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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

CLINICAL AND LABORATORY JUSTIFICATION FOR THE USE OF PROBIOTIC PRODUCTS IN COMPREHENSIVE TREATMENT AND PREVENTION OF INFLAMMATORY PERIODONTAL DISEASES

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GENERAL CHARACTERISTICS OF THE WORK

Relevance of the topic. It is known that among the main dental diseases, inflammatory diseases of periodontal tissues occupy an important place. Periodontal diseases are an important medical and social problem, characterized by steady growth and widespread prevalence among the population.

According to the results of clinical and epidemiological studies, there is a negative unfavorable dynamic in the increase of level of inflammatory periodontal diseases among people of young age, here we can especially note representatives of adolescence, that is also revealed by statistical data from the World Health Organization. These data are based on the results of a survey in all age and sex groups of the population in more than fifty countries of the world, according to which a significant increase in the prevalence and intensity of periodontopathies is often determined among those surveyed who have not yet reached the age of thirty.[1,2] Despite the large number of studies on the problem, today the search of effective treatment methods for periodontal diseases is relevant. According to the literature, antibiotics widely used in dental practice have an anti-inflammatory effect, but with long-term use, resistance to pathogenic agents at the cellular level decreases.

The use of antibiotics and steroid drugs changes the oxidation-reduction potential of saliva, weakens the activity of lysozyme, promotes the development of allergic reactions, and causes a decrease in the body's resistance to pathogenic influences.

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Total suppression of the bacterial flora of the oral cavity creates the preconditions for relapses of periodontal diseases and can lead to superinfection with fungi. Therefore, one of the most important tasks is the development of methods that ensure the restoration and normalization of biocenotic interactions.[3,4.]

Taking into account the above, today the use of probiotic agents in the treatment of inflammatory periodontal diseases is actual. It is known that synbiotics have a multifactorial pathogenic effect, local - on the cellular elements of tissue and general - on various systems and organs. Local effects include normalization of microflora, reduction in the number of pathogenic and opportunistic microorganisms, acceleration and activation of metabolism. General effects are expressed in an increase in nonspecific protective factors, an increase in the general protective and adaptive reactions of the body.[5]

The object of study: patients with inflammatory periodontal diseases undergoing treatment at the Dental educational clinic of the AMU.

The aim of the study: assessment of the effectiveness of the use of modern preventive and probiotic agents in the complex treatment of periodontal diseases.

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The study objectives:

1. The study of the prevalence of various forms of inflammatory periodontal diseases and the severity of their clinical manifestations in the examined patients.

2. Questioning doctors to identify the frequency of prescription of various therapeutic and prophylactic agents in the treatment of inflammatory periodontal diseases.

3. To identify among the examined sick persons burdened with general somatic pathology as an important risk factor for the development of severe forms of inflammatory and destructive periodontal diseases.

4. The study of the influence of the proposed probiotic agent “Multilac” as part of complex periodontal treatment on index indicators of the condition of periodontal tissues.

5. The study of the antibacterial and anti-inflammatory effectiveness of the proposed synbiotic in the complex treatment of periodontal diseases.

6. The evaluation of the effectiveness of the use of modern hygiene product “Curaprox enzycal” in the treatment and prevention of mild periodontal inflammatory diseases.

Research methods:

- Indices Sinless – Loe, PMA, GI, SBI, PI, PHP;
- Questionnaire;
- Microbiological examination of saliva;
-Parametric and non-parametric methods of statistical processing.

The main provisions for the defense:

- The high level of prevalence and intensity of major dental diseases and adverse reactions of some potent medications predetermine the need for optimization and selection of more effective treatment and preventive measures.
- A number of drugs used in modern dental practice often cause an allergic reaction, which is excluded when using probiotic agents that can be used in periodontal treatment.

- The dental status of persons with inflammatory periodontal diseases is associated with an increase in quantitative and qualitative indicators of pathogenic and opportunistic flora.

Scientific novelty of the study:

- New data have been obtained on the incidence of various forms of periodontal diseases and the frequency of doctors' prescription of some traditional and modern therapeutic and prophylactic agents, including probiotics for the treatment of periodontitis.

- The effectiveness of the use of the synbiotic "Multilac" and modern prophylactic agents "Curaprox enzycal" in the complex therapy of catarrhal gingivitis and mild inflammatory periodontal diseases has been established.

The practical significance of the study:

1. The obtained data on the use of the proposed probiotic and modern preventive agents can be widely used in practical dentistry to improve the quality of treatment of mild catarrhal gingivitis and periodontitis and prevent the development of their more severe forms.

2. The obtained data can be used in the educational process of students, as well as in improvement in postgraduate dental education.

