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**DISEASES OF THE PERIODONT IN CHANGES IN THE GENERAL STATE
OF THE BODY**

MONOGRAPHY

Samarqand-2025

UO'K: 616.314.17-002-036.12-031.81

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In this monograph, the authors humbly endeavour to enlighten dentists on contemporary methodologies for the qualitative treatment and timely prevention of oral diseases, with a focus on periodontal diseases in postmenopausal women, clinical and functional changes in periodontitis, and the provision of relevant information to dentists. The monograph seeks to equip dentists with knowledge on the clinical and laboratory parameters that need to be determined when monitoring the effectiveness of treatment used in this form of the disease. The monograph is intended to be relevant to a wide range of professionals, including dentists, therapists, clinical residents, master's students, doctoral students, and students of medical universities.

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ABBREVIATIONS

CRP-C-reactive protein

ET-1-endothelin-1

HT-hormonal therapy

BMD - bone mineral density

MChGP-mild chronic generalized periodontitis

MChGP 2- Moderate chronic generalized periodontitis

SChGP - Severe chronic generalized periodontitis

HRT- hormone replacement therapy

PI - Periodontal index

PMA - papillary-marginal-alveolar index

IL-6-interleukin-6

OHI-S -Hygiene Index

SDP - Soft dental plaque

HDC - Hard dental calculus

ENTRANCE



Today, the life of women in the postmenopausal period is characterized by metabolic disorders in various tissues, including teeth, in the form of tooth loss, periodontal diseases, and increased resorption of the alveolar and jaw bones. Currently, the high prevalence of dental diseases in women in the postmenopausal period and..."the difficulties encountered in their treatment and prevention are largely due to insufficient knowledge of their pathogenesis...." Postmenopause is the physiological period of a woman's life that occurs after the last menstruation. Postmenopause refers to the age-related aging of a woman's body. In many patients, the quality of life deteriorates and the level of health decreases. Therefore, after the cessation of menstruation, women need regular monitoring and, if necessary, therapeutic therapy, including hormone therapy. Postmenopausal symptoms arise from a deficiency of estrogen hormones, synthesized in the ovaries during the reproductive period and acting as the main protectors of the female body. After a persistent cessation of menstruation, a small amount of estrogen is synthesized in the adrenal cortex, but this is not enough to maintain health at a constant level. Usually, at the beginning of the transition to menopause, subjective signs of estrogen deficiency appear (hot flashes, heat sensation, sweating, decreased performance, decreased memory and attention), and later (after several years of postmenopause), signs of target organ damage are added to them. Usually, postmenopause in women

begins approximately after 48-50 years, i.e., within 1-2 years after the complete cessation of menstruation. The average age of menopause worldwide is 48.8 years (95% CI 48.3-49.2), which has significant variations depending on the geographical location of women [15], in the Russian Federation it ranges from 49 to 51 years [3]. At the same time, there is a category of patients with premature ovarian insufficiency who may stop menstruating before the age of 40. These women should undergo hormone replacement therapy, which reduces the risk of secondary damage to bone tissue, heart, blood vessels, and other organs depending on the optimal concentration of estrogens.

Timely treatment of postmenopause is aimed at eliminating unpleasant symptoms, maintaining an active lifestyle, and overall improvement of the body. Women in the postmenopausal period need regular observation, assessment of the risk of osteoporosis, genitourinary atrophy, and other complications that can be successfully treated with early diagnosis. A number of domestic scientific studies have shown that systemic osteoporosis caused by estrogen deficiency affects teeth in postmenopausal women. This is manifested in a decrease in the height of the interdental septum, the appearance of osteoporosis foci in the body of the mandible, and a decrease in the density of the alveolar process.

Taking into account the age period, the postmenopausal period has different types:

- timely cessation of menstruation at 48-55 years;
- very early, when menstruation stops before the age of 40;
 - early, when permanent closure of the ovaries occurs at the age of 40-44;
 - late, when women still have menstruation after 55 years of age (in this case, the risk of cancer increases, therefore appropriate screening is required).

According to the etiological principle, there are 2 types of postmenopause:

- spontaneous cessation of ovarian function without any medical intervention;
- iatrogenic - "removal" of the ovaries is associated with surgical intervention (removal of the gonads), radiation or chemotherapy.

More than 50 million women in the world are in the peri- and postmenopausal period, but one-third of women survive under conditions of female sex hormone

deficiency. In recent years, many studies worldwide have been devoted to studying the nature of the relationship between systemic osteoporosis and generalized periodontitis, however, the available data are contradictory and require further research.

Periodontitis is a multifactorial disease caused by bacterial pathogens, the main cause of tooth loss is a violation of the structure of connective tissue, the formation of deep periodontal pockets, and the loss of alveolar bone tissue. Considering the predominance of bone resorption processes in osteoporosis, certain features should be taken into account when planning the treatment of chronic generalized periodontitis in such cases.

In our country, active measures have been taken to develop the medical sphere, reduce their complications, as well as provide qualified medical care to the population suffering from these diseases, and the following tasks have been defined: "Strengthening support for a healthy lifestyle and disease prevention, including the standardization of the medical system, the introduction of high-tech methods of diagnosis and treatment, effective models of patronage and medical examination, the effectiveness, quality and accessibility of medical services." These tasks determine the priorities of in-depth scientific research, such as increasing the level of modern medical care, diagnosing and treating complications of dental diseases among the population, and using modern technologies in providing quality medical care. In studies conducted to improve the treatment of inflammatory-destructive diseases of the oral cavity in women with general osteoporosis in the postmenopausal period, a number of scientific results have been obtained. In particular, the significance of any disease in modern society is determined by the prevalence of this disease among the population, the severity and severity of the outcome, and the economic losses of the patient and their family or society as a whole (Mukhamedzhanova L.R., 2005). It is known that the disruption of the structure and function of the alveolar bone in general osteoporosis has a very negative effect on periodontal tissue (Povoroznyuk V.V., 2013), as a result of which this cause, together with other negative factors, leads to early tooth loss (Kazakova N.N., 2023). Each of these existing methods of

systematic diagnostics is aimed at determining the indicator of the structure or function of bone tissue. It should be remembered that in clinical practice, a comprehensive examination of patients is carried out relatively rarely. In addition, in 50% of cases, osteoporosis appears asymptotically (Franke Yu., 2014; Rozhinskaya L.Ya., 2013).

CHAPTER I. FEATURES OF THE DEVELOPMENT OF DENTAL DISEASES IN WOMEN IN THE POSTMENOPAUSA PERIOD

(Literature review)

§1.1. Modern concepts of the etiology and pathogenesis of the postmenopausal period



In Western countries, more than a third of the female population over the age of 65 suffers from signs and symptoms of osteoporosis, which is characterized by a low density of bone mass. Estrogen deficiency is the main pathogenetic factor in the development of osteoporosis in women. The influence of estrogen deficiency and osteopenia/osteoporosis on periodontitis has not been sufficiently studied due to the lack of studies that assess the clinical signs of partial gingival inflammation and the development of periodontitis. [145].

Postmenopause predisposes women to osteoporosis due to a decrease in estrogen levels. This leads to a decrease in bone mineral density (BMD) and an increase in bone fractures. Osteoporotic fractures lead to a significant increase in morbidity and are considered one of the largest health priorities by the World Health Organization (WHO). Therefore, it is very important to develop appropriate guidelines for the prevention and management of osteoporosis for women in postmenopause. The Women's Health Initiative's randomized controlled trials

showed that hormonal therapy (HT) reduces the occurrence of all osteoporosis-related fractures in postmenopausal women. However, the study showed that the adverse effects outweighed the potential benefits in the bone, leading to a significant decrease in HT use for menopausal symptoms. [115].

It has been established that the period of the onset of natural menopause depends on genetically determined factors interconnected with the territory of residence, national characteristics, economic and social conditions, mode and conditions of life, and civilization.

A tendency towards the earliest onset of postmenopause was revealed with overweight, increased physical labor, including in women with higher education, as well as in working women. However, it was found that the age of onset of menopause in smoking women decreased by 1 year.

The periodontal disease is very common and can make up almost 90% of the world's population. Periodontitis leads to loss of the density of connective tissue and bone tissue, and this is the main cause of tooth loss in adults. [135].

Classification of menopause:

BKT-10 coding N 95.1 - Menopause and climacteric in women.

Menopause is a natural physiological state that occurs in a woman's body during her lifetime. At this stage, a slowdown in ovarian function occurs, after which the absolute function of the ovaries ceases.

Researchers and medical professionals have agreed to define menopause as the last menstrual period followed by the absence of at least a twelve-month menstrual cycle. The advantage of this definition is that it defines a single variable measured during this transition period. This definition also allows for the calculation of the median and average age of menopause for interpopulation comparison. [124].

Menopause is divided into four periods: premenopause, perimenopause, menopause, and postmenopause.

Premenopause is a period characterised by an irregular menstrual cycle, hormonal instability, and the development of early menopausal symptoms lasting 2-5 years.

Women in menopause are prone to estrogen deficiency, which leads to decreased salivation. As a result, the risk of developing dental and periodontal diseases, as well as dysbiosis of the oral microflora, increases [134].

Perimenopause is a stage of highly pronounced clinical manifestations that includes the pre-menopausal period and 2 years after menopause.

Menopause is the complete cessation of menstruation for more than 12 months, the time is determined retrospectively. This phenomenon is a natural physiological process and is associated with the hereditary origin of the conditioned follicle.

In women with periodontal disease and postmenopausal osteoporosis, estrogen deficiency can affect the activity of bone and immune cells, therefore the decrease and loss of alveolar bone density increases. [116].

The standard diagnostic criterion in menopause is the development of amenorrhea with a decrease in the level of estradiol in the blood below 30 mg/ml and an increase in follicle-stimulating hormone (above 40 IU/l) in the blood.

Considering the need for estrogen in postmenopausal women and the evidence confirming the economic efficiency, safety, and effectiveness of HT, we propose considering HT for the main prevention and treatment of osteoporosis in suitable candidates [115].

There are very early (up to 40 years), early (40-45 years), timely (46-54 years), and long-term (over 55 years) types of menopause.

Postmenopause is the transformation of the menopausal period into the final cessation of ovarian function, which continues until the last year of a woman's life (more than 32% of women correspond to a postmenopausal state). This age period means an increase in the number of diseases associated with estrogen hormone deficiency.

Causes of development

With increasing age in women, the occurrence of the postmenopausal period increases. A third of a woman's life can be attributed to this period. During this period, vital changes, such as the process of ovulation, are an exception, complete

presenile activity begins to develop in the female body.

With the onset of natural menopause, estrogen levels gradually decrease over several years, and the woman's body adapts to life in conditions of hypoestrogenism. A sharp decrease in estrogen levels almost ceases after surgical removal of the ovaries. Within a few days after surgery, 70-90% of women develop postovariectomy syndrome and clinical manifestations of menopause. 60% of women experience menopausal syndrome in a severe form, 26% - in a moderate form, and only 14% - in a mild form. [41].

This process occurs due to profound changes in the nervous and hormonal systems, including age-related changes in the pituitary, central nervous system, hypothalamus and ovaries, thyroid gland, adrenal gland, and other endocrine glands of the body, leading to pathological dysfunctions.

It has been established that the period of development of physiological menopause is associated with genetically determined factors, which depend on the place of residence, national characteristics, social and economic status, the nature of the place of residence, the level of education and culture.

Pathogenetic therapy for menopausal symptoms is hormone replacement therapy selected individually. Since the majority of women in the postmenopausal period have one or another extragenital pathology, the leading causes among them are insulin resistance, lipid metabolism disorders, and arterial hypertension. Scientific studies have shown that the pharmacological profile of drospirenone is closest to natural progesterone. Drospirenone's antimineralocorticoid properties promote sodium excretion from the body and prevent water retention. Like progesterone, drospirenone has high affinity for progesterone and aldosterone receptors and low affinity for androgen receptors. It does not bind to glucocorticoid or estrogen receptors [51].

The earliest period of physiological menopause is associated with a decrease in the risk of developing breast cancer, ovarian cancer, and, conversely, with an increased risk of developing diseases of the cardiovascular system, atherosclerosis, stroke, and osteoporosis. In most cases, fatal outcomes decreased by 3% with an

annual increase in the development of the menopausal period. The risk of further development of menopause leading to death in women is 2-4 times higher than in men of the same age.

A tendency towards delayed menopause was revealed in overweight women. This phenomenon is explained by an excess of estrogen hormones in overweight and obese women, which can lead to a delay in the onset of menopause.

