil count decreased by 37.8% in the main group and by 9.6% in the comparison group. The percentage of monocytes decreased by 12.6% in the comparison group and by 27% in the main group. The percentage of lymphocytes decreased more

considerably in the comparison group by 11.4% and by 27.7% in the main group. At the same time there was an increase in the level of epithelial cells in the comparison group by 1.5 times and in the main group by 2.9 times. An increase in the level of epithelial cells promotes an increase in their adhesive activity and increases the efficiency of the mechanisms of sanitation of the oral cavity. The IB decreased down to $1,08 \pm 0,03$ and statistically insignificantly differed from the data in the group of practically healthy people $0,91 \pm 0,03$.

The mentioned changes are caused by the regulatory influence of the local immunocorrection on the innate immunity system and permits to avoid an abrupt activation of the protective mechanisms, which leads to their depletion in the background of the inflammatory process caused by bacterial flora.

The study of TP (total protein) concentration in the mixed saliva of patients with chronic sialadenitis showed an increase in its concentration in all patients before treatment. The average salivary OB level in comparison patients before treatment was $1,4 \pm 0,06$ g/l with fluctuations of 0,8-1,8 g/l, median - 1,5 g/l. The OB content in the main group patients before treatment averaged $1,35 \pm 0,04$ g/l with fluctuations of 0,7-1,9 g/l, median 1,5. The salivary OB content in the patients of the comparison and basic groups was 14,3 % higher than that in the healthy controls ($p > 0,05$). The OB content in the patients of the comparison group after the basic treatment remained elevated by 6,3% relatively to the practically healthy persons and was $1,28 \pm 0,06$ g/l with the parameter $1,2 \pm 0,03$ g/l in the practically healthy persons. In the main group the level of OB corresponded to the data of practically healthy people. Another marker of inflammation the level of albumin in the oral cavity before treatment was reduced and on the average in the comparison group was $0,41 \pm 0,01$ g/l, in the main group - $0,48 \pm 0,05$ g/l. The albumin content in the saliva of the patients in the comparison group and the main group was 4-18% lower than the albumin content in the practically healthy people. After treatment, the content of albumin in the comparison group increased and averaged $0,62 \pm 0,04$ g/l in the group, and $0,56 \pm 0,02$ g/l in the main group. The value of globulins in comparison group patients before treatment was $0,96 \pm 0,03$ g/l. The level of globulins in the main

group was also increased and was $0,86\pm 0,05\text{g/l}$. The content of globulins after treatment in the 2 groups of patients was close to the practically healthy values and was $0,66\pm 0,04\text{ g/l}$ and $0,64\pm 0,03\text{ g/l}$ respectively.

Before treatment, the ratio of albumin and globulin A/G - coefficient was reduced to $0,5\pm 0,04$ in the comparison group and to $0,65\pm 0,07$ in the main group. After treatment, the A/G ratio of saliva in the comparison group increased by 48.9% relative to the data before treatment, and in the main group it also increased significantly by 34.3% ($p<0.05$) and these changes were statistically significant.

LMMWS (low and middle molecular weight substances) were determined in the mixed saliva of patients with chronic sialadenitis as acute phase criteria as indicators of endogenous intoxication.

During the examination of the control group patients after the conventional treatment, there was no normalization of the LMMWS level, there was only the tendency of Σ LMMWS decrease. So, if before the treatment the level of Σ LMMWS was 0.69 ± 0.058 units, after the treatment it averaged 0.67 ± 0.039 units; i.e. the decrease by 2.8 % was registered and this decrease was statistically insignificant. There was no normalization of the long wavelength LMMWS at 294 nm and 304 nm. There was no significant decrease in LMMWS at 244 nm and 254 nm. To reduce the level of endogenous intoxication in the future, such patients required a longer period of treatment with the use of antibiotic therapy.

Accumulation of LMMWS in mixed saliva was also noted in the main group before treatment. There was normalization of long-wave LMMWS at wavelengths of 294 nm and 304 nm. There was a significant reduction in LMMWS at wavelengths of 244 nm, 254 nm and 264 nm. Thus, a marked decrease in the important parameter of endogenous intoxication - LMMWS - was observed in the patients of the main group. We have found that local immunocorrection reduces the severity of the local inflammatory reaction induced by microorganisms and thereby provides a reduction in the infection load in the oral cavity, which in turn contributes to the reduction in the severity of endogenous intoxication.

Thus, the study allows us to conclude that patients with chronic

sialadenitis have local immune changes in the content of the main cytokines in the oral cavity. Assessment of saliva proteins at the stage of clinical manifestations made it possible to establish the increase of TP and globulins and decrease of albumins that characterized inflammatory process in the oral cavity. Increase of neutrophils, lymphocytes, monocytes on the background of IL-1 β and IL-2 hypercytokinemia and increase of endogenous intoxication were observed.

The use of traditional therapy in patients with chronic sialadenitis leads to incomplete normalization of the state of local immunity. Inclusion of local immunocorrection in complex therapy permits to normalize both indices of adaptive immunity, phagocytic activity and cytokine regulation.

The carried out researches allow to suppose that in pathogenesis of chronic sialadenitis an important role is played by local immune reactions. On this background in most cases using only antibacterial therapy and sanation of salivary glands in these patients is insufficient. In chronic sialadenitis it is necessary to add local immunocorrection to the scheme of medical interventions. It is evident that immunofan has a pronounced immunomodulatory effect due to the influence on the adaptive and innate immunity. Complex therapy contributes to the reduction of inflammatory proteins, cytokines, AI products and decreases the number of relapses. This is the basis for the use of local immunocorrection in the treatment of patients with chronic sialoadenitis.

After clinical and laboratory examination we propose a 2-stage method of treatment of patients with chronic sialoadenitis, consisting of two consecutive courses.