Approbation. The main provisions of the dissertation were reported and discussed at the scientific conference "Питання Експериментальной та клиничной стоматологии". Materials of the scientific and practical conference with international participation "Актуальная стоматология. Наука, практика, педагогика" for the 40th anniversary of the Faculty of Dentistry of the Kharkov National Medical University, Xarkov, issue 13, 2018; "Təbabətin aktual problemləri", materials of scientific-practical conference, Baku, 2018; General question of world science, Collection of scientific papers of the VIII international scientific-practical conference, Part 2, Amsterdam, 2019; Materials of the international scientific and practical Congress on "Təbabətin aktual problemləri-2020" dedicated to the 90th

anniversary of Azerbaijan Medical University, Baku, 19-20 December 2020; Materials "Təbabətin aktual problemləri-2021" dedicated to the 100th anniversary of honored scientist, professor Tamerlan Aziz oglu Aliyev, Baku, 6-8 October 2021.

The materials of the dissertation work were discussed and reported at an extended meeting of employees of the department of therapeutic dentistry simultaneously with employees of other related dental departments of the Azerbaijan Medical University (16.11.2022, protocol No.06), at a scientific seminar that operates under the Dissertation Council ED 2.50 (11.03.2024, protocol No. 09).

Implementation of research results into practice. Scientific and practical data obtained as a result of this research are introduced into the practical activities of the Dental educational clinic of AMU, as well as into the educational process of the departments of therapeutic dentistry and microbiology and immunology of AMU.

The name of the organization where the dissertation work was performed. The dissertation was carried out on the basis of the department of therapeutic dentistry and the department of microbiology and immunology of the Azerbaijan Medical University, using the resources of the Dental educational clinic of the AMU.

Publications: 13 scientific papers were published on the topic of the dissertation, 7 articles - 2 of them in foreign journals, 6 theses - 3 in foreign journals.

The volume and structure of the dissertation. The dissertation is presented on 151 pages of computer text (201230 characters) and consists of an introduction (10935 characters), a review of domestic and foreign literature (64005 characters), material and research methods (32146 characters), chapters of the results of one's own research and their discussion (59047 characters), a final review of the work done, conclusions and practical recommendations (35840 characters), a list of scientific

literature (12 pages), containing 119 authors, both domestic and foreign. The thesis includes 21 tables and 24 charts.

MATERIALS AND METHODS

To achieve this goal, 200 patients aged 20-45 years (average age 32.5 years) with a diagnosis of chronic generalized catarrhal gingivitis – CCG (110 people) and chronic generalized periodontitis of mild degree – CGPmd (90 people) participated in the examination. The inclusion criteria are patients with inflammatory periodontal diseases: chronic catarrhal gingivitis and chronic generalized periodontitis of mild degree. The presence of severe somatic pathologies and pregnancy are the exclusion criteria.

A survey was also conducted with the participation of 30 dentists, among whom monitoring was carried out to identify the most frequently used agents in periodontal treatment by patients. The questionnaire indicated the drugs they most frequently prescribed and noted the most common complications they encountered in their practice.

Patients with catarrhal gingivitis, depending on the used therapeutic and prophylactic agents, were divided into 3 observation groups. The control group (19 people) was trained in the rules of oral hygiene and received professional sanitation of the oral cavity. The comparison group (20 people) received hygienic training, treatment according to the generally accepted standard regimen, and they were recommended the therapeutic and prophylactic toothpaste “Curasept ADS 712” (composed of: 0.12% chlorhexidine bigluconate, which has antimicrobial and antiseptic effects, 0.04% fluoride sodium and ADS system, responsible for preserving the natural whiteness of tooth enamel) as part of measures for individual oral hygiene. The main group (15 people) underwent training in the rules of oral hygiene, standard therapy and were prescribed “Curaprox enzycal 1450” toothpaste (composition - water, sodium fluoride at a

concentration of 1450 ppm, 3 enzymes - glucoseoxidase, lactoperoxidase and amyloglucoseoxidase, which enhance the ability of saliva to reducing the negative impact of pathogenic bacteria, hydrated silicon dioxide, sorbitol, crispy chondral extract, citric acid, peppermint oil, etc.).

Patients with mild chronic generalized periodontitis, depending on used therapeutic and prophylactic agents, were divided into 3 observation groups. In the control group (18 people), in which basic therapy was limited to the inclusion of measures for hygienic training of the examined persons and the implementation of professional oral hygiene measures by a specialist. The comparison group (20 people) received training in the rules of oral care, treatment according to the traditional method, the recommended product “Curasept ADS 712”, which is a gel toothpaste that has antimicrobial and antiseptic effects, and is also responsible for maintaining the whiteness of teeth and their aesthetic properties.

Patients of the main group (20) received hygienic training, standard therapy and were prescribed as an individual hygiene product “Curaprox enzycal 1450” toothpaste with 3 enzymes that enhance the ability of saliva to prevent the negative effects of bacteria, which was recommended for regular cleaning of the oral cavity.