Signs of early menopause include vasomotor symptoms:

- overheating and night sweats, most commonly occurring in premenopause,
- menstrual cycle disorder or early postmenopause.

Urogenital diseases (drying and hyperemia of the mucous membrane, itching, burning sensation, dyspareunia, as well as pollakiuria) are so-called "medium-term" symptoms, but in recent years, these symptoms have often already developed in perimenopause [45].

Many authors believe that ovarian dysfunction has a genetic predisposition. Throughout life, a slow decrease in the concentration of follicle-stimulating hormone, as well as follicles located in the ovaries, is observed. Based on this, the activity of the hypothalamic-pituitary structure system repeatedly responds to estrogen hormone deficiency. Due to an increase in the secretion of gonadotropic hormones of the hypothalamic-pituitary system, profound functional and biochemical disorders lead to a weakening of follicular activity and its sensitivity to gonadotropic motives, a slow decrease in the synthesis of estrogen hormones and progesterone. This reduces FSH synthesis by the adenohypophysis organ. These disorders ultimately lead to a compensatory increase in FSH and LH production by the adenohypophysis organ, which affects the development of the menopausal period.

The average age of menopause worldwide is from 49 to 51 years, and there is a tendency to expand the age range of the physiological period. During this time, general involuntary processes occur in the woman's body. Special attention is paid to the manifestation of menopause in the oral cavity. It has been established that the development of dental diseases such as caries, gingivitis, periodontitis is observed.

Other changes may also occur in the oral mucosa: burning sensation, bad taste in the mouth, increased viscosity of saliva, dryness of the oral cavity. According to a number of authors, the probability of developing burning sensation syndrome in women during perimenopause is considered high [43].

A deficiency of estrogen hormones plays a major role in the pathogenesis of many diseases. It should be noted that early disorders of the cardiovascular, skeletal, and central nervous systems manifest themselves even in premenopause. At this age, osteoclast synthesis increases, osteoblast cell synthesis decreases, calcium adsorption in the intestine decreases, and vitamin D deficiency leads to increased bone tissue resorption. The period of menopause is considered a stage in the development of emotional disorders of any category of belief, from a slight deterioration of mental state and anxiety to depressive phenomena.

In menopause, against the background of age-related changes in the body, various changes predominate, indicating a deficiency of sex hormones and a decrease in the quality of life. Menopause determines the need for correction of vasomotor and other symptoms of estrogen deficiency and allows for preventive measures. During perimenopause, symptoms may indicate both intermittent hyperestrogenism (mastodynia, menorrhagia, migraine, nausea, etc.) and signs of estrogen deficiency (vasomotor, psychological, urogenital, etc.). Early postmenopausal signs of estrogen deficiency predominate, which can begin in perimenopause and continue until the postmenopausal period [37].

The main signs of menopause are divided into two types: early and late. The first signs are sweating, aggression, irritability, depressive syndrome, sleep disturbance, memory impairment, and discoloration of the mucous membrane. Late signs include metabolic (accumulation of central and abdominal adipose tissue), cardiovascular (vascular atherosclerosis), and musculoskeletal (increased loss of bone tissue - osteopenia, osteoporosis, increased risk of fracture, sarcopenia) changes [74].

§1.2. Clinical manifestations and features of the development of dental diseases in women in the postmenopause period

In menopausal age, irreversible hormonal disorders of ovarian activity develop, and the level of estrogens decreases. In particular, during this period, an increase in various diseases is observed [88]. A study of the dental status of women in menopause confirmed the existence of a link between a decrease in estrogens and a significant increase in the development of dental diseases [93]. Based on the presence of estrogen-containing hormone receptors in the oral mucosa and salivary glands, it is possible to identify disorders in the level of hormonal changes in the oral cavity itself [8;132;109]. Lamolo-Vartare et al. proved the presence of mRNA and immunoreactive protein of the estrogen hormone in the mucous membrane and salivary glands, which simultaneously confirms its biological role [94]. In this regard, the menopausal period is a process accompanied by metabolic and functional disorders in the tissues of the oral cavity [114]. As a result, tooth loss, periodontal tissue damage, and high resorption of alveolar processes in bone tissue are observed [58; 126].

Glossalgia

Oral overheating syndrome (glossalgia) is expressed as severe pain affecting various parts of the oral cavity, dry mouth, taste disturbance, and acute heating sensation: the tongue, lips, gums, inner cheek surface, palate, as well as any part of the oral cavity where these changes spread. This condition is characterized by a lack of certain clinical manifestations [117].

At the same time, painful sensations manifest as dryness of the oral cavity, increased sensitivity to food, and a change in taste [128].

The main symptoms of heating in the oral cavity include local (chronic lesions of the oral mucosa, allergic reactions to various metals, foreign substances, and systemic (diseases of the digestive tract; cardiovascular pathologies; neuroendocrine pathologies; vitamin deficiency) causes. In particular, mental disorders, anxiety, and depressive syndrome play a major role. Burns of the oral cavity are observed in women at least 3-7 times more often than in men, and especially after the onset of menopause, its increase from 19% to 32% can be observed [129].

In scientific research, M. Robias and co-authors proved that with psycho-emotional changes, the development of a feeling of burning in the oral cavity in most women during menopause can be observed most often. More than 73% of women complained of a feeling of heating in the oral cavity without specifying a specific location; the tongue (13.2%): anterior (47%), lateral part of the tongue (44%) and middle part of the tongue (12%); and the lips and gums (2.6%). Q. Mankosh et al., studying 370 women in the postmenopausal period, found changes in burning syndrome in the oral cavity (26.1%), dryness of the oral cavity (26.9%), and dysheusia (4.1%) [122].

Oral dryness

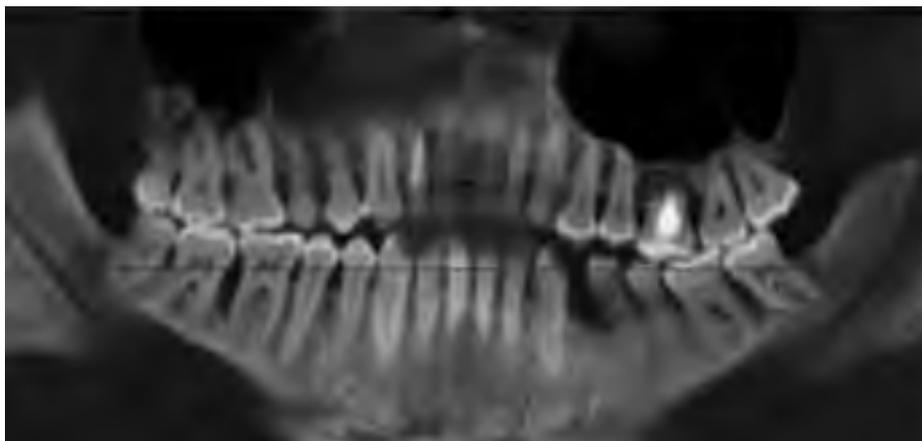
Oral fluid and saliva play an important role in maintaining a healthy oral cavity. Decreased oral fluid secretion increases the risk of caries, discomfort in the oral cavity, and the development of fungi in the oral cavity. The total volume of amylase, calcium, and phosphorus remains unchanged, and the acidity of saliva decreases. Over time, the oral fluid or saliva begins to thicken even more, its secretion decreases - saliva is released, as the amount of ptyalin decreases, mucin and lysozyme increase [25].

T. Naderfox et al. proved that xerostomy is more common in women (28.3%) than in men (20.9%), and the gender difference turned out to be significant [137]. It turned out that 44% of menopausal women and 6.5% of pre-menopausal women experience discomfort in the oral cavity [64]. Thus, J. A. Rakmani et al. in their studies revealed a significant decrease in the pH content of mixed saliva in the slightly acidic direction and a decrease in the amount of saliva (44%), which leads to an increase in the GI and PI, OHI-S, and KPI indices. [110].

Regarding the pH value of mixed oral fluid, the analysis results show the same values according to the Calin Caloja scientific study. At the same time, despite the disruption of taste sensations during the development of menopause, a decrease in the state of altered taste sensitivity thresholds and their preservation within normal limits were noted [148]. R.K. Rohita noted in her study that the unsatisfactory relationship between the duration of menopause and the speed of saliva flow is weak

[119].

Bone tissue alteration



Many authors in their studies have found that a decrease in estrogen levels in the female body leads to osteoporotic changes in bone tissue in 40% of cases, which is a decrease in bone mass and density [125; 75; 118]. Osteoporosis usually develops in elderly people, more often observed in young women than in men. It has been established that increased bone metabolism develops 4-5 years before the onset of menopause [10]. The release of the bone tissue matrix under conditions of weakening of the activity of osteoblast cells increases the development of bone erosion by osteoclast cells.

The course of osteoporosis is slow and without significant changes [47]. According to a number of analyses, osteoporosis should be considered as a risk factor for the progressive course of periodontitis. Resorption of the bone skeleton in osteoporosis was determined due to the loss of periodontal tissue, teeth, and the height of the alveolar bone [95; 88]. During the study of the periodontal condition of women in the postmenopausal period with osteoporosis, S.Falids-Williams revealed a significant deepening of periodontal pockets and damage to periodontal tissue, followed by its decrease, compared to age control groups without osteoporosis [12].

§1.3. Etiology and pathogenesis of periodontal diseases in postmenopausal women

Periodontal disease is one of the most common inflammatory and chronic malignant diseases, recorded in 4 billion people worldwide [48]. At the same time,

the attendance of patients with periodontal diseases in dental clinics has increased, which is almost 65% of all registered patients in the dental office [94].

The formation and development of inflammatory-destructive processes of periodontal tissue are associated not only with local, but also with general factors. According to a number of surveys, periodontal tissue diseases are detected in 81% of postmenopausal women, moreover, among these diseases in various forms, periodontitis is the most common [49].

Great importance is attached to the influence of estrogen hormone deficiency on the formation of periodontal tissue diseases [119]. D. Darpa and G. Jann studied the state of periodontal tissue in women in the postmenopausal period. They studied 95 women with an average age of 54-55 years and an average postmenopausal duration of 9.33 years. When probing the gums in the examined women, the bleeding index was 53.55%, and the periodontal index was PI=4.44%. In 12 women, a mild degree of chronic periodontitis was observed, in 35 - moderate, and in 29 - severe destructive changes of periodontitis. The indicators of this survey show a higher risk of developing severe inflammatory-destructive forms of chronic periodontitis in women in the postmenopausal period [84].

Numerous data on the study of the pathogenesis of periodontal diseases have shown the direct and indirect influence of periodontopathogenic microorganisms on the overall state of the body. Modern epidemiological, clinical, functional, and laboratory experimental studies prove a connection between the microbiological state of the blood or the inflammatory process characterized by damage to periodontal tissues and concomitant diseases of the body as a whole [94].

N. Naozi et al. established a correlation between periodontal disease in women in postmenopause with an increased risk of developing thoracic, esophageal, pulmonary, gallbladder, and melanoma tumors. Consequently, pathogenic microflora in the periodontium can reach the esophagus, including areas where it is difficult to penetrate the circulatory system, through oral fluid into the lungs through respiration [119].

Ko'pgina ilmiy tadqiqotlar tanadagi ko'plab jarayonlarga, jumladan limfa

tugunlari, arteriyalar va o'pkalarga ta'sir qiluvchi parodontit etiologiyasi bo'yicha olib borilgan [89].

Many scientific studies have been conducted on the etiology of periodontitis, which affects many processes in the body, including lymph nodes, arteries, and lungs [89].

Periodontitis is a multifactorial disease caused by bacterial pathogens, causing a protective reaction with loss of connective tissue structure, formation of deep periodontal pockets, resorption of alveolar bone tissue, and is the main cause of tooth loss [76]. In addition, individual dental status, dangerous habits, malnutrition, lack of microelements, uneven occlusion, changes in blood circulation in microvessels, and general lesions are also significant in the formation of periodontitis [131]. As a result of the influence of many causal factors on the formation and development of inflammatory-destructive diseases of periodontal tissues, it is necessary to identify the causes leading to the formation of periodontitis in the early stages [44; 141].

The bioecology of the oral cavity, among the bacterial microflora, is one of the most complex microbial floras of the human body, containing more than 500 different microbes. The bacterial sign of development plays an important role in damage to periodontal tissues, and the diversity of the microbiocology of the oral cavity, belonging to the sequence of immune-specific reactions, causes the formation of inflammatory-destructive changes in periodontal tissues [93]. As a result of an increase in the number of pathogenic and conditionally pathogenic bacteria, the concentration of representatives of ordinary microbiocology decreases [11].