Stage 1 - Antibiotic therapy, irrigation of salivary gland ducts with antiseptic solutions (furacilin, chemotrypsin), desensitizing therapy, enhancement of secretory function of salivary glands.

Stage 2 - stage 7-8 days after purulent content of salivary glands is cleared, local immunity should be corrected. As the practice of the last decades shows, there is a steady increase of recurrence frequency of sialadenitis and almost every patient faces the recurrence of exacerbation. As our studies have shown in the prevention of relapses of

chronic sialadenitis, a positive result can be achieved with 2-stage treatment.

Results of clinical and laboratory studies of patients with sialosis on the background of type 2 diabetes

Clinical-laboratory and functional-diagnostic examination was performed in sialosis 40 patients with type 2 diabetes mellitus (insulin-independent). The patients were aged from 26 to 82 with the disease duration from 2.1 to 9.9 years.

The purpose of the study in this section was to assess the nature of physico-chemical, biochemical, immunological and cytological parameters of saliva in the dynamics of basal and complex treatment.

The first group of patients ($n = 15$) with type 2 diabetes and the age of the disease up to 5 years, when the pathogenic effects of diabetes has time to appear, but it is not yet obscured by the presence of "stimulated" by diabetes various somatic diseases. The duration of type 2 diabetes in the 1st group of patients averaged 3.8 ± 0.2 years, the blood glucose level was 8.2 ± 0.3 mmol/l HBA1- $7.8 \pm 0.3\%$

In the 2nd group of patients ($n=25$) with sialosis and type 2 diabetes over 5 years, the average duration of disease was 8.8 ± 0.2 years blood glucose level- 8.3 ± 0.2 mmol/l HBA1- $8.2 \pm 0.2\%$

The following controls were used to assess the results of treatment. Basic (clinical) ones included: evaluation of the patient's general state, absence of complaints on dryness in the oral cavity, change of the gland's size, its consistency, character of the secret from the gland's ducts. Laboratory controls: sialometry, examination of saliva viscosity. The comparison group consisted of patients with diabetes mellitus type II without enzymotherapy (Suvastin).

Examination of a diabetic patient consisted of a thorough analysis of complaints, history taking and objective examination of the patient. In our researches we established a trusting contact with the patients, asked guiding questions to help the patients to tell successively the history of the disease, during the conversation we determined the neuro-psychological status, the person's intellect, and on this basis we analyzed the complaints, the sequence of the disease symptoms. Investigations were conducted according to all rules of deontology, taking into account the peculiarities of personality.

During clinical examination of the patients, 7 persons experienced a decrease in taste sensitivity to salty and sour food, whereas 11 persons did not have any complaints.

During the interview with patients with diabetes mellitus we found out that the nature of complaints depended on the degree of compensation of the underlying disease.

In 18 patients with less than 5 years of insulin-independent diabetes there was no permanent sensation of xerostomia in the oral cavity, only temporary dryness in the mouth appeared during a long conversation or during stress. Eleven people drew attention to decreased taste sensitivity to salty and sour food. Nine patients had a recurrent burning sensation in the back of the tongue. 16 patients complained of painless mobility of teeth and early loss of them.

In the group of patients with more than 5 years of insulin-independent diabetes, 12 patients complained of painless bilateral "swellings" in the parotid-mandibular areas. Patients indicated frequent feeling of dryness of oral mucosa, which was associated with an exacerbation of diabetes mellitus.

Complaints of dryness in the oral cavity during conversation, emotional excitement, as well as when eating, bothered 9 patients with a compensated form of insulin-dependent carbohydrate metabolism disorder. Unusual taste sensations were noted by 3 people from this group. Five patients complained of burning in the back of the tongue. All patients in this group noticed bleeding of gums when brushing teeth, as well as mobility of teeth and their displacement.

11 patients with more than 5 years of diabetes complained about the constant presence of dryness in the oral cavity, intensifying during meals, so many of them had to drink water with their food. During a long conversation patients of this group felt dryness especially acutely, its intensification occurred during emotional stress. 10 people noted that they had to wake up at night to drink water, and in the morning it was difficult to open their lips and open their mouth. All patients were concerned that two symmetrical masses became noticeable in the submandibular areas when the head was tilted backward, painless on palpation. Nine people complained of decreased taste sensitivity to sweet, salty, sour and bitter, reported difficulty

swallowing food and pain while eating. Four patients had burning of the oral mucosa, pain in the tongue, and an increase in its size. Two patients could not wear removable dentures due to increased mucosal sensitivity. All patients reported painful and bleeding gums when brushing teeth, bad breath, painful tooth mobility and tooth displacement. 3 individuals indicated that they even had to give up some personal dental hygiene measures. 1 patient complained of facial pain occurring during an exacerbation of the underlying disease. Some patients in this group noticed a sharp body weight loss.

All patients with diabetes noted rapid tooth decay and, as a consequence, frequent visits to the dentist.

While collecting anamnestic data we clarified the presence of etiological factors, peculiarities of the course of pathological processes and their pathogenetic relationship. Diagnosis of the underlying disease: glucose tolerance disorder, type I diabetes mellitus or type II diabetes mellitus, degree of compensation was made on the basis of an endocrinologist's report.

The patients were asked about the frequency of dental check-ups and their regularity. 50% of all the examinees (40 people) noted that they visit the dentist 3-4 times a year. 30 patients with type II diabetes observed swelling of parotid salivary glands, and 20 patients reported periodic enlargement of submandibular salivary glands. Moreover, the patients associated the enlargement of the glands with the rise of sugar curve. At the same time, the patients noted that the symptoms of xerostomia were especially acute when the salivary glands were enlarged.

Clinical examination of each group of patients was aimed at identifying dental manifestations, taking into account the individual characteristics of the course of endocrinological disease in each individual patient.