Patients (38 people) with mild chronic periodontitis were also divided into 3 groups. The control group included 12 people who were trained in the rules of oral care and received professional sanitation of the oral cavity. The comparison group consists of 13 people who were also trained in the rules of oral care and received treatment according to the generally accepted standard regimen. In this group, the therapeutic and prophylactic toothpaste “Curasept ADS 712” was prescribed as part of an individual oral hygiene product. The main group includes 13 people who received training in oral care similar to standard treatment, the recommended toothpaste “Curasept ADS 712” and the synbiotic “Multilac” (probiotic + prebiotic) (Bifidobacterium

longum BI-05 $6,75\times10^8$ CFU, Bifidobacterium breve Bb-03 $4,50\times10^8$ CFU, Bifidobacterium bifidum Bb-06 $2,25\times10^8$ CFU, Lactobacillus acidophilus La-14 $9,00\times10^8$ CFU, Lactobacillus rhamnosus Lr-32 $4,50\times10^8$ CFU, Lactobacillus casei Lc-11 $2,25\times10^8$ CFU, Lactobacillus plantarum Lp-115 $2,25\times10^8$ CFU, Lactococcus lactis LI-23 $9,00\times10^8$ CFU, Streptococcus thermophilus St-21 $4,50\times10^8$ CFU and fructooligosaccharides - 63,0 mg).

On the first visit, all patients were taught the necessary hygienic skills and rules for oral care, the hygiene products used by patients were studied, and the necessary recommendations were given. To assess the hygienic condition, the presence of soft and hard dental plaque was determined. All patients underwent professional oral hygiene. Personal hygiene control and clinical examination were carried out using indices before and after treatment. Longer follow-ups were carried out at 1, 3 and 6 months after treatment. Professional oral hygiene was carried out according to the traditional method; scaling and an ultrasonic device were used to remove tartar, after which the gums were irrigated with a 0,05% chlorhexidine solution and the necks of the teeth were polished with a polishing paste. The main reasons for patients with CGPmd to visit a dentist were halitosis, bleeding gums when eating and brushing teeth. After radiography, periodontal pockets up to 3,8 mm deep were identified, with mild destruction of the bone tissue of the alveolar process and expansion of the periodontal gap in the cervical region. The general condition of the patients was assessed by subjective parameters, using a survey, and objective parameters, using examination, probing, palpation and an index assessment of the condition of the oral cavity. We found out the patients complaints, symptoms of the disease, their duration, previous treatment and its effectiveness. Subsequently, study participants were advised to brush their teeth with the prescribed toothpastes twice a day for at least three minutes. According to the treatment plan, all patients underwent a comprehensive clinical and instrumental examination

of the oral cavity with the determination of index indicators: hygiene index Silness-Loe (S-L, 1964), index Muhlemann - SBI (1971), PMA (M.Massler, J.Shour, C.Parma, 1960), PI (A.L.Russel, 1956, 1967). The condition of the gums was assessed using the Gingival Index (GI)-(Loe & Silness,1963r). During control dental examinations, the oral hygiene efficiency index PHP was also assessed (Podshalley, Haley, 1968).

Samples for research were immediately placed in Stewart's transport environment, and for further research they were sent to the research laboratory of the department of microbiology and immunology at AMU. After collection of clinical samples, salivary pH was measured.

The biomaterial was inoculated onto solid and semi-liquid nutrient environment for the cultivation of microorganisms under aerobic and anaerobic conditions. The following set of media was used: 5% blood agar, Sabouraud, Endo, streptococcal selective agar, yolk-salt agar, thioglycollate environment, MRS agar. Microorganisms were identified by morphological, biological and biochemical properties in accordance with regulatory documents.

The rate of salivation was determined by dividing the volume of secreted oral fluid by the time of its collection. At the time of clinical and laboratory studies, patients were warned about the undesirable use of chewing gum, smoking, drinking, etc., which could cause chemical stimulation of salivation due to the influence of various active components included in their composition. At the same time, data within the range of 0,02 – 0,30 ml/min corresponded to hyposecretion, 0,31 – 0,59 ml/min - normal salivary flow rate, and above 0,60 ml/min. - hypersalivation. A well-calibrated graduated cylinder was used as a receiving vessel and measuring device.

Previously, in the course of these studies, the state of acid-base balance and pH value in mixed saliva were measured using pH-metry. To exclude the influence of food residues on the pH value, mixed saliva was obtained in an amount of 3-5 ml and collected in measuring vessels 2 hours after eating. The litmus

paper was dipped into the oral fluid for 1-2 seconds and in the next 10 seconds the color vibrations were compared with the color scale (an indicator test strip for a more accurate determination of the pH of biological fluid “Specialtestpaper 4,5-9,0” of industrial production), which is applied to the packaging with litmus paper.

When comparing proportions in small samples, Fisher's exact test was used. In all statistical analysis procedures, the achieved level of significance (p) was calculated, with the critical level of significance taken equal to 0,05. Statistical processing of the obtained material was carried out using a standard software package for applied statistical analysis (Microsoft Excel, Statistica for Windows v. 7.0).

Thus, comparison of the results of microbiological studies in groups is carried out using the Pearson $\chi 2$ test. To identify significant changes before and after the treatment and preventive measures in terms of Muhlemann and PMA indicators for the compared groups, a parametric Student's t-test for dependent samples was taken, since it can be pointed out that these variables are subject to the law of normal distribution in the examined clinical groups.

Diagnosis of periodontal diseases was carried out in accordance with the classification of periodontal diseases according to the International statistical classification of diseases and related health problems, 10th revision, adopted in 1999 by the Assembly of the World Health Organization(WHO) (ICD-10). To obtain objective results, patients of all three groups were comparable in age, gender, nature and depth of damage to periodontal tissues.