As a result of the proliferation of dental plaque bacteria and the accumulation of their secretions, it was established that it is the main feature that has a mechanical, physical, chemical, and biological effect on periodontal tissue [23; 53; [128]. Microorganisms embedded in easily digestible carbohydrates (sucrose, glucose) lead to the formation of organic acids, the breakdown products of which play a leading role in reducing the pH level of oral fluid and disrupting the mineralization of tooth enamel. As a result of the synthesis of polysaccharides by dental plaque

microorganisms - dextrans and levans, a long-term developmental and harmful long-term effect on dental enamel has been established. With the development of plaque, an increase in gram-negative anaerobic species from gram-positive to gram-negative is observed [44]. Changes in periodontal tissues are detected as a result of the proliferation of dental plaques and plaques containing pathogenic and opportunistic bacteria. This leads to the destruction of the following periodontal tissues: deepening of the dentoalveolar pockets, formation of the periodontal pocket, violation of the strength of the gums to the root surface. In addition, the development of plaques leads to the recession of the gums in the periodontal tissue and the loss of the alveolar bone [117]. The rate of plaque formation is determined by the method of feeding, oral hygiene, the quality and quantity of oral fluid [15; [128].

S.K. Sokrsky identified 5 main microbial bacteria involved in the process of inflammatory and destructive changes in periodontal tissues: *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*, *Prevotella intermedia*, *Treponema denticola*, *Tanarella forsythia* with the participation of indicators, periodontal pathogens activate each other's outcomes [82; 62].

E. Karkuma and Y. Normutra established a relationship between the presence of *P. intermedia*, *P. gingivalis*, *T. Denticola* and *Prevotella nigrescens* in samples of oral fluid or saliva and the development of periodontitis. At the same time, *T. forsythia* and *A. actinomycetemcomitans* have not been reliably identified by sampling from either oral fluid, saliva, or periodontal pockets [139].

Aggregatibacter actinomycetemcomitans, immobile, gram-negative, facultative anaerobic coccobacteria, are associated with microbial bacteria involved in the development of inflammatory and destructive processes of periodontal tissues, and in appearance: rod-shaped with rounded edges [116]. Five serotypes of *A. actinomycetemcomitans* have been identified, which differ from each other by the type of virulence. The observation time of *A. actinomycetemcomitans* on the dental plaque varies. At that time, *A. actinomycetemcomitans* was found in 0-25% of healthy children and 41-100% of those examined with periodontal tissue damage [17; 62; [65]. *A. actinomycetemcomitans* passively binds with other microbial

bacteria. With the help of adezine peptides, *A. actinomycetemcomitans* binds to transferred collagen and fibronectin of species I, II, III, V, and destroys them [123]. The capsule-like polysaccharide antigen protects *A. Actinomycetemcomitans* from phagocytosis. *A. Actinomycetemcomitans* attaches to the outer surface of epithelial cells, causes the formation of a vacuole in the cytoplasm, and breaks down into the cell membrane, leading to its death [59].

§1.4. Methods for determining oral microflora in periodontal diseases

Diagnosis of periodontal tissue damage is based on clinical and functional foundations, which is determined by questionnaires, patient examination, analysis of dental and periodontal status (determination of periodontal pocket depth, gingival bleeding, periodontal and hygienic indicators), and X-ray examination - determination of alveolar bone height [125].

Nevertheless, traditional diagnostics does not have the ability to determine the condition of the periodontium in highly sensitive individuals at risk of exacerbating the progression of processes [15]. Therefore, it is necessary to identify more advanced equipment confirming the exacerbation of periodontal diseases.

According to the results of a number of studies, the development of periodontal tissue diseases leads to an increase in individual microbial flora. Pathogenic microflora of the periodontium: exotoxins and endotoxins produced by *T. forsythia*, *P. intermedia*, *T. denticola*, *P. gingivalis*, and *A. actinomycetemcomitans* determine the duration of inflammatory-dystrophic processes, causing damage to gingival tissues and the alveolar bone.

The most important diagnostic methods for the pathogenic microflora of the periodontium are electron microscopic, bacteriological, and molecular genetic. Electron microscopic diagnostics determines generalized parameters of microbial flora, which do not determine the type of microorganism. Generally accepted types of microorganisms in the diagnosis of periodontal tissue damage, i.e., the proximity of their sex and species, the bacterial environment in an individual nutrient medium has a number of shortcomings: it is necessary to study the need to establish

irreversible processes of changes negatively affecting periodontal tissues, analysis duration from 5 to 7 days, the use of individual specific nutrient agar, and the organization of the necessary requirements for their cultivation [117; 132].

Early detection of bacteria, prevention of their reproduction to prevent inflammatory and destructive changes in periodontal tissues is an important link in innovative periodontology. Today, the most correct, appropriate type of diagnostics is molecular genetic diagnostics, i.e., polymerase chain reaction (PCR), which contributes to a significant increase in the low saturation of the desired nucleic acid fragments (DNA) in biological cells [36; 37; 80].

Positive aspects of PCR diagnostics include:

- In the direct direction, identification of the source of infection (presence of an individual specific DNA segment detected by PCR);
- increasing the individual specificity of the diagnostic type (identification of a DNA fragment characteristic of this source of infection);
- increased sensitivity (allows detection of individual cellular microbes);
- Multilaterality (allows studying a sufficient number of bacteria simultaneously from certain tissues due to the same structure in complete DNA or RNA);
- Taking samples in a short time (3-5 hours);
- Diagnosis of latent infections (if the changes occur in a closed form, it allows for the detection of microbes).

The essence of this method is the synthetic repetition of source DNA fragments in the patient's biological material. As a result of the propagation of the first fragment of the DNA of the detected microbial type, two are formed. The formation period of another DNA molecule is approximately 3 minutes. For precise visual detection of the microorganism using electrophoresis, it takes from 30 to 40 cycles.

It should be noted that, taking into account the use of hormone replacement therapy (HRT), it is necessary to organize PCR testing methods necessary to obtain the necessary information about the bacterial status of the female oral cavity.

§1.5. Etiopathogenetic aspects of the treatment of periodontal diseases in

the postmenopausal period

Due to the direct connection between the general changes in the human body and inflamed organs, the development of microorganism pathology intensifies. In this regard, most researchers [123] in their scientific articles found that the development of a pathological condition in periodontal tissues is often considered a possible complication of the underlying disease, while in another case, it is closely related to this disease [22, 23, 113].

Major inventions in the field of medicine in the past have made it possible to identify multifunctional phenomena based on cell autolysis, unified systemic processes of free radical oxidation [22, 136, 13], cellular transformations of various origins associated with protective incompatibility. [73, 86, 135, 112, 45] and cytokine control [132, 35]. These common system devices directly link the development of most changes, showing their relationship with the same risk methods. The same mechanisms are associated with the formation of inflammatory and destructive changes in periodontal tissues.

Thus, when planning treatment, it is necessary to use a systematic approach, taking into account local tissue damage and complex changes in metabolism [19, 17].

To ensure the strengthening of the defense mechanism, as well as the treatment of antioxidants and compensation for mineral deficiency, most researchers simultaneously noted several enzymes, including: sodium thiosulfate, antioxidant vitamins (E, A, C), products containing mineral substances (clamin, panangin) as complex therapeutic preparations [13, 45, 47, 50].

Information on the use of the antioxidant drug "Mexidol" in the general treatment of periodontal tissue diseases is of great importance [29, 28]. According to the data obtained by the authors, local oral administration of Mechidol and the combination of local and intramuscular administration of the drug to a greater extent leads to a significant increase in the effectiveness of treatment.

These injuries lead to an increase in local active complexes, restoration of tissue balance, and significant improvement in therapeutic procedures [37, 63, 141,

112].

Many researchers have noted a good therapeutic effect when the active substance "Tanakan," Ginkgo biloba leaf extract, is added to the general treatment of periodontal disease. This drug has a multifunctional effect and therefore affects many cells in the development of periodontal inflammation.

Ginkgo biloba leaf extract enhances capillary blood flow, has an antihypoxic, antitumor effect, and limits the formation of free radicals and lipid peroxidation in cell membranes. In addition, this drug has a calming effect and thereby reduces psychological alertness, anxiety, and fear [79].

A necessary trend in the etiopathogenetic treatment of chronic general periodontitis is the correction of the protective balance. In practical dentistry, in particular, Imudon immune system corrector is widely used, which is characterized by the presence of antigens in the polyvalent complex.

The drug's effect is manifested by increased phagocytic stimulation of macrophages, an increase in the level of lysozyme in oral fluid, an increase in the level of strong cells of the immune system and secretory immunoglobulin A. The drug helps stimulate leukocyte migration in the thickness of the mucous membrane. [13, 19, 79].

In turn, among the drugs that modulate the immune system, the use of "Likopid" is recommended - a synthetic agent of natural origin with anti-inflammatory, antibacterial, reparative process-stimulating, antitoxic, and hepatoprotective properties [42].

As a modulator of the immune system, it is proposed to use the drug "Levamisol" (Decaris), which, under the control of immunological indicators, regulates the processes of the immune system at the cellular level, restoring abnormally impaired T-functions [49]. In addition, thymalin, tactivin, thymoptin, and thymogen are used to restore protective forces in the treatment of periodontal diseases.

It should be noted that the correction of the immune system should be carried out precisely together with the immunologist after the necessary laboratory tests of

the immunological status.

To eliminate bone tissue resorption, it is necessary to use nonsteroidal anti-inflammatory drugs (naproxen, ketoprofen, indomethazine), one of which is the increase in prostaglandins and inflammatory mediators in periodontal tissues [48, 54].

These agents, having an antihypoxic effect, restore blood circulation, reduce the effect of hyaluronidase, and prevent the formation of microthrombosis. Indometazine is also effective in the treatment of lesions with autoimmune components in the pathogenesis.

As always, the use of antiseptic solutions, decoctions and infusions of medicinal herbs (turnip, chamomile, oak, calendula), antihistamines, desensitizing and antibacterial therapy for periodontal inflammation is carried out in a timely manner [59, 41, 83, 103].

Calcium thiosulfate (calcium glycerophosphate, chloride solution, calcium gluconate) and sodium thiosulfate, which have pronounced antitoxic and anti-inflammatory effects, are often used as desensitizing agents [49].

In addition to the desensitizing effect, calcium preparations reduce the permeability of the walls of blood capillaries and are important for the complete formation of bone tissue [49].

The use of antihistamines (suprastin, tavegil, fencarol, pipolfen) reduces soft tissue swelling, prevents allergic reactions, and has a sedative and anti-inflammatory effect.

PVP-n agents combine endo- and exotoxins, remove them from the body, normalize the permeability of cell membranes and capillary walls, improve blood circulation in vessels, positively affect aggregation ability, and increase the level of oxygen tension.

Along with an antitoxic effect, these agents affect the concentration of immunoglobulins, bind mobile immune parameters, increase the number of T-suppressors, and stimulate the increase of immunoglobulin E, thereby exhibiting a stimulating immunomodulatory effect. Digispon has antimicrobial (due to

dioxidine) and reparative (due to collagen) effects.

The use of adsorbents in the periodontal pocket and their application to gingival tissues simultaneously affects many aspects of adsorption, antibacterial, anti-inflammatory, and etiopathogenesis.

It is necessary to note the scientific research on the determination of the role of platelet growth factor-BB agents, the fibrin-fibronectin system "Tissukol-Kit" and the hydroxyapatite system "Ostim-100" in the treatment of periodontal tissues by the method of targeted stimulation. [50].

In the treatment of periodontal tissue pathology, physiotherapeutic methods are often used, which have a reparative effect on microcirculation, trophic-capillary activity, enzymatic processes, and prevent inflammatory and destructive changes in periodontal tissues [45, 7, 91].

The effective effect of physiotherapeutic treatment is an increase in the individual nonspecific reactivity of periodontal tissues and the immune forces of the human body [8].

Currently, the following physiotherapeutic treatment methods are used: hydroionotherapy, hydrotherapy, darsonvalization, magnetotherapy, electroseption, vacuum therapy, electrophoresis (vitamins P and C, calcium, heparin, lidaze, trypsin), self-massage, laser therapy, fluctuorization, photodynamic therapy, etc. [22, 48, 88].

Hyperbaric oxygen therapy (HBO) is an etiopathogenetic method of treating periodontal diseases, during which a change in the concentration of periodontal tissues with oxygen is observed and hypoxia decreases. This treatment method improves protein metabolism, normalizes the energy supply of periodontal tissues, capillary blood flow, and transcapillary metabolism of periodontal tissues, thereby increasing their potential for regenerative activity [23,46].