Visual examination of the group of patients with insulin-independent diabetes mellitus less than 5 years gave the following picture. Face - symmetrical, skin - physiological color. Bimanual palpation of salivary glands in 15 patients revealed that parotid salivary glands had smooth, even surface, were of soft consistency, painless, and were located within anatomical borders. The glands were

not fused with the surrounding tissues. Lymph nodes could not be palpated. In the oral cavity in 14 patients interdental papillae were enlarged, pale pink in color, dense to the touch; in 4 patients slightly edematous and hyperemic interdental papillae bled when probing. Oral mucosa was pale pink in color, poorly moistened. Free saliva was present in small amount, frothy in appearance. The back of the tongue of 9 persons had white-gray plaque, tightly adherent to the underlying mucosa. Only 7 persons had white plaque easily removed from slightly swollen surface. Apertures of parotid gland ducts in all patients were weakly expressed, when massaging the gland a few drops of transparent saliva were secreted from the "stenon" ducts. Saliva secretion by submandibular glands was sufficiently preserved.

During the examination of 12 patients with insulin-independent diabetes mellitus over 5 years we could see symmetrical swellings in the parotid-mandibular areas. The skin over them was not discolored and not folded. During bimanual palpation, increased in volume, salivary glands were smooth, painless, not adherent to surrounding tissues, elastic consistency. Regional lymph nodes were not determined.

Red border of lips was dry, 7 people had cracks of lips, 4 people had "gray scale-covered" itches in the corners of mouth. In the oral cavity the interdental papillae were enlarged, edematous, areas of hyperemia were interspersed with areas of cyanosis, palpation of the gums was painful, bleeding was evident. Two patients had pus from periodontal pockets. The back of the tongue of all patients was covered by a gray plaque that was difficult to remove. Five patients had small areas of erosions on the tongue in addition to the plaque. Oral mucosa of this group of patients was atrophic, sticky, pale pink in color, only in the area of the bottom of the mouth there was a small amount of free, frothy saliva. The mouths of the "stenon" ducts were atrophic. Massaging the parotid salivary glands did not yield any secretion from the ducts.

Visual examination of the maxillofacial region of 9 patients with insulin-dependent diabetes mellitus less than 5 years old did not reveal any changes. Whereas bimanual palpation of the floor of the oral cavity, in the submandibular areas revealed a slight, painless in-

crease of salivary glands within the anatomical boundaries. Glands had smooth, even surface, soft consistency, mobile, not fused with surrounding tissues. Regional lymph nodes were not palpated. In the oral cavity in all patients of this group interdental papillae were enlarged, edematous, had glossy surface, when probing they bled, there were areas of hyperemia and cyanosis. Oral mucosa was poorly moistened, atrophic; the back of the tongue was covered with dense gray plaque in 100% of cases. Apertures of salivary gland ducts, especially "wartons" were weakly expressed. When massaging submandibular glands a few drops of transparent saliva were secreted, whereas when massaging parotid glands the secret was secreted in sufficient quantity. There was little free saliva, which looked frothy.

During external examination of 11 patients with insulin-dependent diabetes mellitus for more than 5 years, attention was drawn to dry lips, cracks covered with red blood crusts in some patients. In the corners of the mouth, there were "hard spots". Facial skin was physiologically colored. All subjects in this group had two symmetrical "swellings" in the submandibular areas. On bimanual palpation they were enlarged in size, painless, smooth salivary glands of elastic consistency, not adherent with surrounding tissues. Lymph nodes were not determined. In the oral cavity the mucosa was atrophic, sticky. Interdental papillae were enlarged and hyperemic, bleeding when probing. The tongue of all patients was rough, cracked, covered with gray, indelible plaque. There was no free saliva in the oral cavity. The mouths of the "warton" ducts in all patients of this group were weakly pronounced, atrophic. Massaging of submandibular salivary glands did not obtain a secretion from the mouths. Sublingual rollers were covered with white removable plaque, edematous.

Tremes between teeth were found in almost every patient of these groups, as well as Popov-Godon's phenomenon and multiple complicated caries. There were significant differences ($p < 0,05$) in KPU in patients with type II ($19,05 \pm 3,05$; $19,25 \pm 3,88$) diabetes compare to the comparison group ($9,15 \pm 3,07$). Based on which we can conclude that patients with endocrine pathology have high caries intensity and low tooth hard tissue resistance, saliva sediment has high demineralizing and utilizing activity.

When comparing the indices according to the duration of the disease, no significant differences in the CFE were revealed ($p > 0.05$).

To determine the severity of gingivitis we used the papillary-marginal-alveolar index in Parma modification, the most accessible to the practitioner. Authentic increase ($p < 0.05$) of PMA indices was revealed in patients with insulin-independent diabetes mellitus in comparison with the control group that allows to judge about the generalized inflammatory process in periodontal tissues.

PMA indices in patients with insulin-independent diabetes mellitus ($30,11 \pm 3,16\%$; $73,75 \pm 6,69\%$) were reliably higher than those of the comparison group ($7,05 \pm 2,62\%$) and testified to widespread inflammatory process in periodontal tissues ($p < 0,05$).

Hygienic condition of the oral cavity was determined according to the method of Y.A. Fedorov, V.V. Volodkina. This index allowed to form an opinion about the regular and proper care of the oral cavity. In patients with diabetes mellitus type II more than 5 years, the average value of the Fedorov-Volodkina index was 2.44 ± 0.5 , indicating poor oral hygiene. In patients with diabetes mellitus type II less than 5 years this index was significantly lower and was $1,8 \pm 0,203$, oral hygiene - satisfactory ($p < 0,05$).

A direct correlation between the level of oral hygiene and periodontal tissues condition was revealed. Due to bleeding gums, painfulness, some of the examinees were sparing themselves, oral care was irregular, so the indicators of the Fyodorov-Volodkina index increased.