RESEARCH RESULTS AND THEIR DISCUSSION

A questionnaire survey of 30 dentists showed that all respondents prescribed antiseptics. Most doctors noted that they prescribe these drugs for a period of 10-14 days until the clinical

signs of inflammation are eliminated, and some doctors do not control at all the timing of patients' use of the prescribed drugs. Experts noted that in practice they more often prescribe chlorhexidine and miramistin, and listerine somewhat less frequently. At the same time, many of the surveyed specialists noted that most often in their practice they prescribe chlorhexidine digluconate of various concentrations, in 100% and miramistin in 90% of cases; hydrogen peroxide was prescribed somewhat less frequently. "Curasept ADS 712" is prescribed by an even smaller number of doctors, while chlorhexidine is used by patients for a period of 1-2 weeks, until the clinical signs of the pathological process are eliminated.

Collection of anamnestic data showed that 70,9% in the first group and 61,1% of patients in the group of patients with mild periodontitis turned out to be practically healthy, that is, without the presence of general somatic pathology. The rest noted the presence of concomitant general somatic diseases: cardiovascular system - 12% and 13,3%, respectively, in the first and second groups; bronchopulmonary system (2% and 7%); gastrointestinal tract (28% and 35%); otolaryngological pathology were more often detected in patients with periodontitis – 7,8% and much less often in the presence of catarrhal gingivitis – 1,8%.

It should be noted that in the control group, immediately 6 months after completion of treatment and prophylactic measures, the incidence of bleeding during probing reached 100%, and in the comparison group, a similar picture was observed only 6 months after basic therapy. More favorable dynamics emerged in the main group, where the results for the above factor were 73,7% and 89,5%, respectively, after 6 months. 60,0%, 100,0% and 100,0% are figures indicating the prevalence of bleeding gums during eating and brushing teeth in the main group of patients with mild periodontitis, the comparison group and the control group 12 months after treatment, that is, at the final stage of research. Similar data were revealed by group and by gum bleeding during probing – 90,0%, 100,0% and 100,0% of patients with CCG.

At the examination after 12 months, certain differences were also recorded in the data on the frequency of detection of heavy dental plaque between the main and two other groups of patients examined, both with CGPmd and with CCG.

During an intraoral examination, a small amount of dental plaque was noted in the interdental spaces and in the cervical area of the teeth in 18 (90,0%) cases in the main group. At the same time, both in the control group and in the comparison group of patients with CGPmd, the maximum indicators were recorded, that is, 100,0% before treatment, the PI index in all study groups significantly exceeded the intact indicators, which indicated the development of a pathological process in the gums (chart 1).

The decrease in PI values in patients of all treatment groups after treatment confirms the anti-inflammatory effect of the therapeutic and prophylactic agents used.

However, a comparison of the obtained statistical data on the PI and SBI indices shows that the preventive and therapeutic effectiveness of “Curaprox enzycal 1450” toothpaste exceeds that of “Curasept ADS 712” and traditional products in individual oral hygiene.

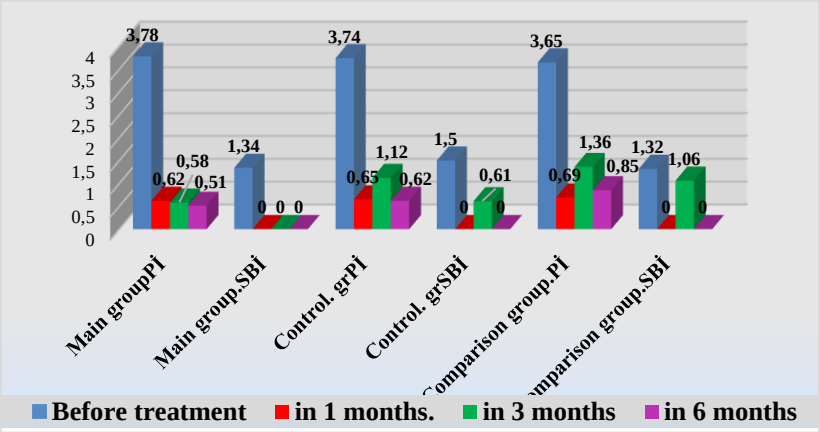

Chart 1. Dynamics of periodontal indices after treatment with chronic catarrhal gingivitis (M=m)

We conducted a comparative assessment of the dynamics of changes in clinical parameters at the final stage of complex treatment and management of patients with chronic catarrhal gingivitis.

In the comparison group and in the control group after 6 months, the values of the SBI bleeding index increased to 1,06±0,028 and 0,61±0,039, which indicated the presence of a sign of inflammation of periodontal tissue in some patients, while the data obtained at similar times in the main group group, allows us to conclude that there are significantly better results when using "Curaprox enzycal 1450" toothpaste, which has greater anti-inflammatory and preventive effectiveness.