Eastern therapies associated with physiotherapy, cryotherapy, and hirudotherapy have gained wide recognition in the development of periodontal pathology therapy.

Apitherapy, in other words - treatment with products containing beekeeping

products, became widespread after a number of scientific studies that revealed the role of honey in its immunobiological, antibacterial, anti-inflammatory, stimulating tissue renewal, analgesic, sedative, and desensitizing effects. For the treatment of periodontal pathology, rinsing, applying a bandage to the gum surface, and electrophoresis with a 30% aqueous solution of honey are used.

At the same time, end products of bees, such as electrophoresis with an aqueous or alcoholic solution of propolis and electrophoresis with a 0.5% aqueous solution of apilak, can be widely used for treatment [86].

Today, hirudotherapy is very often used in the treatment of general periodontitis. The positive effect of such treatment is explained by the ability to stop the accumulation of platelets and aggressive indicators of blood coagulation, which participate in the course of biological and chemical reactions aimed at thrombin formation. Dragee-type models or gelatin capsules were created for peroral use [66]. Probably, simultaneously, in the oral cavity, at the stage of rehabilitation of systemic therapy, it is necessary to use medical leeches [77, 9].

In the general treatment of periodontal pathology, the following preparations are also used to prevent microcirculatory changes - complamin, especially trental, acetylsalicylic acid, nicotinic acid (vitamin PP), rutin (vitamin P), ascorbic acid [55]. The above-mentioned drugs improve capillary permeability, have an antithrombotic effect, normalize the rheological properties of blood, and enhance metabolic functions in the walls of blood vessels.

The development of therapeutic measures in patients with periodontal tissue changes, especially in long-term and severe periodontal diseases, cannot be carried out without surgical intervention, the task of which is the restoration of irreparably lost, irreversible periodontal tissues.

Innovative scientific research allows solving the problem of restoring the bone structure of the periodontium by replacing bone tissue with various osteotropic materials. The use of such raw materials and treatment methods allows for an increase in the size of the bone structure of the periodontal tissue complex by 2.9-4.9 mm and osteoregeneration of the dentogingival joint [113].

In the systemic treatment of periodontal tissue diseases, local orthopedic treatment is equally important, since among local factors, the severity of clinical and functional traumatic occlusion, changes in the occlusal-articular relationship play an important role in the development of periodontal diseases.

The task of orthopedic treatment is to prevent functional overpressure caused by the loss of teeth or changes in their position and to replenish the arch of the common dental arch in a lost functional state [26, 25, 45, 49]. To prevent premature tooth loss and ensure free movement of the mandible, selective grinding of hard dental tissues is often used as an orthopedic treatment method.

Selective grinding of teeth is used in severe degrees of periodontal inflammation, final grinding is used in many visiting stages only after the completion of conservative treatment of processes in severe degrees of periodontal inflammation and before the surgical stage with phased implementation [54, 154, 92].

For initial and surgical treatment, temporary splinting of the teeth is used, which prevents their movement, reduces it if present, prevents and reduces functional overload of periodontal tissues and overpressure [1, 2, 4, 17]. Direct prosthetics is used for the purpose of long-term immobilization of moving teeth, equal distribution of chewing pressure on existing teeth of alveolar processes and the alveolar bone, improvement of chewing and speech functions, increasing the effectiveness of dental treatment, and long-term treatment [11, 22, 99]. This process is carried out with removable and non-removable orthopedic prostheses.

§1.6. The role of hormone replacement therapy in the treatment of periodontal diseases in women in the postmenopausal period

Many studies have etiopathogenetically confirmed the use of complex hormone replacement based on the use of estrogen-containing hormones or their combination with progestogens in the treatment of periodontal pathology in women with estrogen hormone deficiency.

Due to the compactness of estrogen-containing hormone receptors in connective cells, as well as the density of alveolar bone tissue and the density of

other bones in the body being approximately 10 times less, the use of complex hormone replacement therapy for the treatment of periodontal changes in women in the postmenopausal period does not give significant results and allows only to ensure the stability of the inflammatory-destructive phenomenon [80, 121, 132, 15].

Thus, the additional use of estrogen-containing agents in periodontal diseases in the oral cavity has a positive effect on the state of periodontal tissues in the body of women in surgical and natural menopause.

Hormones are individual specific biologically active substances that participate in maintaining the organic sphere of the body, metabolic phenomena, and controlling the growth and development of the female body [47]. Estrogen and progesterone are bioregulators of reproductive function and have a strong effect on the nervous, cardiovascular, and musculoskeletal systems, including the organs and tissues of the oral cavity [22].

GAT is an effective method of treating postmenopausal symptoms [35]. This treatment leads to a return to the normal level of estrogen-containing hormones in blood serum and, as a result, plays a good role in preventing the development of inflammatory and destructive diseases, since the development of osteoporosis and destructive processes is observed in postmenopause. [114].

In the USA, 35-45% of postmenopausal women use GAT, in Australia this figure is 27%, in European countries this figure is from 15 to 32%, and in Russia - 0.3% [45].

There are two types of estrogen-containing hormone administration: enteral (sublingual, oral) and parenteral (nasal, vaginal or gel, injection).

Classification of drugs for hormone replacement therapy:

- Monopreparations (estrogens, progestogens);
- Combined preparations containing estrogen and progestogen (monophasic, two-phase, three-phase);
- Combined preparations containing estrogens and androgens;
- Combined preparations containing estrogens and antiandrogens;
- Combined preparations with estrogenic, gestogenic, and mild androgenic

activity;

- Selective estrogen receptor modulators - SERMs.

In their scientific work, P. Maskarenkas and S. Garskia proved that periodontal diseases are no less common in postmenopausal women who do not receive GAT than in the recipient's body [115]. From another point of view, women in the postmenopause period and women in the premenopause period who received GAT were in the same periodontal condition [102].

Many scientific studies have shown that women using GIS demonstrate complete restoration of life activity. In addition, minimal discomfort is felt in the oral cavity and is combined with increased salivation [21; 35; 63].

In postmenopausal women receiving estrogen-hormonal therapy, the density of the lumbar spine and other bones in the body was higher than in the control group, while similar analyses were also found in the alveolar bone [37].

To date, no one has denied the reliability of hormone replacement therapy, both for preventive and therapeutic purposes. Long-term GAT can increase the risk of developing breast cancer and cardiovascular diseases (vascular thrombosis, thromboembolism, myocardial infarction, stroke) [17].

In particular, a number of scientific works deny the positive effect of GAT on periodontal tissues [131]. The results of the studied works are contradictory. In this regard, the use of GAT in the future requires a thorough analysis of the woman's well-being, identification of signs of risk of vascular thrombosis and oncological changes [56].

Based on this, when complicating and studying scientific research, the need for further analysis of this problem and the creation of an individual algorithm for the diagnosis and treatment of periodontal diseases in women in the postmenopause period is determined.

Complex hormone replacement therapy should be predicted to normalize the life activity of women in the postmenopausal period, primarily due to the prevention and treatment of systemic osteoporotic changes [81, 122].

However, when receiving hormone replacement therapy, in addition to the

beneficial effect, it is recommended to consider the risk of developing complications, side effects, contraindications, and individual tolerance to hormonal drugs [43, 75]. Precisely for this reason, in world literature, recommendations for the use of GAT (hormone replacement therapy) and intensified studies of other treatment methods are considered [23, 104, 18, 133]. Despite the numerous reasons for improving the effectiveness of GIS, doubts about its effectiveness and weaknesses remain unresolved.

In this regard, the task of another treatment method is to choose a treatment with fewer advantages and disadvantages, without the risk of developing cancer and having minimal side effects [87].

Today, along with other types of treatment, there is also a method of receiving general vitamin therapy. It has been established that many vitamins have a significant effect on the activity of the reproductive complex [21, 731, 119]. Vitamins B1, B2, B6, and folic acid participate in estrogen metabolism and the formation of target receptors [24, 103]. With a decrease in the production of estrogen-containing hormones in the ovaries, the adrenal cortex produces estrogens and androgens.

The specific nanofunctional activity of B vitamins lies in the fact that they, as prosthetic groups, are part of the progressive centers of protein enzymes and, therefore, may be necessary for the implementation of metabolic phenomena induced by these enzymes, in which all growth reactions, self-formation, and vital activity of each organism lie at the forefront [83, 109].

Folic acid participates in the metabolism of purine and pyrimidine bases, the methionine complex, syrin, glycine, glutamic acid, choline, nucleic acid and protein metabolism, and cell division. At the same time, folic acid is a necessary indicator against anemia, necessary for natural biological hematopoiesis, participates in the complex of serotonin and norepinephrine production, which has a positive effect on the psycho-emotional state [83, 22, 10].

High doses of folic acid have an estrogen-like effect, which leads to a reduction in the dose of hormone replacement therapy for postmoneopausal

syndrome. With folic acid deficiency, the level of homocysteine in blood plasma increases [121, 124].

Homocysteine is a sulfur-containing amino acid, an intermediate product of methionine metabolism. Homocysteine is not a structural element of protein and therefore does not enter the body with food. Under natural physiological conditions, the sole basis of homocysteine in a woman's body is methionine metabolism.

The metabolism of homocysteine is carried out in two separate ways. The first is the presence of folic acid and methylenetetrahydrofolate reductase (MTHFR).

The second method is the transsulfurization of vitamin B12, free betaine, by homocysteine-methyltransferase, which is characterized by insignificant tissue elementarity and is therefore considered incapable of replenishing homocysteine metabolism in folic acid deficiency [119, 125].

With impaired metabolism of homocysteine characterised by decreased intake of folic acid and B vitamins into the female body or conversely with increased intake of methionine Hyperhomocysteinemia (HHC) develops.

It was also found that, in addition to the genetic deficiency of enzymes involved in homocysteine metabolism and dietary cutting of vitamin cofactors, sex steroid hormones, in turn, alter the level of homocysteine in blood serum [21].

Information about a close relationship between homocysteine metabolism and the level of sex steroid hormones is confirmed by the fact that the level of homocysteine in the woman's blood plasma before menopause is low, and after menopause it increases [130].

Homocysteine is characterized by a pronounced cytotoxic effect, which is due to its oxidative activity, as well as its ability to inhibit natural biological antioxidant systems that lead to endothelial damage [112, 132]. In addition, homocysteine blocks cyclooxygenase in endothelial cells, which contributes to an increase in platelet binding activity as a result of a decrease in prostacyclin production and an increase in thromboxane A2 production, while the binding reactivity of platelets increases, however, the effect of natural anticoagulants and tissue plasminogen activators is reduced. From this it follows that HHC contributes to the proliferation

of the platelet and coagulation complex of hemostasis.

To date, no studies have been conducted in dentistry aimed at analyzing the possible relationship between inflammatory periodontal diseases and the level of homocysteine in the blood, and therefore, in general, there is no data on the use of folate agents. Our research is aimed at the treatment and rehabilitation of changes in periodontal tissues in the female body during the postmenopausal period.

II BOB. MODERN METHODS OF EXAMINATION OF DENTAL DISEASES IN WOMEN IN THE POSTMENOPAUSA PERIOD.

§2.1. General characteristics of observations and materials used and modern research methods

It is important to determine the clinical, functional, and laboratory characteristics of the state of the organs and tissues of the oral cavity and the relationship between the high level of homocysteine in the blood and the integral inflammatory-destructive process. The study of the influence of the proposed therapeutic and preventive measures on periodontal tissues was conducted in 75 postmenopausal women diagnosed with chronic generalized periodontitis.

§2.2. Disease Investigation Object and Implementation Composition

A typical approximate observed comparative study is conducted in interconnected groups lasting 12-14 weeks. The study was conducted with several analyses, where the same patients were used at two different stages of the study - before treatment (comparison group) and after treatment (main group) in the form of control and main groups.

The research team members who concluded a written voluntary contract met the following criteria:

1. A certain group of women aged 45 to 55 living in the Samarkand region.
2. A certain group of women with clinically confirmed natural postmenopause lasting at least 12 months (postmenopausal syndrome).
3. Conducting therapeutic and preventive measures.

Exclusion options

1. A category of persons who do not understand the specific task and purpose of the planned research.
2. Women with significantly severe menopausal syndrome.
3. Women with a confirmed diagnosis of diabetes mellitus of all types and any severity.
4. Development of acute myocardial infarction (AMI), which developed six months before the study, as well as acute cerebrovascular accident (ACV), which formed six months before the study.
5. Certain contraindications to the use of medications for the study.
6. Use of non-recommended medications during the study.
7. Women with drug and/or toxic (i.e., alcohol) dependence, which can be identified based on anamnestic data, as well as at different study periods.
8. Refusal to sign the information consent.