Thus, studies have shown that in patients with type II diabetes especially > 5 years, the dental status of the patient deteriorated significantly and also depended on the severity of the disease.

The above results of the clinical examination allow us to say that the groups of patients were selected correctly and can be used to conduct studies of mixed saliva and detection of changes in the salivary glands, as well as to study the results of treatment of salivary gland pathology.

The results of studies in 10 patients in the comparison group and 15 patients in the main group showed that salivary secretion before treatment was reduced and averaged $0,31 \pm 0,03$ ml/min and

0,29±0,02 ml/min, and these values were 1,2 times lower than in healthy persons ($p<0,05$). Saliva secretion in the main group after basal treatment in combination with enzymotherapy increased up to 0,67±0,02 ml/min and was 1,2 times higher than in the comparison group ($p<0,05$).

The results demonstrate that the secretion of mixed saliva was significantly reduced before treatment and did not recover to normal after basal treatment. After complex treatment, positive results were obtained with regard to salivation in the main group of patients.

Salivary viscosity before treatment was increased in the patient groups and averaged 7.3±0.4 mm in the comparison group and 7.2±0.2 mm in the main group. After treatment, the saliva viscosity decreased in the comparison group and averaged 5.8±0.21 mm, which was 1.3 times ($p<0.05$) more than in patients nearly healthy i.e. indexes of saliva viscosity didn't restore completely after the conducted basic therapy.

After the basic therapy and enzymotherapy the viscosity of saliva decreased 1,4 times ($p<0,05$) relative to the pre-treatment data and statistically insignificantly differed from the data for healthy people ($p<0,05$).

It has been shown that cytokines (IL-1, IFN- γ and others) can stimulate the immunoinflammatory process in type 2 diabetes mellitus patients. Cytokines, being intercellular mediators of immune system, determine not only the character of inflammatory processes, but also regulate cell reproduction and repair, participate in pathological processes leading to fatty tissue inclusion as well as form insulin resistance.

Proinflammatory cytokines form an inflammatory reaction leading to inhibition of insulin production by β -cells of islets of Langerhans, subsequently causing their death.

The results of the studies showed that enzymotherapy, in contrast to basic therapy, was accompanied by a tendency toward normalization of the cytokine profile in RA and was accompanied by a decrease in the elevated indices of IL-1 β and IL-2 and an increase in IFN- γ . Basal therapy caused normalization of these parameters, but their level in most cases differed significantly from the values of

practically healthy patients (table 2).

Table 2

The content of cytokines in gastric cancer in patients with sialosis and type 2 diabetes in the dynamics of treatment (M±m)

| | Practically healthy (n=10) | Comparison group (n=10) | | Main group (n=15) | |
|--------------|----------------------------|-------------------------|-----------------|-------------------|-----------------------|
| | | Before treatment | After treatment | Before treatment | After treatment |
| IL-1β, pq/ml | 45,2±4,8 | 46,3±2,5 | 46,2±2,3 | 48,4±0,8 | 45,0±0,4 [^] |
| IL-2 pq/ml | 11,4±2,1 | 13,6±0,3 | 13,3±0,3 | 13,9±6,4 | 11,9±0,2 [^] |
| IFN-γ pq/ml | 8,8±0,8 | 6,9±0,3* | 7,3±0,2 | 6,7±0,2* | 8,3±0,1 [^] |

Note: *- statistically significant differences in relation to practically healthy (p<0.05); ^- statistically significant differences between groups of patients

Thus, the inclusion of enzymotherapy into the complex therapy of patients with sialosis on the background of type 2 diabetes mellitus in contrast to the traditional methods of therapy allowed to provide more rapid positive clinical dynamics, namely, under the influence of this drug in a short time there was increased salivation, reduction of swelling and disappearance of the feeling of dryness. The cytokine profile was normalized along with a faster resolution of clinical symptoms due to a decrease in the inflammatory mediators IL-1 β and IL-2 in the RA and increase of IFN-γ by the end of treatment.

Sialosis patients against the background of type 2 diabetes before treatment revealed changes in the cytological profile of smears-prints, which was expressed in neutrophilosis, lymphocytosis, monocytosis and reduction of epithelial cells at the local level. Neutrophilosis was accompanied by functional disorders of phagocytosis, which was manifested by a decrease in the number of neutrophils phagocytizing autoflora and an increase in the percentage of destructive neutrophils in the FAN-2 test.

After baseline therapy in comparison group 2 and after complex

therapy in the main group 2 with enzymotherapy, the patients showed clinical improvement. Clinical improvement corresponded to the data of cytomorphological studies. In both groups of patients after treatment a decrease in the level of neutrophils, lymphocytes, monocytes and the inflammation index (II) was revealed. Percentage of neutrophils after treatment in comparison group 2 decreased by 4.6%, in the main group 2 by 17.8%. Percentage of monocytes after treatment decreased in comparison group 2 by 8.3% and by 15.6% in the main group. Along with this the specific weight of lymphocytes decreased in the control group by 6.3% and 8.3% in the main group. The number of phagocytes actively phagocytizing autoflora increased in the comparison group by 4,8%, and in patients with enzymotherapy by 7,8%. All these data indicate a decrease in the inflammatory process and an increase in the protective forces and nonspecific resistance of the oral cavity in patients with sialosis and type 2 diabetes after comprehensive therapy.

A comparative analysis of the levels of albumin against the background of treatment in 2 groups of patients showed no statistically significant changes. There was a decrease of the globulins from $0,84 \pm 0,02$ g/l up to $0,7 \pm 0,03$ g/l ($p < 0,05$) against the background of Suvastin complex therapy, and in the comparison group there was a tendency for the globulins to increase from $0,77 \pm 0,06$ g/l up to $1,02 \pm 0,02$ g/l ($p < 0,05$). These changes resulted in the reduction of A/G coefficient in the comparison group to $0,53 \pm 0,02$ and increase of A/G coefficient in the main group from $0,67 \pm 0,07$ to $0,75 \pm 0,05$ ($p < 0,05$).

