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STUDY OF THE DEGREE OF DYSBIOSIS IN THE ORAL FLUID OF PATIENTS FOLLOWING SURGICAL TUMOUR REMOVAL AND CHEMOTHERAPY DURING THE APPLICATION OF A THERAPEUTIC AND PREVENTIVE COMPLEX

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The study aimed to evaluate the effect of a therapeutic and preventive complex on the degree of dysbiosis in the oral fluid of patients following surgical removal of head and neck tumours and chemotherapy. Thirty-five adults aged 25–55 years were examined: 10 healthy controls, 10 patients receiving standard oncological care, and 15 patients receiving standard care combined with the proposed complex. The degree of dysbiosis was calculated from the ratio of relative urease and lysozyme activities in oral fluid at baseline and after 1, 3, 6, and 12 months. At baseline, the indicator exceeded the reference value approximately 15-fold in both patient groups. Standard treatment produced only a partial and temporary reduction. In the main group, the degree of dysbiosis decreased 1.7-, 4.1-, 6.5-, and 9.3-fold after 1, 3, 6, and 12 months, respectively, approaching the physiological range. The proposed complex promoted sustained restoration of oral microbial homeostasis.

Key words: head and neck tumours, oral dysbiosis, oral fluid, therapeutic and preventive complex.

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ДОСЛІДЖЕННЯ СТУПЕНЯ ДИСБІОЗУ У РОТОВІЙ РІДИНІ ПАЦІЄНТІВ ПІСЛЯ ОПЕРАТИВНОГО ВТРУЧАННЯ З ВИДАЛЕННЯ ПУХЛИН І ХІМІОТЕРАПІЇ НА ТЛІ ЛІКУВАЛЬНО-ПРОФІЛАКТИЧНОГО КОМЛЕКСУ

Дослідження було присвячене оцінці впливу лікувально-профілактичного комплексу на ступінь дисбіозу в ротовій рідині пацієнтів після хірургічного видалення пухлин голови та шиї і хіміотерапії. Обстежено 35 дорослих віком 25–55 років: 10 здорових осіб контрольної групи, 10 пацієнтів, які отримували стандартне онкологічне лікування, та 15 пацієнтів, яким додатково призначали запропонований комплекс. Ступінь дисбіозу розраховували за співвідношенням відносних активностей уреази та лізоциму в ротовій рідині у вихідному стані й через 1, 3, 6 і 12 місяців. На початку дослідження показник в обох групах пацієнтів приблизно у 15 разів перевищував норму. Стандартне лікування забезпечувало лише часткове й тимчасове зниження. В основній групі ступінь дисбіозу зменшився відповідно у 1,7; 4,1; 6,5 та 9,3 раза, наближаючись через 12 місяців до фізіологічного рівня. Запропонований комплекс сприяв стійкому відновленню мікробного гомеостазу порожнини рота.

Ключові слова: пухлини голови та шиї, дисбіоз порожнини рота, ротова рідина, лікувально-профілактичний комплекс.

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The oral cavity is a complex ecological system in which epithelial tissues, saliva, resident microorganisms, and local immune mechanisms continuously interact. Under physiological conditions, mucosal integrity, saliva, antimicrobial proteins, immunoglobulins, and commensal microorganisms maintain homeostasis and prevent excessive colonisation by opportunistic species [12, 14]. Disruption of this balance may impair mucosal resistance, activate inflammation, and promote oral dysbiosis.

Saliva is a central component of oral defence. It contains numerous immune factors in addition to components responsible for lubrication, buffering, digestion, and remineralisation. Lysozyme is one of the most important salivary antimicrobial proteins and restricts bacterial growth through hydrolysis of peptidoglycan in bacterial cell walls. It also regulates microbial adhesion, biofilm formation, and local immune responses [7]. Together with lactoferrin, peroxidases, histatins, defensins, and secretory immunoglobulin A, lysozyme supports microbial stability and mucosal protection [7, 9, 14]. Reduced activity of these factors may therefore facilitate microbial overgrowth and transition from a balanced microbiota to dysbiosis.

Oral dysbiosis is not merely an increase in total microbial load. It is a qualitative and functional disturbance characterised by depletion of health-associated commensals, enrichment of potentially pathogenic taxa, altered microbial metabolism, and impaired host-microbial interactions [8–10]. These changes may increase the production of microbial enzymes, toxins, and inflammatory metabolites that damage epithelial tissues and sustain inflammation. Biochemical analysis of oral fluid therefore permits assessment of microbial activity and endogenous antimicrobial defense.