Research design

Based on the set tasks, 75 postmenopausal women underwent in-depth clinical, functional, and laboratory studies on the state of the periodontium, hormonal background, complex inflammation, and the main indicators of blood homocysteine levels.

As a study group, 75 postmenopausal women aged 45-55 years (including 30 in the comparison group and 45 in the main group) underwent in-depth clinical and laboratory examination of the main parameters of the periodontal condition. The study was conducted at the 1st clinic of SamSMU, as well as at the Samarkand Regional Dental Polyclinic, where 25 patients in the main group had a mild form of generalized periodontitis, 29 women had a moderate form of periodontitis, and 21 patients had a severe form of periodontitis. Patients were examined as both the comparison group and the main group, i.e., at two stages of the study - the comparison group (30 people, comparison group) with the traditional treatment method and the improved treatment method (45 people, main group).

The main group included 45 women in the postmenopausal period, who

received continuous treatment with the Angiovit vitamin complex for 2-2.5 months 21-28 days after the end of local treatment, the effectiveness of which was assessed 1-1.5 months after the end of treatment.

The study examined the dental status of patients, the state of the FSH hormone background (E2, LH), the criteria for a complex systemic inflammatory process in blood serum (IL-6, CRP, ET-1) and the level of homocysteine, the condition of the bone tissue of the alveolar process, gingival tissue, the patient's predisposition to therapeutic measures, the frequency and severity of side effects of the administered drug, and oral fluid indicators (salivation rate, pH, Na, K, Ca, concentration of inorganic phosphorus ions).

2.1 table

Research Parameters	Research process	
	onset	after 3-3,5 months
Voluntary consent	±	
Outpatient dental patient card	±	±
Manage exclusion options	±	
Use of complex treatment methods	-	±
Study of Organs and Tissues of the Oral Cavity	±	±
Study of hormonal status	±	-
Analysis of integral inflammatory criteria	±	±
Analysis of oral fluid parameters	±	±
Determination of blood homocysteine	±	±
Orthopantomogram	±	±
Application of treatment	±	

§2.3. Criteria of treatment effectiveness

Effectiveness of therapeutic measures in accordance with the analysis of clinical, functional, and laboratory studies.

1. Restoration or reduction of clinical and functional parameters of the oral cavity appearance:

- a decrease in the values of the PMA index by at least 15% from the initial value;

- Equalizing or reducing the indicators of the periodontal index (PI) by 10% of the initial value.

2. Course of development of clinical and functional indicators of periodontal tissue inflammation (reduction in the severity and saturation of periodontal tissue inflammation, decrease in gingival bleeding, decrease in the depth of periodontal pockets).

3. Development of laboratory parameters (normalization or adjustment of the studied parameters of the integral inflammatory process, hormonal background, homocysteine content).

Davolashning samaradorligi klinik va funksional ko'rsatkichlarga ko'ra soxta terminal chegarasi (davolash tugaganidan keyin 1-1,5 oy o'tgach) bilan baholandi.

§2.4. Modern research methods

Determination of the OHI-S hygiene index.

To study the state of oral hygiene, we used the OHI-S index (Green, Vermillion, 1964), which consists of examining and analyzing the surfaces of the tooth covered with soft and hard dental plaque. Examination was carried out on the vestibular surface of teeth 16, 11, 26, 31, and on the lingual surface of teeth 36, 46 using a periodontal probe, as well as using Curaprox PCA 260. Determining this method and establishing the OHI-S hygiene status is shown in Figure 2.1. Study analyses were determined in points.

The codes and parameters of the OHI-S hygiene index, consisting of two criteria: the plaque index and the dental calculus evaluation index, are presented in Tables 2.2 and 2.3.



Figure 2.1. The condition of the patient's teeth and periodontal tissues in the climacteric period with moderate periodontitis before and after professional oral hygiene.

Table 2.2

Codes and parameters for the analysis of soft dental plaque (CDP)

Points	Indicators
0	Soft dental plaque not detected
1	Soft dental plaque covers up to 1/3 of the tooth surface
2	Soft dental plaque covers 1/3 to 2/3 of the tooth surface.
3	Soft tooth deposits cover more than 2/3 of the tooth surface.

Table 2.3

Codes and parameters for the analysis of hard dental calculus (QTT)

Points	Indicators
0	Hard dental calculus not found
1	Supragingival calculus covers no more than 1/3 of the tooth surface
2	Supragingival stones correspond to 1/3 to 2/3 of the tooth surface, or subgingival hard dental stones are present only in the cervical part of the teeth.
3	Supragingival calculus covers more than 2/3 of the tooth surface, or several subgingival calculus are found on each side in the cervical region of the teeth.

The data obtained for all criteria were summed separately and divided by the number of studied areas, then the result of these indicators was analyzed. The calculation of the hygienic condition of OHI-S was carried out using the following formula (2):

$$\text{OHI-S} = \frac{X \text{ YTK}}{n} + \frac{X \text{ QTT}}{n},$$

where YTK - soft dental plaque,

QTT - hard dental calculus,

n - number of examined teeth (6).

Table 2.4

Interpretation of OHI-S index setup analysis

Index values	Hygiene status
0,0-1,2	Good
1,3-3,0	Satisfactory
3,1-6,0	Unsatisfied

Figure 2.1. Determination of the hygienic index according to Green-Vermilion

§2.5. Methods of examination of periodontal tissues and examination of oral fluid

The study of patients was carried out at the Department of Orthopedic Dentistry of the Samarkand State Medical University and the gynecology department of the first clinic of the Samarkand State Medical University after 4-6 weeks before individual treatment according to a specialized program. The patient's complaints were studied, anamnesis and objective studies were collected, and treatment was completed, attached to a specially created card for analyzing the results of laboratory and functional studies.

Basic (anamnestic, examination, objective examination) and auxiliary (radiographic, transillumination) methods are used to determine the demineralization surface of teeth. In each of the examined, the presence of demineralization surfaces, the presence of fillings, and the presence of extracted teeth were identified and recorded. The frequency of caries detection was studied by calculating the KPU and KPUp indices.

The depth of periodontal pathological pockets was determined from all surfaces of the teeth using a specialized periodontal graduated probe. Three sectors (one anterior and two lateral) were identified in the maxilla and mandible, in which the largest deep position of the periodontal pathological pouch was noted. According to WHO recommendations, pockets deeper than 1 mm were in a pathological state (WHO, Technical Report Series No. 207, Periodontal Diseases, Geneva, 1968). The index of H. P. Muhleman, S. Son (1971) was used to determine gingival bleeding. It was determined by the following evaluation criteria:

0 - no bleeding;

1 - small bleeding is observed when the tooth is touched to the gingival pocket with a probe;

2 - spot detection;

3 - the space between the teeth is filled with blood;

4 - gingival pocket is filled with blood and protrudes beyond its borders.

In order to fully assess the objective state of periodontal tissues, the periodontal index PI was conducted (Russel, 1956) (Table 2.5).

Table 2.5

Parameters of periodontal index analysis

PI (points)	Evaluation options	Auxiliary X-ray examinations
0	No signs of inflammation	:
1	Gingival mild inflammation that does not	No pathological changes in the X-ray image

	surround the tooth in a circular pattern	
2	Inflammation of gingival margin without disruption of circular ligaments of tooth	-
4	It is analyzed only in X-rays.	First-degree resorption of the upper part of the interdental alveolar process reaches half the root length.
6	Periodontitis, circulatory ligament disorders, absence of chewing dysfunction, absence of tooth mobility.	Resorption reaches 1/3 of the root length, interdental bone pockets appear.
8	Destructive changes are observed in the tissues of the periodontium, manifested by the absence of chewing function, mobility, and displacement of the 1st-degree tooth.	

Collection of oral fluid was carried out in the morning on an empty stomach before brushing teeth. Patients are recommended to lower their chin to the chest and, after activation, spit up to 3 ml into a mixed saliva tube using dynamic tongue movements, chewing muscles, and cheeks.



Figure 2.2. Measuring the depth of the periodontal pocket.

Oral fluid examination

The frequency of oral fluid release was calculated by dividing the level of oral fluid secretion (3 ml) by its release time (min). The pH value of mixed saliva was

determined on an ABL 330 automatic analyzer (Radiometer (Denmark)). The basis of the system is the direct measurement of pH using ion-selective electrodes. The study was conducted in an amount not exceeding 0.1 ml.

To determine the content of sodium, potassium, and calcium ions in mixed saliva, the AL 9180 electrolyte analyzer from Roche Diagnostics (Switzerland) was used. Rules of Use: The AVL electrolyte analyzer uses the Ionic Selective Electrode (ISE) rule for targeted determination of electrolyte parameters.

In ion-selective shells, specific processes occur with the electrolytes located in the sample. These shells - ion exchangers - respond with the electric charge of the ion, which leads to a change in the membrane capacitance or the specified voltage generated between the sample and the shell. The galvanic determination of the yarn located in the middle of the electrode reveals the difference between two reservoirs on any surface of the shell. The galvanic circuit is connected in one position through a sample using a corresponding recording electrode, a connecting electrolyte, and a "precise terminal."

The shell, inner electrolyte, and inner electrode close the circuit from the reverse side. The difference in the number of ions between the inner electrolyte and the sample causes the formation of an electrochemical reserve in the shell of the aggressive electrode.

The reserve potential is distributed to the amplifier through a high-conductivity internal electrode. The test electrode is grounded similarly to the amplifier. The number of ions in the following example is established by a calibration curve constructed at the ends of a banal solution with the accuracy of the natural number of ions.

To determine the saturation of inorganic phosphorus in mixed saliva, the composition of reagents from the biochemical analyzer SLIM (Italy) and Vital Diagnostics (Germany) was used.

§2.6. Laboratory research methods

Measurement of homocysteine concentration, signs of inflammation, and vascular endothelial damage

The level of homocysteine in blood serum was measured using the Multiscan ELISA analyzer from Labsystem (Finland) and Axis (Norway) diagnostic boxes. The test system was created to fully determine total homocysteine in plasma (serum) blood. The accuracy of this research method is 1 micromole/l.

Blood was collected in cold plastic tubes, which were stored in an ice container until serum was obtained. Centrifugation was carried out using a K-23 freezing centrifuge (Germany) within 30 minutes after assembly in the air conditioner environment. Test tubes containing blood serum (plasma) are stored in the refrigerator at a temperature of 3-8°C for up to 3 months.

According to the American Association of Cardiologists, when calculating the "norm" for homocysteine in the blood, one should refer to the formula $M \pm 2SD$, the "norm" should be taken as the amount of homocysteine in the blood from 5 to 15 $\mu\text{mol/l}$. [124]. In our studies, the correct level of homocysteine in blood serum for truly healthy patients was $9.5 \pm 2SD$ (up to 10.0 $\mu\text{mol/l}$).

Determination of interleukin-6 (IL-6) in blood serum was carried out using the Multiscan enzyme immunoassay analyzer from Lab-system (Finland) and a set of diagnostic kits from Peninsula Laboratories Inc. (CIHA). The accuracy of the method is 3 pg/ml.

Research method. In this case, in the study example, a gray monoclonal antibody developed against human IL-6 is used to detect IL-6. An increase in the concentration of IL-6 in blood serum indicates the beginning of the inflammatory process.

Determination of the concentration of C-reactive protein (CRP) in blood serum was carried out using the Multiscan enzyme immunoassay analyzer from Labsystem (Finland) and diagnostic kits from Peninsula Laboratories Inc. (USA). The accuracy of the method increases by 1.0 pg/ml.

Research method. This test is based on enzyme-linked immunosorbent assay. The method uses only specific monoclonal antibodies to some antigenic determinants of the CRP molecule. Gray monoclonal antibodies to CRP are immobilized on a microplate. After 45 minutes of incubation at ambient temperature,

the microplate wells are rinsed with water to remove unassembled components. During the subsequent removal period (20 minutes), a blue color is formed with tetramethylbenzidine (TMB) medium. The formation of the color is delayed by the addition of a suspension solution (1N hydrochloric acid), and the color changes to yellow. The amount of CRP corresponds to the color saturation. Absorbance is calculated spectrophotometrically at a wavelength of 450 nm.

Endothelin-1 (ET-1) in blood serum is a sign of damage to the endothelial layer of blood vessels, the determination of its content was carried out using the Multiscan enzyme immunoassay analyzer from Labsystem (Finland) and the Peninsula Laboratories Inc complex of diagnostic kits. (USA). The accuracy of the method is 0.04-0.06 ng/ml.