Thus when comparing the methods of treatment used with regard to the protein component there was found out that in the main group of patients with sialosis in the background of type 2 diabetes mellitus the results were considerably better which can be explained by the use of enzymotherapy in treatment.

Changes in LMMWS levels in patients with sialosis with type 2 diabetes indicated the intensity of catabolic processes and accumulation of low and middle molecular weight metabolites in RM before treatment. After sialosis therapy, it is advisable to conduct a study of LMMWS in RW, which can be used as an integral indicator of meta-

bolic disorders in the oral cavity, as well as a parameter characterizing the effectiveness of treatment.

Thus, the determination of biochemical and immunological parameters of the oral cavity in patients with sialosis and type 2 diabetes mellitus with a course of >5 years indicate that in general they are characterized by the same changes as in patients with sialosis and type 2 diabetes mellitus ≤5 years. The essence of these changes was determined by the accumulation of endotoxemia products (LMMWS), the appearance of laboratory signs of inflammation (increased IL-1 β , IL-2, inflammation index) and suppression of local immunity factors. The studies revealed that the correction of immune and biochemical changes can be carried out with enzyme preparation Suvastin, which has a wide range of effects with anti-inflammatory and immunomodulatory activity.

Clinical examination and treatment results for patients with end-stage chronic renal disease receiving outpatient program hemodialysis

The next section was devoted to determining the effectiveness of sorbent therapy in patients with sialosis against a background of CKD.

We observed 60 patients with the terminal stage of chronic renal failure developed against the background of previous glomerulonephritis (34%), pyelonephritis (20%), diabetic nephropathy (15%), polycystic kidney disease (9%), hypertensive nephroangiosclerosis (8%), congenital and hereditary kidney damage (5%), interstitial nephritis (3%), renal amyloidosis (2%), and chronic renal failure of unknown etiology (7%).

In the M. Mirkasimov Republican Hospital and the laboratory of the ASATFD. A. Aliyev we conducted additional laboratory and clinical studies and treatment of 39 patients, who were divided into two groups depending on the duration of GD-treatment. The first group included 12 patients with less than 5 years of GD-treatment and the second group consisted of 27 patients with more than 5 years of GD-treatment. The average duration of GD treatment in group 1 was 2.5 ± 0.4 years (minimum 0.5 years, maximum 5 years). In the second group 9.1 ± 0.6 years (minimum 6, maximum 14 years). The

age of patients in the first group averaged 49.8 ± 3.7 years (minimum 31, maximum 78 years), in the second group 52.3 ± 3.1 years (minimum 18, maximum 87 years).

Our attention was attracted by the drug "Azeomed" relating to the group of sorbents on the basis of zeolites. Zeolites have expressed sorption qualities thanks to which they reduce the degree of organism intoxication at any pathological processes. However, the use of zeolite-based sorbents in dentistry is still limited.

We divided all the patients with sialosis and CKD we examined into 2 groups: the control group consists of 16 patients for whom we used the conventional treatment (irrigation of the gland ducts. Furacilin (antiseptic agent), trypsin (proteolytic enzyme) were used during lavage. Besides, brine compress with Luvomecol ointment was put on the swollen parotid glands. Locally No spa tablets two times a day and the main group (n=23) for which besides basic sialosis treatment we used sorbent natural zeolite in powder form for 7-10 days putting it on the oral cavity mucosa.

Concentration of urea in RL before treatment in patients with sialylozygia was 2.4 times higher ($p < 0,05$) and averaged 20.5 ± 1.1 mmol/l in the comparison group and 20.7 ± 0.8 mmol/l in the main group. At the same time, in the comparison group the decrease of urea concentration after traditional therapy was statistically insignificant ($p < 0,05$). Significant decrease of urea concentration was determined by us in the main group, where its level after the treatment was 16.5 ± 0.5 mmol/l. The observed decrease of urea is associated with the use of natural sorbent zeolite, capable of reducing the level of endotoxins, which includes urea. Thus, biochemical studies in patients with sialosis and CKD before treatment in all patients showed an increase in creatinine and urea in RL. In the course of oral correction in patients with sialosis the best results have been obtained with application of natural zeolite, which was determined by local decrease of urea by 20.2% and creatinine by 12.1% as compared with the comparison group: urea by 4.8%, creatinine by 5.2%. Total treatment efficacy in creatinine and urea in the comparison group was 5,2%, while in the main group - 16,2%.

The results of our studies showed that the viscosity of saliva was

increased in all patients with sialosis in the comparison group and the main group before treatment. After treatment, viscosity tended to decrease, and the degree of decrease correlated with the rate of salivation in both the comparison and main groups. The decreased salivation rate and increased salivary viscosity detected during the study are obviously due to dystrophic changes in the SG as well as to kidney disease.

Our results show that the pH of mixed saliva in patients with sialosis and CKD was shifted towards alkaline. Increased pH values of the RL may be associated with both an increase in bicarbonates and an increase in the amount of ammonia in patients with CKD. Ammonia is formed in the process of urea hydrolysis by ureolytic bacteria. The average pH of the mixed saliva in the comparison group was 7.6 ± 0.1 units, and in the main group - 7.7 ± 0.05 units. The performed basal and comprehensive treatment allowed to lower the pH in saliva to 7.5 ± 0.1 units in the comparison group and to 7.4 ± 0.1 units in the main group. Thus, the use of natural zeolite insignificantly affects the rate of secretion of its viscosity and to a greater extent shifts the pH from alkaline to neutral.