Patients with malignant head and neck tumours are particularly susceptible to disturbances of oral microbial homeostasis. The disease may be associated with tissue destruction, inflammation, malnutrition, impaired salivary secretion, and poor oral hygiene. Surgical treatment adds mechanical trauma and may lead to pain, restricted mouth opening, altered dietary habits, and difficulty in maintaining oral care. Subsequent chemotherapy may further suppress epithelial regeneration, modify immune responses, increase oxidative stress, and reduce mucosal resistance to microbial colonisation [3, 9–11].

Anticancer therapy may substantially alter the composition and function of the oral microbiome. Chemotherapy-associated oral mucositis has been linked to a reduction in health-associated genera, including Streptococcus, Actinomyces, Gemella, Granulicatella, and Veillonella, together with enrichment of Gram-negative and inflammation-associated microorganisms [10]. Such alterations may intensify inflammation, delay epithelial recovery, and increase infectious risk. In patients with head and neck cancer, treatment-related changes have also been identified in salivary proteins involved in innate immunity, antimicrobial protection, inflammation, and tissue repair [3]. Thus, the postoperative and post-chemotherapy period may combine increased microbial aggression with weakening of local protective mechanisms.

The consequences of dysbiosis extend beyond local discomfort. Microbial imbalance may contribute to oral mucositis, gingival inflammation, candidal infection, periodontal damage, impaired wound healing, and secondary bacterial complications. Mucosal barrier damage may facilitate microbial translocation into deeper tissues or the bloodstream, particularly in immunosuppressed patients. These complications may reduce food intake, worsen quality of life, delay rehabilitation, and necessitate modification of anticancer treatment [3, 10].

The balance between microbial contamination and nonspecific antimicrobial protection can be evaluated using oral-fluid biochemical indicators. Urease activity reflects the metabolic activity of urease-producing microorganisms and may indirectly characterise microbial contamination. In contrast, lysozyme activity represents an important component of local nonspecific antimicrobial defence [5, 7, 9]. Their ratio provides an integrated measure of microbial aggression and host protection. Increased urease activity accompanied by reduced lysozyme activity indicates a shift towards dysbiosis, whereas normalisation of their relationship may reflect restoration of microbial homeostasis.

Standard oncological management remains the principal treatment for head and neck malignancies; however, it does not always sufficiently correct secondary disturbances in the oral ecosystem. Accordingly, adjunctive interventions supporting microbial balance, local immunity, antioxidant defence, and mucosal recovery have attracted increasing attention. Probiotic administration may reduce the incidence and severity of oral mucositis associated with anticancer therapy, particularly when multistrain formulations are used [15]. Antioxidant and anti-inflammatory agents may also help. Curcumin and other plant-derived polyphenols can modulate oxidative stress, inflammatory signalling, microbial growth, and epithelial repair [4, 6]. Comparative analyses indicate that multimodal preventive strategies addressing several pathogenic mechanisms simultaneously may be more effective than isolated symptomatic interventions [13].

These findings provide a rationale for multicomponent therapeutic and preventive regimens combining probiotics, vitamin and mineral components, antioxidant flavonoids, local antimicrobial agents, and topical preparations supporting mucosal healing. Their combined action may reduce microbial contamination, strengthen nonspecific antimicrobial defence, and promote restoration of oral homeostasis. Nevertheless, evidence regarding the long-term dynamics of oral dysbiosis after surgical tumour removal and chemotherapy remains limited.

The purpose of the study was to evaluate the effect of a therapeutic complex of drugs on the degree of dysbiosis in the oral fluid of patients after surgical removal of tumors and chemotherapy.

Materials and methods. Biochemical studies of oral fluid were conducted in 35 patients aged 25–55 years. The study cohort comprised 25 patients with histologically verified malignant tumours of the head and neck who had undergone tumour-resection surgery at the clinical base of the SE “The Institute of stomatology and maxilla-facial surgery National academy of medical sciences of Ukraine” (SE “ISMFS NAMS”), Odesa and were scheduled for adjuvant chemotherapy; the control cohort comprised 10 somatically and dentally healthy volunteers whose systemic medical examination and oral status were within normal limits. Individuals who did not meet these inclusion criteria or declined informed consent were excluded. No participants were withdrawn, replaced, or lost to follow-up after enrolment. Biochemical studies were carried out in the “Laboratory of biochemistry and vivarium” of the SE “The Institute of stomatology and maxilla-facial surgery National academy of medical sciences of Ukraine” (SE “ISMFS NAMS”). The study was carried out from 6 February 2023 to 19 February 2024.