Research method. Endothelin-1, biotininated endothelin-1, and monoclonal antibodies to the studied blood serum sample were inserted into the plate and mixed. Antibodies to endothelin-1 are combined with a specially processed surface of the lamellar fossae. Biotininated endothelium-1 fights for the binding sites of antibodies with unlabeled endothelin-1 in the studied blood serum. After removal, unconjugated biotininated endothelium-1 is destroyed by washing the plate, then horseradish peroxidase is introduced into the fossa together with streptavidine, thereby creating a "sandwich" system with immobilized antibodies and biotininated endothelium-1 in wells. After washing, the excess of horseradish peroxidase conjugated with streptavidine is removed, a chromogenic substrate, tetramethylbenzidine, is added to the well, which is reflected by peroxidase in the "sandwich" system with the formation of the building.

The intensity of developing staining is equal to the concentration of biotininated endothelin-1, combined with antibodies isolated in the plate. At the same time, the concentration of combined biotininated endothelin-1 contradicts the rational concentration of endothelin-1 in the studied blood serum.

Determination of interleukin-6 (IL-6) in gingival fluid was carried out using the Multiscan enzyme immunoassay analyzer from Labsystem (Finland) and diagnostic kits from Peninsula Laboratories Inc. (USA). The accuracy of the method

is 3 pg/ml.

Collection of material from the periodontal pocket is carried out by KENDOL (USA) by turning the needle towards the root of the tooth using a syringe for endodontic manipulations. Then the obtained material was frozen, and after freezing, medium centrifugation.

§2.7. Methods of studying bone tissue and methods of statistical data processing

Orthopantomography was used to determine the degree of destructive changes in the bone tissue of the jaws, which allows us to see the position of the upper and lower jaws on a single film. The study was conducted by the firm Trophy-radiologie (Germany) on an Opontorama pc 100 orthopantomograph before treatment and 1-1.5 months after the completion of therapeutic and preventive measures in the X-ray room. When studying the radiographs, much attention was paid to the d-shape - the height of the interalveolar process, as well as to the image of the cortical plate of the alveolar process, which indicates the manifestation of osteoporosis and osteosclerotic transformations.

Methods of statistical data processing

Several statistical processing methods were used in the studies, depending on the type of parameters not observed and the intended purpose [111].

To analyze the correctness of the distribution of causes, situation parameters and imbalances were used, which determine the nature of the assignment curve. The location was considered correct with a parameter value from -2 to 2.

In situations of similar order, the results are described in the format $X \pm S_{\sim}$, where X is the sample mean and S is the standard error of the mean. Segments are indicated for ordinal values (points).

Student's t-test was used to compare similar units, along with the correct placement, the unity of qualified units. The adequacy of the selection subdivisions was assessed according to the F-criterion.

The relationship between the dominant traits was checked using Spearman's rank correlation coefficient (R).

Materials and methods of laboratory study of oral microflora

In our study, we used the domestic PCR reagent kit "Multident-5" (SPF "Genlab," Russia). They are designed to identify five of the most important periodontopathogenic bacteria: *P. intermedia*, *T. forsythia*, *T. denticola*, *A. actinomycetemcomitans*, *P. gingivalis*. Sensitivity of the set: 100 copies of the DNA template in the 5 µl analyzed sample (approximately 2×10^4 copies per ml). All procedures were performed on a Tercic amplifier. Sampling of the material for the study was carried out on an empty stomach. A sterile paper dot (No 25) was placed in the gingival pocket (periodontal pocket) with a sterile forceps and left for a few seconds. Then the paper spot was immersed in an Eppendorf-type tube containing physiological saline, the contents of the tube were mixed and sent to the laboratory for further diagnostics. Figure 6 shows the removal of material from the periodontal pocket.

The interpretation of the results was carried out in the form of pluses:

- + - illumination below control (the pathogen is present, but its level is within normal range, treatment is not required);
- ++ - brightness at the control level (within the limits of the pathogenic norm (104 units/ml), treatment depends on symptoms);
- +++ - brightness significantly higher than the control, but below the maximum (prescribed pathology (105 units/ml), requires treatment);
- +++ - brightness is very strong (the amount of the pathogen is higher than 106 units/ml, treatment is required). An example of electrophoresis is shown in Figure 11.



Figure 6 - Sampling of periodontal pocket microflora

III CHAPTER. RESULTS OF THE STUDY OF THE HYGIENIC STATE AND CLINICAL AND LABORATORY PARAMETERS OF THE ORAL CAVITY IN WOMEN

§3.1. Study of clinical and laboratory parameters

The pre- and postmenopausal period in women is characterized by a lack of metabolism in many organs, including the dentoalveolar system, and primarily by disruption of periodontal tissues, which leads to premature tooth loss [60].

To date, a decrease in the concentration of estrogen-containing hormones in postmenopausal women is accompanied by a deficiency of folic acid, as well as methionine metabolism due to a deficiency of vitamins B6 and B12, characterized by a pronounced cytotoxic effect, expressed in an increase in the level of homocysteine in the indicated blood, contributing to the aggregation of platelets and an increase in osteoporotic changes [12, 38, 123].

To determine the relationship between the manifestation of chronic periodontitis and the concentration of homocysteine, signs of vascular endothelial damage, and the intensity of the complex inflammatory-destructive process, we conducted a thorough clinical and laboratory examination of a woman in the postmenopausal period (menopause). In this case, patients aged 45 to 55 with a diagnosis of chronic generalized periodontitis who underwent generally accepted therapeutic measures for sanitary and professional hygienic cleaning of the oral cavity without hormonal correction.

At the same time, a number of categories of women were divided into three groups depending on the severity of periodontitis: 25 women with moderate periodontitis, 25 patients with mild periodontitis, and 25 women with severe periodontitis.

The conducted surveys show that the majority of the examined patients showed a significant decrease in the level of estrogens (E-2) in the blood to 25.0 ± 0.3

pg/ml against the background of an increase in follicle-stimulating hormone (65.1 ± 0.3 pg/ml). (0.5 IU/ml), which is a characteristic feature of the postmenopausal period. The level of luteinizing hormone (LH) was approximately 22.0 ± 0.3 IU/ml.

§3.2. Results of Green-Vermillion Index Indicators

The results of the Green-Vermillion index indicators (Table 3.1, Fig. 3.1) show that there are no significant differences in the hygienic appearance of the oral cavity between women diagnosed with moderate and mild generalized periodontitis (Mann-Whitney, U. -test, $P = 0.325$) and it should have been normal. Thus, it was established that in women with severe periodontitis, the parameters of the studied value were significantly higher than in the comparison group and were equivalent to poor oral hygiene (Mann-Whitney, U-test, $P < 0.003$).

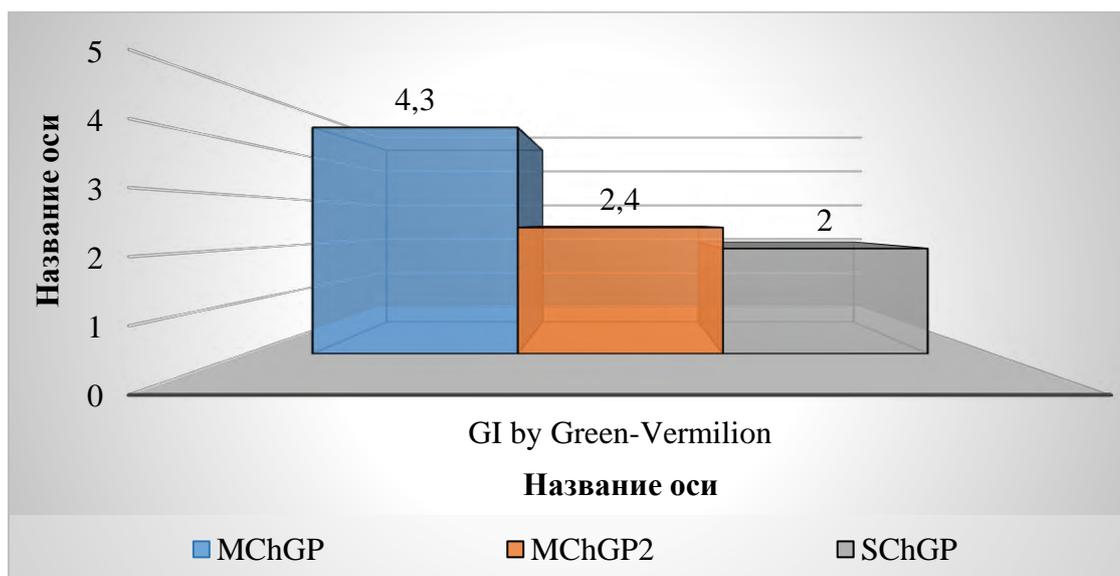


Figure 3.1.

Table 3.1
Results of oral hygiene indicators according to Green-Vermillion in women with chronic generalized periodontitis in the postmenopausal period.

Studied parameters	Postmoneapause period				
	MChGP (p=25)	MChGP2 (p=25)	P1	SChGP (p=25)	P2
GI by Green-Vermilion	1,58±0,18	1,82±0,17	0,335	3,18±0,37	≤0,003

Note: P1 - statistical significance of differences between groups, mild and moderate periodontitis;

P2 - statistical significance of differences between groups of moderate and severe generalized periodontitis (Mann-Whitney, U-test).

The study of the state of the hard tissues of the teeth (Table 3.2) showed that in the postmenopausal period, in the studied women with moderate generalized periodontitis, the saturation of the caries process in the hard tissues increased significantly. Teeth, assessed according to the KPU and KPU_p indices (Mann-Whitney, U-test, P<0.02), were obtained in relation to patients with mild periodontitis. At the same time, despite the fact that there were no significant differences in the estimated indicators between the groups of patients with moderate and severe generalized periodontitis, significant tooth loss was observed in these women compared to those treated.

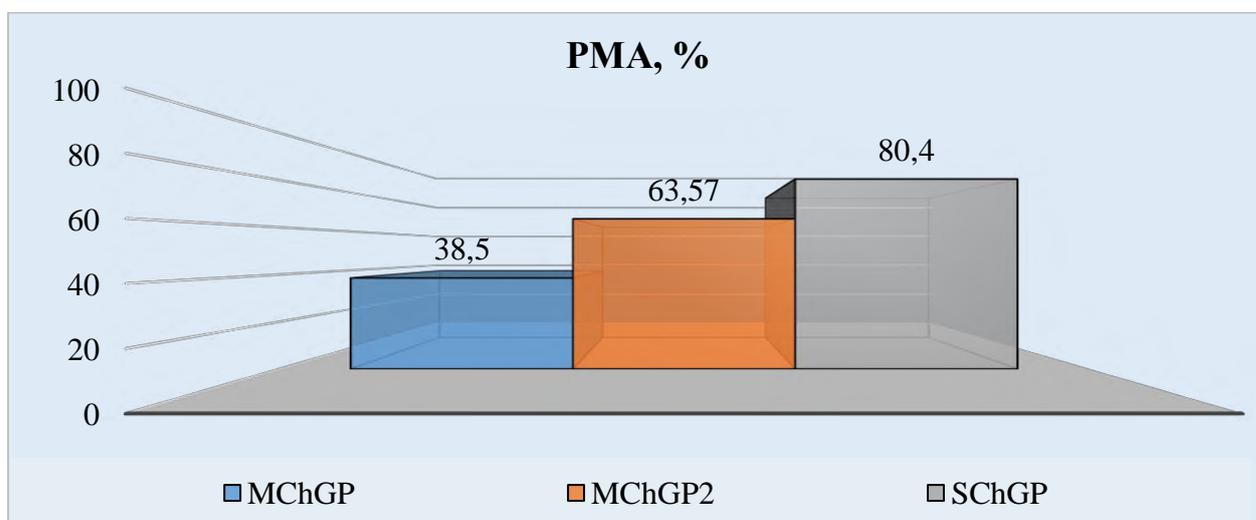
Table 3.2

Studied parameters	Postmenopausal period				
	MChGP (p=25)	MChGP2 (p=25)	P1	SChGP (p=25)	P2
<u>KPU</u>	<u>7,62±0,80</u>	<u>15,69±1,11</u>	<u>P<0,002</u>	<u>14,29±1,12</u>	<u>P>0,04</u>
<u>KPU_p</u>	<u>8,21±0,93</u>	<u>16,31±1,12</u>	<u>P<0,002</u>	<u>15,07±1,12</u>	<u>P>0,04</u>

Note: P1 - statistical significance of differences between groups, mild and moderate generalized periodontitis;

P2 - statistical significance of differences between groups of moderate and severe generalized periodontitis (Mann-Whitney, U-test).