Thus, in the groups of patients before treatment, salivary flow rate was significantly reduced and was 6.3 ± 0.02 and 0.32 ± 0.01 ml/min, respectively. Viscosity and pH were significantly increased and were 7.6 ± 0.3 cm, 7.5 ± 0.2 cm and 7.6 ± 0.1 units and 7.7 ± 0.05 units, respectively.

The use of sorbent therapy with natural zeolite in the complex treatment of patients with sialosis and CKD being on GD treatment did not reveal reliable quantitative results in terms of physico-chemical indices of OL.

Cytological examination revealed that the percentage of neutrophils, monocytes, and lymphocytes in the comparison group decreased statistically insignificantly after the treatment. At the same time the percentage of epithelial cells increased statistically significantly ($p < 0.05$). The percentage of phagocytic cells increased in the FAN-1 test statistically insignificantly, while the percentage of destructive neutrophils (FAN-2) did not change and was $6.4 \pm 0.2\%$ after treatment.

Before treatment, the level of IL-1 β was 53.6 ± 1.3 pg/ml in the comparison group and 53.2 ± 0.9 pg/ml in the main group. The increased concentration of proinflammatory cytokine IL-1 β was evidence of an inflammatory process in the oral cavity of sialosis patients. After treatment in the comparison group, despite the fact that patients received general and local medical therapy, the content of IL-1 β didn't decrease statistically reliably ($p < 0,05$) and averaged $51,4 \pm 1,2$ pg/ml in the patient group. After sorbent therapy in the main group there were positive dynamics of IL-1 β characterized by a decrease in the average values in this group. In particular, the level of IL-1 β significantly decreased by 11.1% compared to the pre-treatment values and was 47.3 ± 0.7 pg/ml.

The analysis of the results of IL-2 concentration in OL showed that before treatment its content was elevated in the clinical groups, and after the traditional and complex treatment the increase of this cytokine was observed. IL-2 concentration in the comparison group before treatment was $15,6 \pm 0,8$ pg/ml, and after treatment was $14,7 \pm 0,7$ pg/ml, which was 5,8% less than before treatment and this difference was statistically unreliable ($p < 0,05$).

The inclusion of local sorbent therapy caused a reduction of LMMWS level in the wave range of 244 nm and 254 nm from 0.014 ± 0.0009 units and 0.013 ± 0.0009 units up to 0.011 ± 0.0006 units and 0.008 ± 0.0009 units of optic plasma, respectively. In the dynamics of treatment in the control group, there was also a decrease in LMMWS in the 244 nm and 254 nm wavelength ranges, although it was less pronounced. Also, the changes in LMMWS are probably related to both the rate of urea formation and the rate of elimination. Recommendations for the practical use of the treatment results follow from the performed work. It is recommended to include local sorbent therapy in the complex therapy of patients with sialosis and CKD on GD-treatment. Sorbent therapy is carried out locally by applying powdered zeolite to the oral mucosa. The application of natural zeolite insignificantly affects the secretion rate and to a greater extent shifts the pH from alkaline to neutral. The results obtained testify to a certain relief of the inflammatory process by the sorbent against the background of basic treatment and the impact of this drug

on the local immunity of the oral cavity of patients with sialosis against the background of CKD. The above-described dynamics of cytokine levels in OL was associated with stabilization of clinical manifestations of SG. After treatment, positive dynamics of clinical symptoms was noted in the examination groups, but nevertheless the effectiveness of traditional therapy was inferior to the complex treatment with the use of natural zeolite. The developed method of complex therapy enables to reduce endotoxemia in the oral cavity due to reduction of short wave fractions of LMMWS (244 and 254nm) which contain uremic toxin-urea. In the course of complex therapy we have established the possibility of increasing the sorption of LMMWS fraction 244 nm and 254 nm in RL.

Sialolithiasis

Among the examined patients who underwent therapeutic treatment, 39 patients had spontaneous exit of a concrement from the salivary gland duct. In 36 patients sialoliths were located in the duct of submandibular salivary gland, in 1 patient - in the duct of parotid gland. Among them, 17 patients had 2 or more concretions in the affected gland (15 - submandibular, 2 - parotid salivary gland), and 6 patients had concretions in both submandibular salivary glands. It should be noted that these concretions were not more than 2 mm in diameter and were located in the duct.

Since 2015, remote lithotripsy of salivary stones in the Nasreddin Tusi Clinic was performed in 41 patients, of whom 36 patients had stones located in the submandibular salivary gland and its duct and 5 patients had stones in the parotid salivary gland and its duct. The age of the patients ranged from 22 to 75 years. In the course of our research work in patients, the concretion was located in the duct of the parotid salivary gland, the effect of the absence of teeth on the side of sialolithotripsy was determined. In patients with complete adentia as well as with partial adentia on the side of sialolithotripsy, no changes were noted on ultrasound after the first two sessions of sialolithotripsy. After that it was decided to place in the oral cavity of these patients in the projection of the concrement a medical spatula for the tongue. Already during the first session with the placed spatula fragmentation was noted. However, when studying scientific

works written earlier by other authors, devoted to the lithotripsy of salivary stones, we did not find information about the effect of adentia on the effectiveness of sialolithotripsy.

Some authors point out in their works that in most cases in order to remove fragments of the split stone the surgery was made to create a new duct according to Afanasiev-Starodubtsev method. Prescribed by us therapeutic treatment and stone crushing up to smallest fragments allowed us to achieve the complete removal of the fragments in 35 patients, without additional surgical manipulations.

Our studies have shown that this method is especially effective for concretions not more than 2,0 cm in size, localized in the ducts of salivary glands.

Sialolithotripsy resulted in the stone fragmentation in 38 of 41 (92,6%) examined patients. However, it should be noted that the number of sialolithotripsy sessions to achieve stone fragmentation varied among the patients (chart 1).