Thus, the results obtained allow us to recommend its use for rapid and long-term relief of inflammatory signs in patients. An important indicator of the effectiveness of the therapy and improvement of the condition of periodontal soft tissues is a decrease in the frequency of diagnosis of bleeding gums during the study period, which is characterized by a decrease in the SBI index (table 1).

Table 1.

Muhlemann index values in patients with chronic generalized periodontitis of mild severity before and after treatment

Groups of patients	Before treatment	in 1 months	in 3 months	in 6 months
Main group (n=20)	2,93±0,023	0,12±0,021*	0,93±0,026*#	1,27±0,049*#
Control. gr. (n=18)	2,90±0,020	0,14±0,028*	1,51±0,034*	1,78±0,047*
Comparison group (n=20)	2,81±0,018	0,97±0,023	1,93±0,039	2,49±0,031

Note: * - the difference relative to the control group is statistically significant ($p<0,05$);

- the difference relative to the comparison group is statistically significant ($p<0,05$) (according to Student's t-test)

During the initial examination of patients in all three treatment groups, before professional oral hygiene and the prescription of prophylactic agents, high index values were recorded, indicating the development of an inflammatory process in periodontal tissues.

Regular use of “Curaprox enzycal 1450” toothpaste during the therapeutic course contributed to a significant reduction in bleeding gums. In the long-term period of clinical observations in the comparison group and in the control group, a more pronounced tendency was recorded in the growth of index data and their return to initial values than in the main group, where the values of the Muhlemann index after 6 months were 1,27 ± 0,049, versus 1,78 ±0,047 and 2,49±0,031, given in the control group and in the comparison group, at similar times.

One of the main factors determining dental status is the hygienic condition of the oral cavity. Before treatment, all patients without exception had an unsatisfactory level of oral hygiene. As the results of the studies showed, treatment of CGPmd using the proposed therapeutic and prophylactic agents had a beneficial effect on the “ecological” state of the oral cavity in patients. Thus, the values of the Silness-Loe (S-L) hygienic index after a course of basic therapy decreased significantly in all three groups of periodontal patients ($p < 0,05$). Although the level of hygiene after treatment generally remained satisfactory, the structure of this indicator in the study groups was different. More pronounced changes were observed in the comparison group, where the indicators at the final stage decreased to 1,21±0,032 points, while in the control group they were similar and amounted to 1,48±0,033 points (table 2).

The main purpose of the local treatment was a comparative assessment of the influence of the hygiene products used on the composition of the studied microorganisms in the oral cavity. Therefore, one of the main tasks was to compare the level of microbial contamination of the oral cavity before and after treatment.

Table 2.
Dynamics of S-L index values in patients before and after treatmen

Groups of patients	Before treatment	in 1 months	in 3 months	in 6 months
Main group (n=20)	2,96±0,008	0,12±0,008 *#	1,12±0,038#	1,28±0,046#
Control. gr. (n=18)	2,91±0,011	0,15±0,012*	1,30±0,028*	1,48±0,033*
Comparison group (n=20)	2,88±0,010	0,98±0,037	1,13±0,041	1,21±0,032

Note: * - the difference relative to the control group is statistically significant ($p<0,05$);

- the difference relative to the comparison group is statistically significant ($p<0,05$) (according to Student's t-test).

The following microbial picture was typical for inflammatory diseases of periodontal tissues. It should be said that the development of periodontitis was accompanied by a significant increase in the level of microbial contamination, as evidenced by a comparative assessment of the data obtained in the main group of periodontal patients and in the first group of people with healthy periodontium.

At the second stage of the study, as a result of the action of the therapeutic and prophylactic toothpaste "Curasept ADS 712", a decrease in the number of opportunistic microorganisms in the saliva content was revealed. In the contents of the oral cavity biopsy, we detected the elimination of Candida spp., which indicated a relatively lower susceptibility of microorganisms

pathogenetically associated with periodontal tissues to the action of the above paste.

As a result of the action of “Curasept ADS 712”, when examining the contents of mixed oral fluid, a decrease in the number of Streptococcus spp, Staphylococcus aureus and gram-negative microorganisms was revealed.

Positive dynamics in indicators at all stages of clinical and laboratory studies indicated the need for maintenance therapy once every six months.

Basic periodontal therapy using “Curasept ADS 712” with 0,12% chlorhexidine and “Curaprox enzycal 1450” as part of individual oral hygiene should become a real alternative to traditional methods with a relatively weak antibacterial and antiseptic effect. Thus, if in the control group the frequency of occurrence of A. actinomycetemcomitans and P. intermedia three months after completion of treatment and preventive measures was 5,6 ± 5,4% and 11,1 ± 7,4%, then in the comparison group, where toothpaste “Curasept ADS 712”, the indicators for the above bacteria decreased to zero. The revealed dynamics of the hygienic index values in patients before and after treatment and the obtained statistical data (1,12±0,038; 1,30±0,028 and 1,13±0,041 – Silness-Loe index values three months after treatment in the main, control groups and in the comparison group, respectively) allow us to assert the effectiveness of the use of the above means in improving dental status.