Patients with head and neck cancer underwent surgery to remove tumors and were prescribed chemotherapy. The patients observed were divided into two groups as follows:

– Comparison group – after surgery, patients were prescribed treatment in accordance with the “Standards for the Diagnosis and Treatment of Cancer Patients”, n=10;

– Main group – after surgery, patients were prescribed a therapeutic and prophylactic complex in addition to the basic standard treatment for cancer patients, n=15.

Both cohorts received guideline-based oncologic care (tumour resection followed by adjuvant chemotherapy in accordance with Order No. 247/2016), while the main cohort additionally underwent a staged therapeutic-prophylactic complex designed to modulate gut/oral microbiota, enhance osteogenesis, and limit oxidative-inflammatory damage. Pre-operative phase (days – 14 to 0): Orthomol Pro 6 (INN: Lactobacillus spp. + Bifidobacterium spp. multistrain probiotic; Orthomol GmbH, Germany) – one capsule once daily after meals for 14 days. Post-operative phase: Orthomol Osteo® granules (INN: cholecalciferol 20 µg with calcium, vitamin K1, magnesium and collagen-supporting micronutrients; Orthomol GmbH, Germany) – one sachet dissolved in 150–200 mL water, taken once daily after meals for 30 days; Quertin chewable tablets (INN: quercetin 60 mg; InterChem S.A., Ukraine) – one tablet three times daily 30 min before meals for 60 days; Lizomucoid dental elixir (INN: lysozyme hydrochloride 1 mg mL^{-1} with herbal antiseptics; SPA "Odeska Biotekhnolohiya", Ukraine) – 1 teaspoon diluted in 60 mL of water, rinse for 1 min after meals twice daily for 30 days; Maripolymiel® phytogel (INN: seawater trace-element concentrate 2 % + peppermint hydro-alcoholic extract 5 % with sodium benzoate, carboxymethylcellulose and menthol; SPA "Odeska Biotekhnolohiya", Ukraine) – thin-layer gingival applications (one pump) three to four times daily after meals for 10 days. The entire regimen was re-initiated six months post-surgery to consolidate clinical benefits; no dose modifications or patient withdrawals occurred.

Patients were treated in accordance with the Standards for Diagnosis and Treatment of Cancer Patients, in particular the clinical protocol for providing medical care to patients with oral and oropharyngeal cancer – Order of the Ministry of Health of Ukraine No. 247 of March 28, 2016. "On Amendments to Order No. 554 of the Ministry of Health of Ukraine dated September 17, 2007, "On Approval of Protocols for the Provision of Medical Care in the Specialty of Oncology" as well as the protocols for the provision of medical care to patients with malignant neoplasms developed by the National Cancer Institute in 2011.

All treatment, preventive and diagnostic measures were carried out only after the patients signed a voluntary informed consent in accordance with the principles of bioethics set forth in the Declaration of Helsinki "for Ethical Principles for Medical Research Involving Human Subjects" and "Universal Declaration on Bioethics and Human Rights (UNESCO)". All participants were adults, cognitively competent, and not otherwise classified as a vulnerable population under Good Clinical Practice. Studies recommended by the Commission on Bioethical Expertise (conclusion of the bioethics commission of the SE "ISMFS NAMS", protocol No. 1011 of 04/14/2022).

Oral fluid was collected in the morning, on an empty stomach, by spitting into sterile centrifuge tubes (without prior cleaning or rinsing of the oral cavity) for 5–10 minutes. Before performing biochemical analysis, the oral fluid was thawed at room temperature, centrifuged at 2,500 rpm for 20 minutes at a temperature of +4°C (bench centrifuge RS-6, MedTech, Ukraine), and the supernatant was collected for biochemical analysis. The degree of dysbiosis (DD) was calculated from the ratio of the relative activities of urease to lysozyme according to the method of A.P. Levytskyi [1].