§3.3. Results of the papillary-marginal-alveolar index (PMA) and Muleman parameters.



3.2- Fig. Papillary-marginal-alveolar index in patients with chronic generalized periodontitis in the postmenopausal period

Significant disorders of important periodontal parameters were noted in the studied women in the postmenopausal period with an exacerbation of chronic generalized periodontitis under conditions of certain parameters of conditions in the hard tissues of the teeth and the hygienic state of the oral cavity. For example, this is evidenced by the parameters of the papillary-marginal-alveolar index (PMA), which is the development of an inflammatory phenomenon in the gums (Fig. 3.2). According to the studied data, in the group of patients with moderate generalized periodontitis, the PMA index indicators were 66% higher than in this type of patients with mild disease. In women with pronounced changes in periodontal tissues, the highest increase in the PMA index was revealed, which is more than 25% of the studied indicator analysis in patients with moderate generalized periodontitis.

As a result of the analysis, it can be concluded that in the studied patients, respectively, the exacerbation of generalized periodontitis, along with an increase in morbidity, increased the intensity of inflammation of the gingival tissues, calculated using the Schiller-Pisarev test. (Table 3.3). Patients with mild generalized periodontitis most often exhibited a light brown color, while

women with moderate generalized periodontitis most often exhibited a brown to dark brown color of the gingival tissues. At the same time, the color of the gums became brown even more intensively with severe periodontitis. Quantitative analysis of the sample (Table 3.3) revealed that in women with moderate general periodontitis, color saturation was 1.9 times stronger than in mild periodontitis. When comparing this value between women with severe general periodontitis (1.2 times more) and moderate severity, no statistically significant differences were found.

Table 3.3

Schiller-Pisarev test parameters in the postmenopausal period, points (X±m)

Studied parameters	Postmenopausal period				
	MChGP (p=25)	MChGP2 (p=25)	P1	SChGP (p=25)	P2
Schiller-Pisarev test	1,64±0,08	3,30±0,05	P<0,002	3,57±0,12	P>0,03

Note: P1 - statistical significance of differences between groups, mild and moderate periodontitis;

P2 - statistical significance of differences between groups of moderate and severe generalized periodontitis (Mann-Whitney, U-test).

According to the data presented by Muleman, the results of the study of gingival bleeding (Table 3.4) showed that in most patients with mild generalized periodontitis, this indicator was 2.1 points (a spot was detected when examining the gingival fossa with light), and in patients with moderate generalized periodontitis - 3.3 points (the periodontal fissure was filled with blood with a light probe). Bleeding of the gingival tissues was more pronounced in patients with severe generalized periodontitis and received approximately 3.71 points (blood flows into the gingival cavity and leaks beyond its borders).

Table 3.4.

Parameters of gingival bleeding according to Muhlemann in patients with

chronic generalized periodontitis in the postmenopausal period ($X\pm m$)

Studied parameters	Postmenopausal period				
	MChGP (p=25)	MChGP2 (p=25)	\underline{P}_1	SChGP (p=25)	\underline{P}_2
Muhlemann gingival haemorrhage, points	<u>2,25±0,11</u>	<u>3,21±0,13</u>	<u>P<0,03</u>	<u>3,68±0,12</u>	<u>P<0,002</u>

Note: P1 - statistical significance of differences between groups, mild and moderate periodontitis;

P2 - statistical significance of differences between groups of moderate and severe generalized periodontitis (Mann-Whitney, U-test).

The expected result of the above changes in the periodontal complex is observed in the depth of the periodontal pockets.

According to the data in Table 3.5, in the studied patients with moderate generalized periodontitis, significant lesions were detected in the depth of the periodontal pockets in the zone of lateral and anterior sections of both jaws, which is determined in comparison with generalized periodontitis of mild severity in the region. Such a correspondence of the studied values was also noted when comparing moderate and severe chronic generalized periodontitis in patients in the postmenopausal period.

Thus, in the studied patients, an exacerbation of chronic generalized periodontitis was noted, an increase in the parameters of the complex periodontal index (PI), which is substantiated by the data of Table 3.6, which indicates that if in mild periodontitis the value of the studied indicator averaged 2.51 points, then in patients with moderate periodontitis it increased to 4.71 points, and in patients with severe periodontitis - to 6.40 points (Table 3.7).

Table 3.5

Depth of periodontal pockets in patients with chronic generalized periodontitis in the postmenopausal period, mm ($X\pm m$)

Studied parameters	Postmenopausal period				
	MChGP (p=25)	MChGP2 (p=25)	\underline{P}_1	SChGP (p=25)	\underline{P}_2

Depth of periodontal pockets, mm					
top sextants	<u>3,29±0,06</u>	<u>4,21±0,07</u>	<u>P<0,002</u>	<u>6,29±0,22</u>	<u>P<0,002</u>
Front Sextants	<u>3,20±0,05</u>	<u>3,59±0,12</u>	<u>P<0,03</u>	<u>5,80±0,16</u>	<u>P<0,002</u>
Lower side sextants	<u>3,39±0,05</u>	<u>4,59±0,09</u>	<u>P<0,002</u>	<u>6,79±0,25</u>	<u>P<0,002</u>

Note: P1 - statistical significance of differences between groups, mild and moderate periodontitis;

P2 - statistical significance of differences between groups of moderate and severe generalized periodontitis (Mann-Whitney, U-test).

From the point of view of this information, special attention is paid to the data of work on the level of IL-6 in the thickness of periodontal pockets. An analysis was also conducted to determine the CRP value in the contents of the periodontal pockets, but it was possible to determine this parameter in a small number of the examined women, which is probably associated with a high molar biomass content and a small number of prescribed sources.

According to the analysis presented in Table 3.7, in women with moderate periodontitis, a significant increase in the level of IL-6 in the fluid of periodontal fissures was observed compared to mild periodontitis. In addition, it is possible to identify a significant increase in the studied indicators in women with severe generalized periodontitis.

Table 3.6

Parameters of the periodontal index (PI) in patients with chronic generalized periodontitis in the postmenopausal period (X±m)

Studied parameters	Postmenopausal period				
	MChGP (p=25)	MChGP2 (p=25)	<u>P₁</u>	SChGP (p=25)	<u>P₂</u>
PI Points	<u>2,50±0,04</u>	<u>4,70±0,01</u>	<u>P<0,002</u>	<u>6,40±0,07</u>	<u>P<0,002</u>

Note: P1 - statistical significance of differences between groups, mild and moderate generalized periodontitis;

P2 - statistical significance of differences between groups of moderate and severe generalized periodontitis (Mann-Whitney, U-test).

Table 3.7

IL-6 content in periodontal pockets in patients with chronic generalized periodontitis in the postmenopausal period ($X\pm m$)

Studied parameters	Postmenopausal period				
	MChGP (p=25)	MChGP2 (p=25)	\underline{P}_1	SChGP (p=25)	\underline{P}_2
Interleukin-6, pg/ml	<u>2,49±0,08</u>	<u>4,61±0,07</u>	<u>P<0,002</u>	<u>5,69±0,04</u>	<u>P<0,002</u>

Note: P1 - statistical significance of differences between groups, mild and moderate generalized periodontitis;

P2 - statistical significance of differences between groups of moderate and severe generalized periodontitis (Mann-Whitney, U-test).

The basis for the ratio of the studied component to the depth of periodontal damage in the compared groups was proven by the presence of a strong correlation between the parameters of the IL-6 level and the degree of periodontal tissue damage ($R=0.890$, Spearman; $P<0.002$).

Analysis of the content of mixed saliva in patients with chronic generalized periodontitis in the postmenopausal period showed that in a certain part of them the content of total calcium was up to 3.3 ± 0.2 mmol/l, ionized potassium up to 29.9 ± 0.7 mmol/l, and total phosphates up to 4.3 ± 0.2 mmol/l.

In each of the three groups of patients, under conditions of pronounced hypoestrogenism, the level of homocysteine in blood serum significantly increased (Table 3.9), accordingly, the development of periodontitis was observed.

§3.4. Analysis of general indicators of the body in patients with periodontitis in the postmenopausal period.

Table 3.8

Parameters of homocysteine levels in patients with chronic generalized periodontitis in the postmenopausal period ($X\pm m$)

Studied parameters	Postmenopausal period				
	MChGP	MChGP2	\underline{P}_1	SChGP	\underline{P}_2

	(p=25)	(p=25)		(p=25)	
Homocysteine, mkmol/l	11,08±0,20	13,69±0,16	P<0,002	15,69±0,15	P<0,002

Note: P1 - statistical significance of differences between groups, mild and moderate generalized periodontitis;

P2 - statistical significance of differences between groups of moderate and severe generalized periodontitis (Mann-Whitney, U-test).

In patients with moderate generalized periodontitis, the level of homocysteine increased by 25% compared to mild periodontitis and by 16% compared to moderate periodontitis in patients with severe periodontitis. When conducting statistical studies, a high degree of clear correlation was noted between the severity of the development of chronic periodontitis and the level of homocysteine in blood serum, which indicates a possible correlation of these indicators.

In our opinion, the analysis conducted by us is of great importance for studying the composition of complex mediators of inflammation (C-reactive protein and interleukin-6) in the blood serum of the studied category of patients.

The results of the study of C-reactive protein parameters in the blood serum of the examined women (Table 3.9) showed a significant increase in this indicator depending on the severity of the periodontitis, i.e., with its progression.

Table 3.9

Parameters of the level of CRP and IL-6 in blood serum in patients with chronic generalized periodontitis in the postmenopausal period (X ± m)

Studied parameters	Postmenopausal period				
	MChGP (p=25)	MChGP2 (p=25)	<u>P</u> ₁	SChGP (p=25)	<u>P</u> ₂
CRO, mg/ml	4,59±0,08	6,39±0,11	P<0,002	8,1±0,9	P<0,002
IL-6, pg/ml	2,49±0,08	4,31±0,11	P<0,002	6,91±0,31	P<0,002

Note: P1 - statistical significance of differences between groups, mild and moderate generalized periodontitis;

P2 - statistical significance of differences between groups of moderate and severe generalized periodontitis (Mann-Whitney, U-test).

At the same time, in women with mild periodontitis, the CRP level was 4.59 mg/ml, while with moderate periodontitis, this indicator increased by 40% and was 6.39 mg/ml. In patients with the studied severe periodontitis, the CRP level increased by 24% (7.8 mg/ml) compared to similar periodontitis of moderate severity.

At this stage, there is a significant degree of reliable correlation between the severity of generalized periodontitis and the level of CRP ($R=0.891$, Spearman; $P<0.002$) indicates a high degree of their interdependence.

This situation was noted when assessing the level of interleukin-6 in the blood serum of patients in the postmenopausal period. As for the study of this parameter, accordingly, a steady increase was noted in periodontitis, exacerbating inflammation (Table 3.9).

It was established that the concentration of IL-6 in patients with moderate periodontitis was 4.31 pg/ml, which is 69% higher than the indicator established for mild periodontitis. In the group with severe periodontitis, the level of IL-6 increased to 6.90 pg/ml, and compared to women with moderate periodontitis, it increased by 60%.

The probability of a significant increase in the concentration of IL-6 in blood serum in patients in the postmenopausal period is associated with the severity of periodontitis ($P=0.891$, Spearman; $P<0.002$), which, in turn, confirms their possible correlation.

In turn, we conducted a survey of the results of assessing the concentration of endothelin-1 - the only sign of endothelial damage - in the blood serum of the studied category of patients, which indirectly proves the manifestation of inflammatory phenomena of periodontal tissues.

The conducted analyses (Table 3.10) show that the content of the ET-1 level in patients with moderate periodontitis increased by 30% compared to the concentration of the studied value, and in patients with mild periodontitis, the severity of periodontitis increased by 36% compared to the studied women with moderate periodontitis.

A significantly higher level of direct correlation was noted between the level of IL-6 and the pro-inflammatory index, ($P=0.891$, Spearman; $P<0.002$) indicates a high degree of correlation between them.

Table 3.10**Endothelin-1 value in the blood serum of patients with chronic generalized periodontitis in the postmenopausal period ($X\pm m$)**

Studied parameters	Postmenopausal period				
	MChGP (p=25)	MChGP2 (p=25)	\underline{P}_1	SChGP (p=25)	\underline{P}_2
Endotelin-1, ng/ml	0,31±0,002	0,36±0,02	P<0,002	0,51±0,03	P<0,002

Note: P1 - statistical significance of differences between groups, mild and moderate generalized periodontitis;

P2 - statistical significance of differences between groups of moderate and severe chronic generalized periodontitis (Mann-Whitney, U-test).