Therapeutic and preventive measures, including modern toothpastes and probiotic agents, actively influenced the frequency of detection of periodontopathogenic bacterial species in patients with chronic generalized periodontitis. The use of a synbiotic as an additional supportive therapy led to a significant reduction in bacterial contamination of the oral cavity and periodontal tissues in patients of all examined groups, including a significant elimination of P. intermedia, T. forsythia and A. actinomycetemcomitans in the examined patients. That is, after completion of the complex treatment in all three groups, the

average concentration of all identified types of periodontal pathogens decreased significantly. Thus, in patients of the 1st main group, the content of A. actinomycetemcomitans in the oral cavity decreased almost 2,5 times from 1,05±0.144 to 0,47±0.057 points, the difference was not statistically significant ($p<0,05$). The number of P.gingivalis in the studied samples of this group also decreased from 1,25±0.068 to 0,58±0,069 points.

In patients with periodontopathies (the main group), a more pronounced decrease in quantitative indicators was recorded in relation to the content of P.intermedia in the oral fluid. As for T. denticola, in the above group, according to its quantitative data, less pronounced changes were recorded.

The maximum results were revealed in the dynamics of the decrease in T. denticola content in patients in the comparison group. It should be noted that initially, with an almost equal average content of three types of periodontopathogens in patients with periodontitis before the start of treatment and prophylactic measures, then after completion of treatment in the content of A. actinomycetemcomitans and P. gingivalis in patients of the main, control and comparison groups, some differences were observed in indicators. Antimicrobial effectiven using the proposed therapeutic and prophylactic agents on the studied microbial species was different in all three groups of studies. In relation to periodontopathogenic microflora, the greatest activity was determined for the probiotic agent. The activity of the drugs prescribed in the comparison group and in the control group was slightly lower. After complex treatment in the main group, the average content of all types of pathogens identified before treatment decreased significantly. When analyzing the frequency of detection of the above bacteria, it was found that out of 30,8% of patients in the main group, after completion of therapeutic measures, A. actinomycetemcomitans was detected again in only 2 (15,4%) people ($\chi = 0,87$, $p = 0,352$). The frequency of detection of P.intermedia before treatment in

this group as a whole was 61,5%, which is almost 4 times more – 15,4% - than after treatment ($\chi 2 = 5,85$, $p = 0,016$).

The therapeutic measures taken did not affect the frequency of P.intermedia inoculation in patients in the control group – 33,3%, before and after treatment. In patients of the comparison group, just like in the main group, but less pronounced, there was a decrease in P.intermedia, 7 (53,8%) and 4 (30,8%), respectively, before and after completion of treatment and preventive measures with using "Curasept ADS 712" toothpaste ($\chi 2=1,42$, $p=0,234$). The basic treatment carried out with elements of additional supportive therapy led to a statistically significant decrease in the frequency of identification of T. forsythia in the main group and in the comparison group. The introduction of a probiotic agent into the treatment process led to a more than threefold decrease in the inoculation rate of the studied microorganism 9 (69,2%) and 3 (23,1%), respectively, before and after treatment ($\chi 2 = 5,57$, $p = 0,018$).

In patients with mild periodontitis in all groups except the control group, the frequency of detection of P. gingivalis also decreased. In the main group, it was determined in 8 (61,5%) people before treatment and 2 (15,4%) after therapy ($\chi 2=5,85$, $p=0,016$). That is, in patients of this group it decreased by almost 4 times. In patients in the comparison group, it decreased only by almost 2,2 times, while in patients in the control group, the indicators before and after treatment did not change, which indicated the lack of effectiveness of the treatment and preventive measures taken - 4 (33,3%) and 4 (33,3%), respectively, before and after treatment – 2 times – 12 (67%) and 6 (33%) ($\chi 2=0,00$, $p=1,000$). Thus, the work presents the results of identifying periodontopathogenic species of bacteria, and the best results were obtained in patients of the main group who received a synbiotic as part of complex treatment (chart 2.) The treatment measures carried out in the control group did not affect the frequency of detection of periodontopathogenic bacterial species.

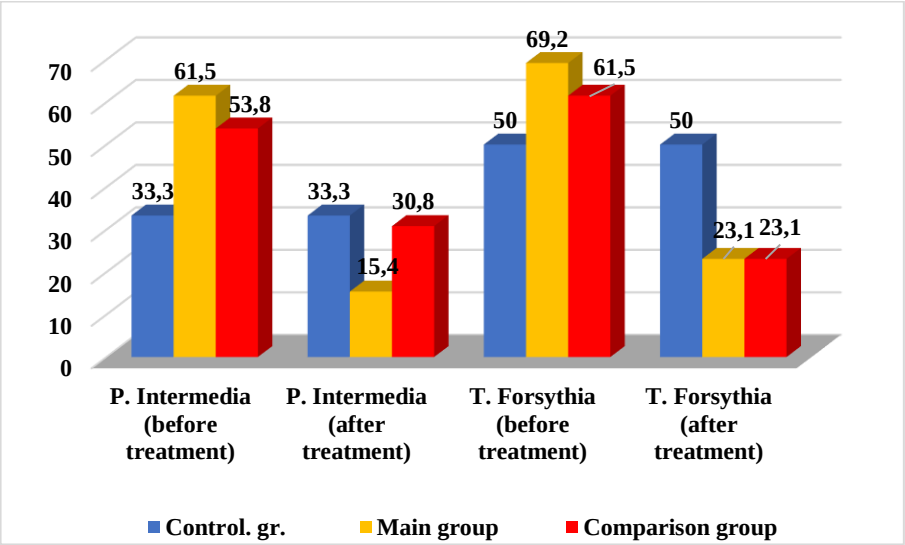

Chart 2. Frequency of inoculation in the oral cavity of P.intermedia and T.forsythia before and after treatment (%)