Data processing was carried out with STATISTICA 6.1. Prior to parametric testing, the Shapiro-Wilk normality test was applied to each continuous variable; none showed significant deviation from a Gaussian distribution ($p>0.05$). Therefore, inter-group comparisons were performed with the two-tailed Student's t-test. When pair-wise contrasts were required (Control × Comparison, Control × Intervention, Comparison × Intervention), the family-wise type-I error rate was controlled with the Bonferroni adjustment. Between-group differences were deemed statistically significant at $p<0.003$ [2].

Results of the study. The degree of oral dysbiosis reflects the relationship between microbial contamination and the state of nonspecific antimicrobial defence in the oral cavity. Since this indicator is calculated from the ratio of relative urease and lysozyme activities, it makes it possible to assess not only the increase in opportunistic microbial activity but also the weakening of salivary protective mechanisms. Therefore, its dynamic evaluation after surgical treatment and chemotherapy is informative for determining the effectiveness of therapeutic and preventive measures aimed at restoring oral microbial homeostasis.

The balance between antimicrobial protection in the oral cavity and the degree of contamination by opportunistic and pathogenic microbiota is most clearly reflected by the degree of dysbiosis calculated according to the method of A.P. Levytskyi, as presented in Table 1.

Normally, the degree of dysbiosis is equal to 1; however, under pathological conditions, this indicator ranges from 1.5 to 20 units. A value of up to 3 units corresponds to moderate dysbiosis, up to 8 units to marked dysbiosis, and more than 8 units to severe dysbiosis.

In patients in the comparison group with head and neck cancer, the baseline degree of dysbiosis in oral fluid was 15 times higher than the reference value. Treatment of patients in the comparison group according to the standard protocol for patients with cancer resulted, after 1 month, in a 29.8% reduction in the degree of dysbiosis ($p_1<0.02$) relative to baseline. It should be noted that at 3 and 6 months, the investigated indicator remained at the level recorded 1 month after initiation of treatment ($p_1<0.002$), whereas at 12 months it showed a slight increase ($p_1>0.1$) compared with the previous observation point and remained significantly elevated relative to the reference value.

Table 1

Degree of dysbiosis in the oral fluid of patients with head and neck cancer during therapeutic and preventive measures over the course of rehabilitation, conventional units (M±m)

Terms / Groups	Terms of the study				
	Initial state	After 1 month	After 3 months	After 6 months	After 1 year
Reference values for the norm, n=10	1.0±0.1				
Comparison, n=10	15.1±1.2 p<0.001	10.6±0.8 p<0.001 p_1<0.002	10.7±0.9 p<0.001 p_1<0.002	10.2±0.8 p<0.001 p_1<0.002	12.4±1.0 p<0.001 p_1>0.1
Main, n=15	14.9±1.0 p<0.001 p_2>0.8	8.8±0.7 p<0.001 p_1<0.001 p_2>0.1	3.6±0.2 p<0.001 p_1<0.001 p_2<0.001	2.3±0.2 p<0.001 p_1<0.001 p_2<0.001	1.6±0.1 p<0.001 p_1<0.001 p_2<0.001

Note. p – significance of differences from the norm; p_1 – significance of differences from the initial state. p_2 – significance of differences from the indices in groups.

It was established that the use of the therapeutic and preventive complex as part of the comprehensive treatment of patients in the main group with oncological pathology after surgery and chemotherapy resulted in a substantial decrease in DD over time: 1.7-fold after 1 month (p_1<0.001), 4.1-fold after 3 months (p_1<0.001), 6.5-fold after 6 months (p_1<0.001), and 9.3-fold after 12 months (p_1<0.001) compared with baseline. It should be emphasised that from 3 to 12 months, DD in patients in the main group was significantly lower than that in the comparison group (p_2<0.001).

Thus, the results of the biochemical analysis of oral fluid in patients in the main group after removal of malignant head and neck tumours during chemotherapy indicate that the proposed therapeutic and preventive complex can reduce the degree of microbial contamination and increase the level of nonspecific antimicrobial protection, thereby normalising the oral microbiocenosis in patients with cancer through a substantial reduction in the degree of dysbiosis both in the short term (after 1 month) and in the longer term (after 12 months).

The results of the present study demonstrate that patients with malignant head and neck tumours exhibit a pronounced disturbance of oral microbial homeostasis following surgical treatment and during chemotherapy. At baseline, the degree of dysbiosis was 15.1±1.2 conventional units in the comparison group and 14.9±1.0 conventional units in the main group, whereas the corresponding reference value in somatically and dentally healthy individuals was 1.0±0.1 conventional units. Thus, the initial values in both groups of patients with cancer were approximately 15-fold higher than normal and corresponded to severe oral dysbiosis. The absence of a statistically significant baseline difference between the comparison and main groups confirms their comparability before the initiation of the differentiated therapeutic and preventive measures.