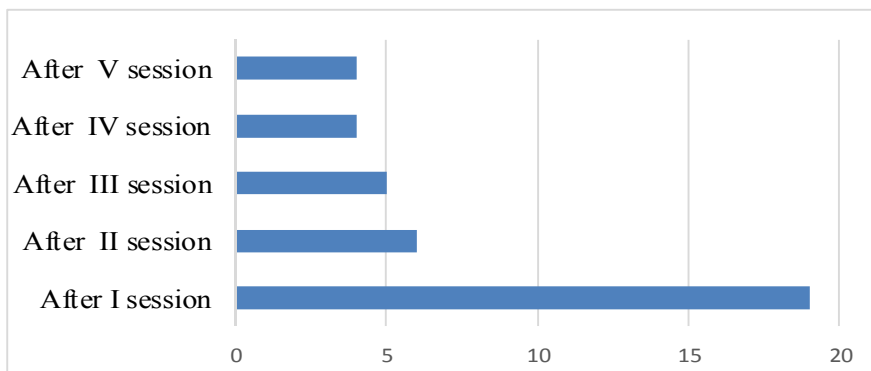


Chart 1. The ratio of the number of patients and the number of lithotripsy sessions required to crush the calculus

Initially a decision about surgical treatment was made in 57 patients with advanced stage of the disease or with very large concretions; however, later it was also decided to perform surgery in 6 other patients for whom sialolithotripsy was not effective: in 3 patients the fragmentation was achieved, but due to the narrow lumen of the duct of submandibular salivary gland, the evacuation of con-

crements did not occur; in another 3 patients with concrements of large size (more than 2 cm) located in the submandibular salivary gland the fragmentation was not achieved.

It is worth mentioning that we managed to avoid surgical intervention in patients with parotid glands affected by parotid stone disease because the risk of postoperative complications is the highest in different types of parotidectomy. Sialolithotripsy method was successful in 5 patients, therapeutic treatment was enough in 2 patients with bilateral involvement of parotid glands. For the patients whose concrements were located in the duct of submandibular salivary gland the function of the gland itself was not lost; that is why they underwent the organ-preserving operation "Ductotomy". For patients whose concrements were in the gland itself, the functionality of the gland itself was lost (for the same reason they were not conducted sialolithotripsy), so they underwent "Total sialoadenoectomy" of submandibular salivary gland - removal of the gland with the concrement. Removal of submandibular salivary gland was performed in 26 patients. Three patients came to us with a complication - phlegmon of the submandibular region. The phlegmon was dissected in the hospital, treatment was prescribed, daily check-ups were conducted, after which the patients were discharged on the 6th-7th day. A month later they were re-admitted for the main surgery. The operation was carried out under general anesthesia, the patients were admitted to the maxillofacial surgery department of the Republican Clinical Hospital. More extended investigation was made before the operation because the operation was carried out under the anesthesia (ECG, X-ray of the chest cavity organs, general and biochemical blood tests, coagulogram, tests for HIV, syphilis, hepatitis B and C, general urine test, general stool test). Four patients were diagnosed with type II diabetes mellitus and three patients had cardiovascular diseases. They underwent additional consultations with an endocrinologist and a cardiologist, respectively, and additional treatment was prescribed.

To find out the chemical composition and structure of concrements, formed in the salivary glands, for the purpose of further determination of regularity of their formation there was carried out a study of the mineral composition and structure of the salivary stones.

Stones were removed from the duct of submandibular gland.

Investigations of mineral composition were carried out in the laboratory of the Institute of Geology of the Academy of Sciences of the Azerbaijan Republic. For this purpose were used diffractometry (Rigaku Miniflex 600) and infrared (IR) spectroscopy (X-ray fluorescent spectrometer S8 TIGER).

Examination of salivary stones gave the following results: most salivary stones (80%) consist of apatite, the rest (20%) - of apatite and vitlockite.

Since the study found that most salivary stones were composed of oxalate, patients were prescribed a diet. Patients were divided into two groups. The first group was assigned to drink plenty of fluids. Fluids were evenly absorbed during the day and special attention was paid to the cases of fluid loss.

Besides drinking plenty of fluids the second group was advised to avoid excessive consumption of oxalate-rich foods.

Diet should be the most usual balanced diet, including all foods without a preference for any one type. Excessive consumption of oxalate-rich foods (rhubarb, sorrel, beet, spinach, chocolate, wheat bran, nuts, black tea) should be avoided. Consumption of fruits and vegetables should be encouraged, because of the beneficial effects of fiber. However, beware of the consumption of fruits and vegetables rich in oxalates. Wheat bran is rich in oxalates and should not be eaten. This was especially true for those patients who were found to have high levels of oxalate excretion. High levels of oxalate are found in the following foods:

- Rhubarb 530 mg oxalates/100 g
- Spinach 570 mg oxalates/100 g
- Cocoa 625 mg oxalates / 100 g
- Tea 375 - 1,450 mg oxalates / 100 g
- Nuts 200 - 600 mg oxalates / 100 g

One year after the study in patients who were prescribed prophylactic treatment there was a decrease in the recurrent formation of salivary gland stones. The frequency of formation of stones in the second group during the year was reduced from 3.1 to 1.1 and the number of patients who had no recurrent stones was 65%. These

findings can be compared with those of a study in which only increased fluid intake was prescribed and the frequency of stone formation decreased from 2.65 to 0.9 and stone formation was not detected in 52% of cases.

Prophylaxis according to the mineral composition of the stones considerably reduced the recurrence of formation of oxalate calcium stones within three years.