The prescription of a probiotic agent led to a significant reduction in the bacterial load and pronounced elimination of P. intermedia and T. forsythia. As a result, there was also a decrease in the frequency of seeding of pigment-forming periodontopathogenic bacterial species, including A. actinomycetemcomitans. In patients with mild chronic generalized periodontitis, the use of effective prophylactic agents had an impact on the elimination of the studied microorganisms and a significant reduction in the frequency of their identification.

Patients who participated in the study in the main group and in the control group testified to a persistent feeling of fresh breath and the absence of bleeding gums when brushing their teeth. However, according to the results of clinical studies conducted after 6 months, there was a clear dynamics of increase in PHP index values in the group of patients treated in the traditional way. During control dental examinations at the final

stage of observation, signs of the preventive effect of therapeutic measures in the main group were revealed, which was proven by the indicators of the oral hygiene effectiveness index – 1,14±0,053 and 1,82±0,052, respectively, 6 months after treatment in the main and control groups ($p<0,001$).

In the comparison group, where patients were prescribed hygienic procedures using “Curasept ADS 712” toothpaste for therapeutic and prophylactic purposes, a statistically significant improvement in the hygienic condition of the oral cavity was also observed at almost all stages. This indicated the effectiveness of preventive measures with training in all the necessary rules for oral care and positive motivation of the subjects to carry out regular hygienic care, the index values of which before and three months after the start of treatment and preventive measures were 2,54 ± 0,057 and 1,09 ±0,049 respectively.

At the beginning of the study, the average value of the PHP index in patients was fixed at a level corresponding to an unsatisfactory hygienic state of the oral cavity. Daily use of the proposed therapeutic and prophylactic agents for two weeks contributed to a significant decrease in index indicators ($p<0,001$). During follow-up examinations, patients who used “Curasept ADS 712” toothpaste showed a significant improvement in the hygienic condition of the mouth and periodontal tissues.

The oral hygiene efficiency index PHP used in the work and the data obtained from it indicated a good level of oral hygiene in patients of two groups - the comparison group and the main group, where a synbiotic was used as an additional supportive therapy, which confirmed, on the one hand, the effectiveness of professional oral hygiene mouth, and on the other hand, the effectiveness of including the synbiotic “Multilac” in basic complex therapy. Thus, in patients of the main group there was a more pronounced decrease in the values of the hygiene index, compared to other groups, which was especially clearly seen in the third month after completion of treatment and preventive measures – 0,92±0,059 in the main group, versus 1,78±

0,047 in the control group, at similar times. But, at the same time, the data obtained neither in these nor in subsequent periods of observation did not reach the critical initial value.

In patients with periodontopathies, the index values increased noticeably by the end of the study in the control group of patients; the difference at these stages of observation turned out to be significant ($p < 0,001$). During a phased examination in the main group at all periods of observation, a decrease in the intensity of deposition and a decrease in the amount of dental plaque was revealed, and the level of oral hygiene was assessed as satisfactory. The positive dynamics of the hygienic index PHP in treatment and prophylactic groups may indicate that the examined patients have developed motivation for proper oral care.

Thus, the cleansing effectiveness of "Curasept ADS 712" toothpaste, when used regularly during the first two weeks, turned out to be higher than traditional preventive agents. The initial and subsequent GI index indicators revealed a relatively more pronounced anti-inflammatory effectiveness of complex therapy with the addition of probiotic agents. The use of the synbiotic "Multilac" led to a sharp decrease in the gingival index.

An important indicator of improvement in the condition of soft periodontal tissues is a decrease in bleeding of the gingival sulcus after the start of a course of basic therapy in all treatment and prophylactic groups for the entire study period, which was characterized by a significant decrease in the SBI index. For example, from 51,9±4,18 at the initial examination to 11,5±2.43 ($p < 0,001$) after two weeks and to 9,6±2,23 ($p < 0,001$) after a month.

Regular use of "Curasept ADS 712" toothpaste and "Multilac" synbiotic during the therapeutic course contributed to a significant reduction in gum bleeding. In the long-term period of clinical observations, a more pronounced tendency in the growth of index data and their return to initial values was recorded in the control group than in the comparison group and in the main group – 23,8 ± 1,25; 9,7±0,61; 8,8±1,62, respectively, in the indicated groups, at similar times.

The clinical picture in patients of the main group showed a more pronounced disappearance of signs of the inflammatory process and its stabilization. The study confirmed that the inclusion of the synbiotic “Multilac” in the treatment regimen in patients with periodontopathies helps to improve the condition of the periodontium and increase the preventive effectiveness of basic therapy.