Discussion. The marked baseline increase in the degree of dysbiosis may be explained by the combined influence of the malignant process, surgical trauma, postoperative changes in oral hygiene and nutrition, and the adverse effects of chemotherapy on epithelial renewal and immune protection. The oral mucosa constitutes an integrated mechanical, immunological, and microbiological barrier whose stability depends on epithelial integrity, salivary secretion, antimicrobial proteins, and balanced interactions with the resident microbiota [14]. Surgical tumour removal disrupts tissue integrity and may temporarily impair normal oral care, while chemotherapy can inhibit epithelial regeneration and alter both local and systemic immune responses. The simultaneous action of these factors creates favourable conditions for the proliferation and increased metabolic activity of opportunistic microorganisms.

Our findings are consistent with the results reported by Hong et al., who demonstrated that chemotherapy-induced oral mucositis is accompanied by detrimental bacterial dysbiosis, including depletion of health-associated taxa and enrichment of microorganisms associated with inflammatory and destructive changes [10]. Although the present study did not determine the taxonomic composition of the microbiota, the considerable increase in the urease-to-lysozyme ratio indicates a substantial functional imbalance between microbial contamination and nonspecific antimicrobial protection. Therefore, the biochemical degree of dysbiosis may be regarded as an integrated marker reflecting not only the presence of microorganisms but also their metabolic activity in relation to the functional capacity of the host defence system.

The importance of evaluating salivary defence mechanisms in patients with head and neck cancer is also supported by the findings of Almhöjd et al. Their proteomic investigation revealed treatment-associated alterations in stimulated saliva, including changes in proteins involved in antimicrobial protection, inflammation, and tissue repair [3]. These data support the assumption that oncological treatment modifies the biochemical environment of the oral cavity and may reduce its ability to control microbial colonisation. The high initial degree of dysbiosis observed in our patients may therefore reflect both an increase in microbial activity and a reduction in the effectiveness of endogenous salivary defence.

In the comparison group, standard oncological treatment was accompanied by a reduction in the degree of dysbiosis from 15.1±1.2 to 10.6±0.8

conventional units after one month. However, the indicator subsequently remained almost unchanged, amounting to 10.7±0.9 after three months and 10.2±0.8 after six months. After 12 months, it increased to 12.4±1.0 conventional units. Despite the initial improvement, all follow-up values remained substantially higher than normal and corresponded to severe dysbiosis. These findings indicate that standard treatment and routine supportive measures may partially reduce the acute postoperative disturbance but are insufficient to achieve stable restoration of oral microbial homeostasis.

A different pattern was observed in the main group. The degree of dysbiosis decreased from 14.9±1.0 to 8.8±0.7 conventional units after one month, representing a 1.7-fold reduction. After three months, it decreased to 3.6±0.2 conventional units, which was 4.1 times lower than the baseline value. Further reductions were observed after six months and one year, when the indicator reached 2.3±0.2 and 1.6±0.1 conventional units, respectively. Thus, by the end of the observation period, the degree of dysbiosis was reduced 9.3-fold and approached the physiological reference range.

The absence of a significant intergroup difference after one month, followed by highly significant differences after three, six, and twelve months, suggests that the therapeutic effect developed gradually. This delayed but sustained response may be related to the time required for modification of the microbial environment, enhancement of local antimicrobial defence, epithelial recovery, and stabilisation of metabolic processes. Re-administration of the therapeutic and preventive complex six months after surgery may also have contributed to the continued improvement observed at the 12-month examination. Nevertheless, because the complex included several systemic and topical agents, the relative contribution of each component cannot be determined separately.

The selected biochemical approach provides a plausible explanation for the observed changes. Urease activity reflects the metabolic activity of urease-producing microorganisms, whereas lysozyme is an important component of innate antimicrobial defence. Lysozyme exerts bacteriolytic activity through hydrolysis of bacterial cell-wall peptidoglycan and may additionally affect microbial adhesion and biofilm organisation [7]. Consequently, a reduction in the urease-to-lysozyme ratio may indicate simultaneous suppression of microbial activity and strengthening of nonspecific antimicrobial protection. The progressive normalisation of this ratio in the main group suggests that the therapeutic and preventive complex acted on both components of oral dysbiosis.