FINDINGS

1. Studies in patients with salivary gland diseases revealed a high incidence of dental caries (KPU - 19.4 ± 1.8), inflammatory periodontal diseases ($26.3 \pm 1.5\%$) and the presence of low oral hygiene (IG - 2.3 ± 0.2) [19, 21, 30].
2. The results of a complex laboratory study of patients with sialosis and sialadenitis showed pronounced shifts in all studied parameters ($p < 0.05$) [3, 8, 16, 23, 29].
3. In patients with chronic sialadenitis local immunity changes significantly on the background of a sharp decrease in salivation (2.3 times). Increase of IL- 1β , IL-2 and decrease of IFN- γ in RW was revealed. As a result of local immunocorrection in the complex treatment of patients with chronic sialadenitis the cytokine concentration of IL- 1β and IL-2 was decreased by 20,3% and 38,8% respectively, while IFN- γ was increased by 21,2%; $p < 0.05$ [8, 10, 12].
4. Urea and creatinine levels were elevated in OL in patients with CKD and sialosis. Urea level was 1.6 times higher in the group of patients with GD treatment duration ≤ 5 years, and 1.8 times higher in the group of patients with GD treatment duration > 5 years. Creatinine content in OL was also increased in the groups of patients by 1.1 times on the average, but this increase was statistically insignificant ($p > 0.05$). Increased content of urea and creatinine in OL in patients with CKD and sialosis is the evidence of increased excretion of toxins of nitrogenous metabolism by salivary glands. The concentration of IL- 1β and IL-2 in OL was found to be significantly higher and IFN- γ - lower than that of cytokines in healthy controls. Along with this, the duration of GD-treatment has an immunosuppressive

- effect on the content of cytokines in OL in patients with sialosis [3, 28].
5. The study of endotoxemia products in the oral fluid showed that after a 3-week course of sorbent therapy with natural zeolite in patients with sialosis and CKD revealed a decrease in the short-wave fractions of substances of low and middle molecular weight in which uremic toxin-urea is determined [6, 15].
 6. In patients with sialosis and type 2 diabetes with a duration of more than 5 years there was a more significant increase in the viscosity of saliva, decreased salivation and changes in pH of mixed saliva towards acidity. Enzymotherapy used in the complex treatment of patients with sialosis on the background of diabetes mellitus 2 type showed anti-inflammatory effect as evidenced by the data of clinical examination, reliable decrease of total protein, globulins and inflammation index in the oral liquid. Clinical efficacy of enzymotherapy is confirmed by immunomodulatory activity of suvastin (decrease in levels of IL-1 β , IL-2, increase in IFN- γ in RG) to the value in healthy individuals in 1 month after the start of treatment [13, 14, 29].
 7. Prophylaxis based on the obtained mineral composition of the stones can significantly reduce the recurrent formation of calcium oxalate stones within three years. Extracorporeal lithotripsy is a promising alternative method for the treatment of patients with salivary stone disease. Crushing and subsequent reduction of the stone volume without complete removal of its fragments can restore salivary flow, eliminating the symptoms of salivary colic. As a palliative method of treatment, sialolithotripsy is especially relevant for patients with severe general somatic pathology, in which surgical intervention is contraindicated [9, 11, 18, 25, 27].

PRACTICAL RECOMMENDATIONS

1. To estimate the disease severity, to provide full-fledged treatment taking into account individual peculiarities of inflammation course and organism protective reactions as well as to predict outcomes of inflammatory processes in clinical practice it is reasonable to include local immunocorrection in-

- to complex therapy of chronic sialadenitis allowing to normalize both indices of adaptive immunity, phagocytic activity as well as cytokine regulation.
2. To improve the quality of care for patients with relapsed chronic sialadenitis a constant analysis of clinical and laboratory examinations is necessary, which will improve methods of prevention of chronic forms and prevent the development of severe complications.
 3. The use of Suvastin in the complex treatment of sialosis in diabetic patients can improve the quality and quantity of oral fluid, normalize the consistency and size of salivary glands, as well as affect the reduction of pathological changes in the periodontium and the oral mucosa.
 4. In the complex therapy of patients with sialosis and CKD under GD-treatment it is recommended to include local sorbent therapy. The developed method of complex therapy can reduce endotoxemia in the oral cavity by reducing the short-wave fractions of LMMWS(244 and 254 nm) in which uremic toxin-urea is determined.
 5. Patients with sialosis against the background of terminal stage of chronic renal disease and diabetes mellitus need dental treatment and prevention of inflammatory periodontal diseases, especially these measures are necessary for patients who are on hemodialysis program for more than 5 years.
 6. In order to speed up the process of excretion of concrements and increase the efficiency of the sialolithotripsy method, it is recommended after 2 - 3 sessions to administer drugs that increase salivation (1% solution of pilocarpine hydrochloride, 5-7 drops 3 times a day 30 minutes before meals, or taking Kovalenko mixture 1 tablespoon 3 times a day for half an hour before meals).
 7. The results of clinical studies suggest that for a more efficient sialolithotripsy session it is recommended to make an ultrasound examination before the procedure and mark the projection of the concrement location on the skin, and to increase the efficiency of the waves during sialolithotripsy it is rec-

ommended to put a metal spatula in the salivary stone projection area from the oral cavity during the procedure.

8. In order to prevent stone formation in patients with salivary gland disease it is advisable to study the physicochemical and mineralogical properties using diffractometry and infrared spectroscopy
9. To prevent recurrence of salivary gland stones, it is recommended to avoid excessive consumption of oxalate-rich foods in addition to drinking plenty of fluids.

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LIST OF ABBREVIATIONS AND SYMBOLS

| | |
|-------------------|--|
| CFE | – carious, filled, extracton index |
| FAN | – phagocytic activity of neutrophils |
| Hb | – hemoglobin |
| HbA _{1c} | – glycated hemoglobin |
| HD | – hemodialysis |
| IFA | – immunoferment analysis |
| IL-2 | – interleukin-2 |
| IL-1 β | – interleukin-1 β |
| INF- γ | – interferon- γ |
| LMMWS | – low and middle molecular weight substances |
| PMA | – papillary marginal alveolar index |

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