Analysis of the clinical effectiveness of complex treatment and preventive measures in patients with periodontal diseases allows us to conclude that there are significantly better results when using “Curasept ADS 712” and the synbiotic “Multilac”, which have a greater cleansing and anti-inflammatory effect, and more effectively reduce gum bleeding during probing.

It should be noted that in the control group during the above periods, a further decrease in the GI index was observed. But between the data recorded in this group and in the other two groups, a statistically significant difference in indicators was revealed – 0,65 ± 0,020 and 1,12 ± 0,014, respectively, in the main and control groups one month after treatment ($p < 0,001$). An important indicator of the effectiveness of the therapy and improvement of the condition of periodontal soft tissues is a decrease in the frequency of diagnosis of bleeding gums during the study period, which is characterized by a decrease in the SBI index. During the initial examination of patients in all three treatment groups, before professional oral hygiene and the prescription of prophylactic agents, high index values were recorded, indicating the development of an inflammatory process in periodontal tissues. During the observations, regular use of “Curasept ADS 712” toothpaste and the probiotic product “Multilac” contributed to a more pronounced reduction in gum bleeding compared to the control group.

Thus, increasing the level of diagnostic measures in order to identify factors contributing to the formation of deep pathological changes and insufficient effectiveness of therapy is today an urgent problem in modern practical dentistry. The

optimal choice of methods and means for the management of patients with periodontal diseases, the number of which, especially among people of young working age, continues to grow, which makes the organization of dispensary registration and the widespread introduction of preventive measures more relevant and which, in turn, will allow timely identification of the epidemiological situation and timely organize and implement the entire necessary volume of dental periodontal care in other regions. Much attention from domestic and foreign scientists is paid to conducting multilateral research, including clinical, laboratory, and experimental methods, for an in-depth study and identification of the main etiopathogenetic causes and risk factors for the occurrence and development of periodontitis. The use of potent drugs in the process of complex periodontal therapy, in particular broad-spectrum antibiotics, with prolonged use can suppress the growth and functional activity of some microorganisms from among the resident normal microflora of the oral cavity.

This, in turn, predetermined the growth in the number of scientific studies of the aggressiveness and degree of pathogenicity of pathogenic and conditionally pathogenic microflora that constantly lives in the oral cavity of people exposed to a negative attitude towards hygienic oral care, and, as a result, pathological changes in the oral cavity. The importance of analyzing their quantitative and qualitative values is associated with the pronounced negative impact of these bacteria and their metabolic products, against the background of certain favorable conditions, on the state of the local immune system, on the functional state of the salivary glands and the buffer capacity of the saliva itself.

CONCLUSIONS

1. During examination, the examined patients with frequently diagnosed chronic catarrhal gingivitis (n=110) were more likely to have hyperemia in the area of the papillary gum and intensive deposition of dental plaque in the interdental spaces [3, 5, 7].
2. Slightly less than half of the surveyed doctors indicated side effects in patients taking antibiotics, and, unfortunately, only 16.7% of the total number of dentists surveyed prescribed probiotic agents in their practice for the complex treatment of periodontal diseases. [2, 3, 4].
3. Diseases of the gastrointestinal tract, cardiovascular system and pathologies of allergic origin were most often observed in patients with mild periodontitis than in those examined with catarrhal gingivitis [3].
4. More pronounced dynamics at all stages of the study in reducing the periodontal indices PHP, GI and SBI in the main group indicates the high effectiveness of the use of the synbiotic "Multilac" in the complex treatment of periodontal diseases [2, 4].
5. The administration of a probiotic agent led to a significant decrease in the quantitative indicators and activity of periodontopathogenic microflora P. intermedia, P. gingivalis and A. Actinomycetemcomitans, while a statistically significant decrease in the frequency of identification of T. forsythia was also observed - 9 (69,2%) and 3 (23,1%), respectively, before and after treatment ($\chi 2 = 5,57$, $p = 0,018$) [4].
6. The inclusion of the drug "Curaprox enzycal 1450" in patients with catarrhal gingivitis and mild periodontitis [7] showed its pronounced both preventive and therapeutic effectiveness, as evidenced by the Muhlemann bleeding index data, which by the end of the study in the main the group of patients with gingivitis was 0 points, against an average of 0,61 and 1,06 points given to the control group and comparison group, at similar times [2,5].

PRACTICAL RECOMMENDATIONS

1. “Multilac” (synbiotic) can be used in combination with hygiene products modern and effective means to prevent the development of relapses of catarrhal gingivitis and periodontitis of mild degree, as well as to prevent their transition to more severe forms.
2. “Multilac” is recommended for use by patients with initial forms of periodontopathies in the presence of allergic reactions to the use of potent antiseptic and antibacterial drugs.
3. Synbiotic “Multilac” is used according to the following scheme: after isolating from saliva, the product is injected into the periodontal pocket area once a day. Exposure time is 10 minutes; duration of application is 10 days. After the procedure, it is recommended to refrain from eating for an hour**.**

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