The probiotic component may have contributed to the restoration of microbial balance through competitive inhibition of opportunistic microorganisms, modulation of host immunity, and production of metabolites favourable to mucosal homeostasis. Yang et al. reported that probiotics may reduce the risk and severity of oral mucositis associated with anticancer treatment, particularly when multistrain preparations are used [15]. Although mucositis severity was not the principal outcome of the present investigation, the observed improvement in the degree of dysbiosis is compatible with the microbiome-modulating and barrier-supporting effects described in that meta-analysis.

The complex also included quercetin and topical phytotherapeutic agents with potential antioxidant and anti-inflammatory properties. Plant-derived polyphenols have been reported to reduce oxidative stress, regulate pro-inflammatory signalling, support epithelial repair, and influence microbial growth in patients receiving chemotherapy or radiotherapy [4]. Oxidative and inflammatory injury is closely connected with microbial imbalance because damaged epithelial tissues provide favourable conditions for microbial adhesion and penetration. Reduction of oxidative-inflammatory damage may therefore indirectly support restoration of the oral microbiocenosis.

The observed effect is also consistent with the current concept that supportive care in oncology should address several interrelated pathogenic mechanisms simultaneously. Network meta-analysis has shown that the effectiveness of preventive interventions for oral complications varies considerably and that multimodal approaches may provide advantages over isolated symptomatic measures [13]. In the present study, probiotics, antioxidant support, topical lysozyme, mineral and vitamin supplementation, and local phytotherapy were combined within a staged regimen. This approach was intended to influence microbial ecology, innate defence, tissue metabolism, and mucosal recovery rather than targeting only one clinical manifestation.

Current evidence indicates that the oral microbiome and salivary metabolites form an interconnected system capable of influencing inflammation, tumour-associated processes, and treatment-related complications in patients with head and neck cancer [9]. The sustained reduction in the degree of dysbiosis recorded in the main group supports the clinical relevance of monitoring functional salivary markers throughout rehabilitation. Unlike a single microbiological examination, repeated determination of the urease-to-lysozyme ratio enables assessment of the direction and persistence of changes in the balance between microbial aggression and host protection.

Results indicate that standard oncological treatment alone produces only a limited and temporary reduction in oral dysbiosis. The addition of the proposed therapeutic and preventive complex was associated with a progressive and sustained normalisation of the biochemical marker throughout the one-year follow-up period. These findings substantiate the incorporation of targeted oral-supportive measures into the multidisciplinary rehabilitation of patients following surgical treatment of head and neck tumours and chemotherapy.

Limitations. A limitation of this study is that the evaluation was performed within a single-centre clinical design and focused on one defined follow-up model after surgery and chemotherapy, which may limit extrapolation of the results to other treatment settings. In addition, the observation period, although sufficient to assess one-year dynamics, does not allow conclusions to be drawn regarding the longer-term stability of the obtained effects.

Conclusions

1. Patients with malignant head and neck tumours following surgical treatment and chemotherapy demonstrated severe oral dysbiosis, as evidenced by an approximately 15-fold increase in the urease-to-lysozyme ratio compared with healthy individuals.

2. Standard oncological treatment produced only a partial and temporary reduction in the degree of dysbiosis. The indicator remained markedly elevated throughout the observation period and increased again by the 12-month examination.

3. The addition of the proposed therapeutic and preventive complex resulted in a progressive decrease in the degree of dysbiosis: 1.7-fold after one month, 4.1-fold after three months, 6.5-fold after six months, and 9.3-fold after one year compared with baseline.

4. After three, six, and twelve months, the degree of dysbiosis in the main group was significantly lower than that in the comparison group. By the end of the study, the indicator approached the physiological reference range.

5. The findings suggest that the proposed complex reduces microbial contamination, supports nonspecific antimicrobial defence, and promotes sustained restoration of oral microbial homeostasis in patients with head and neck cancer during postoperative and post-chemotherapy rehabilitation.

Further research should focus on the dynamic evaluation of haematological blood parameters in patients with head and neck cancer after surgical treatment and chemotherapy in order to determine whether systemic haematological recovery correlates with the microbiological and biochemical effects of the therapeutic-prophylactic complex during rehabilitation.

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