As a result of the analysis conducted, we received information that in patients in the postmenopausal period, accordingly, there was an exacerbation of chronic generalized periodontitis, a significant deterioration of the situation in periodontal tissues, calculated according to PMA indices, we can see changes in the state of gingival bleeding and the depth of periodontal pockets according to PI, Mulman data.

Along with the noted changes in the studied category of patients, the level of homocysteine, signs of systemic inflammation, and the concentration of endothelin-1 in blood serum, including IL-6 in periodontal fluid, increased significantly. In addition, a direct relationship was revealed between the noted parameters and the degree of periodontal damage, which can be proven by our previous opinion about the influence of HHC on the formation of inflammation in periodontal tissues in postmenopausal women.

Considering the indicators obtained during our study, it is necessary to take into account the inevitability of implementing a regimen of therapeutic and preventive measures aimed at correcting hyperhomocysteinemia and restoring periodontal parameters in patients in the postmenopausal period.

IV CHAPTER. RESULTS OF THE STUDY OF THE STATE OF THE ORAL CAVITY AFTER THE IMPROVED COMPLEX TREATMENT OF WOMEN WITH PERIODONTITIS IN THE POSTMENOPAUSA PERIOD.

§4.1. Improved complex treatment method. Algorithm of therapeutic and preventive measures.

According to the results presented in the above chapter, inflammation of periodontal tissues in postmenopausal women is accompanied by an increase in the concentration of homocysteine in blood serum, signs of systemic inflammation (CRP, IL-6), endothelial damage (ET-1), while a direct correlation was found between the severity of chronic generalized periodontitis and the above indicators.

Based on these data, in order to increase the effectiveness of treatment of periodontal diseases in women in the postmenopausal period, coupled with hyperhomocysteinemia, we assessed the influence of the improved treatment complex for generalized periodontitis on the parameters and level of dental status.

In the complex treatment of chronic generalized periodontitis, the following is carried out:

- therapeutic (with and without medications),
- surgically,
- orthodontically
- orthopedic treatment aimed at eliminating inflammatory phenomena in periodontal tissues, eliminating pathological dentogingival pockets, strengthening reparative osteogenesis, restoring the function of the dentoalveolar system.

Algorithm of therapeutic and preventive measures:

- professional oral hygiene;
- training and monitoring of personal oral hygiene;
- removal of supra- and subgingival dental calculus;
- correction and elimination of factors leading to the development of

inflammatory phenomena in the periodontium, for example: overhanging edges of fillings, carious cavities, wedge-shaped defects;

- early elimination of identified etiological causes;
- functional selective grinding;
- prescription or use of antimicrobial and anti-inflammatory therapy:

As a biologically active food supplement, "Osteomed-forte" has a multi-level effect: regulates phosphorus-calcium metabolism, contributes to the effective and safe restoration and regeneration of bone tissue structure; stops bone resorption and stimulates osteogenesis; increases bone mineral density. The product, which is a natural source of prohormones, contributes to the safe normalization of hormone levels and the formation of collagen.

It is well absorbed and does not reduce the acidity of gastric juice due to its calcium citrate content.

Properties of biologically active components:

Calcium citrate ensures complete and safe absorption of calcium from the gastrointestinal tract, helps regulate the production of parathyroid hormone and prevent bone resorption, which is an effective and safe form of calcium necessary for strengthening bones (increases bone mineral density).

Vitamin B6 (organic complex HDBA) contributes to an increase in the level of androgens, which improves the restructuring of bone tissue, indirectly stimulates the activity of osteoblasts, increases the number of osteocytes, amino acids participate in the formation of collagen, which forms the bone matrix. 2 tablets 2 times a day during meals. The duration of admission is 1 month.

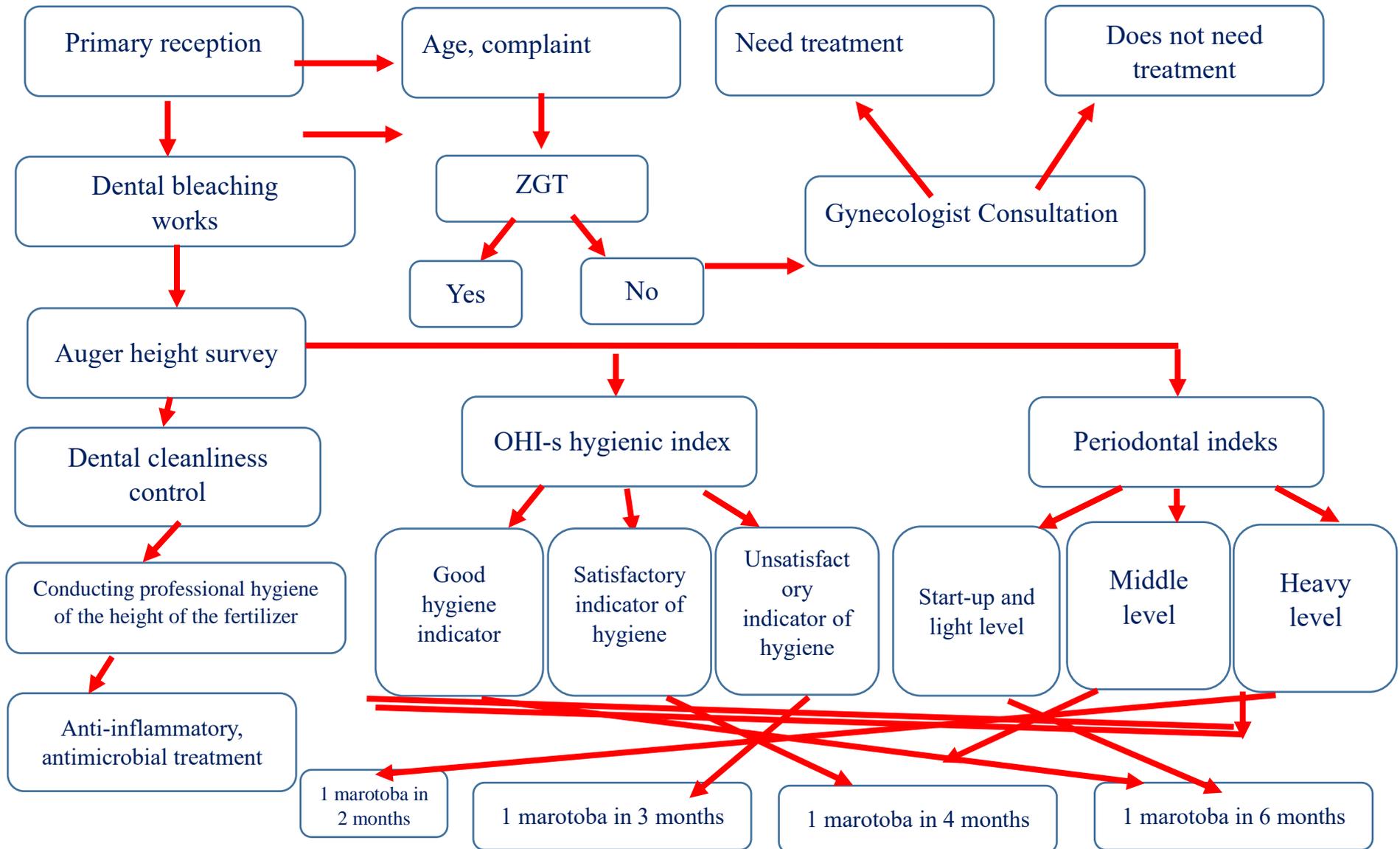
Vitamin D3 (colecalciferol) stimulates the absorption of calcium, magnesium, and phosphorus and is responsible for reducing the excretion of these substances through the kidneys with urine. Vitamin D3 is essential for skeletal growth, muscle strengthening, and the mineralization of bones and teeth.

Regular treatment of women in the postmenopausal period with chronic generalized periodontitis was carried out using the Angiovit vitamin complex.

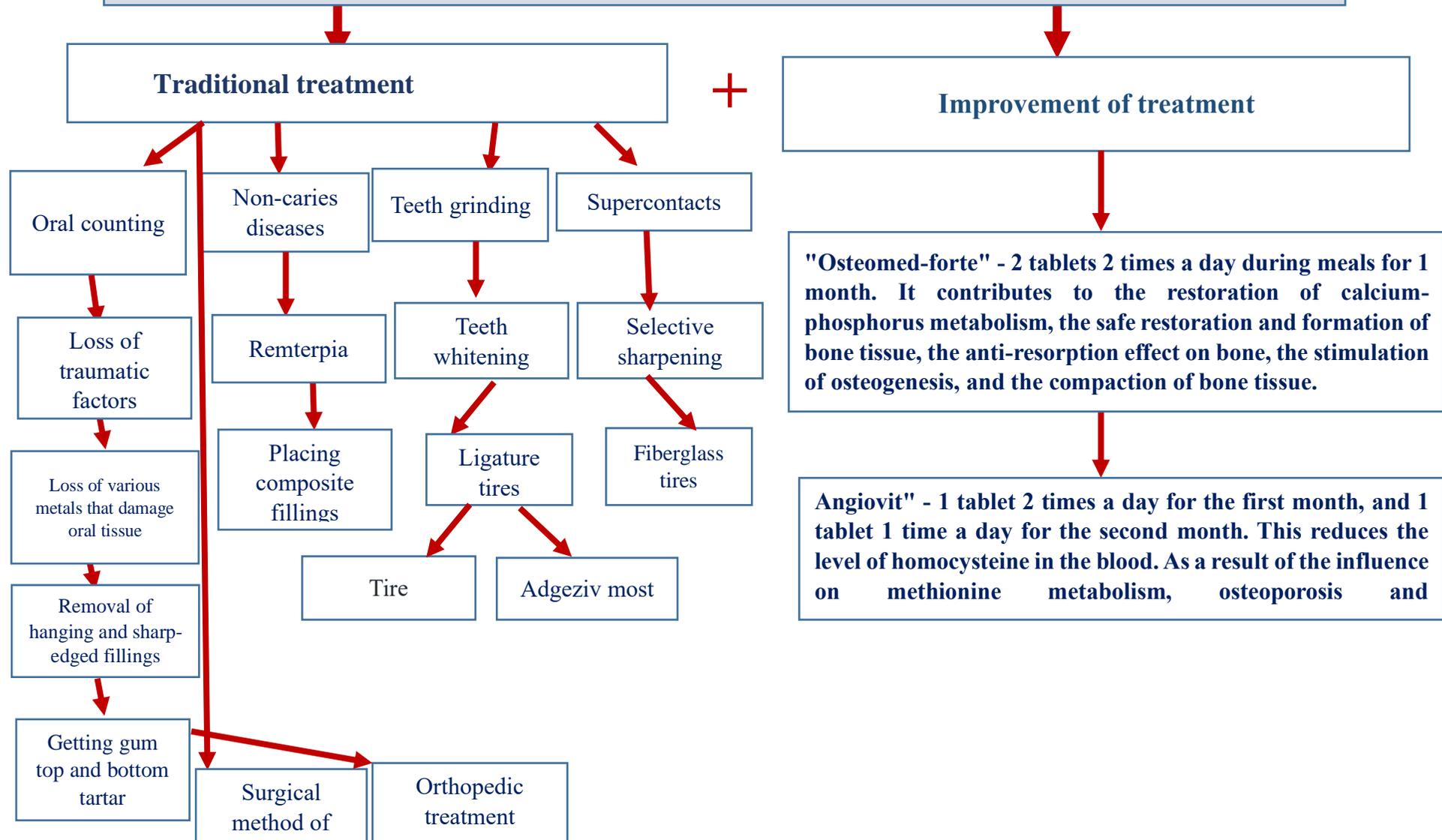
Scheme of administration: first month - 1 tablet - containing vitamin B6 - 0.04 g, vit. B12 - 0.000006g, folic acid - 0.005g, 2 times a day, second month, 1 tablet 1 time a day. For the period of exacerbation of the disease, repeated treatment courses are conducted. "Angiovit" is a drug specifically designed to correct hyperhomocysteinemia. The current therapy was carried out within two months after traditional sanitary and occupational hygiene measures of the oral cavity. The effectiveness of the treatment was assessed 4-6 weeks after its completion.

To determine the effectiveness of complex treatment of chronic generalized periodontitis in postmenopausal women, we studied 75 women in three groups (mild, moderate, and severe) depending on the severity of generalized periodontitis 21-28 days after traditional local therapy, while this experimental group continued the proposed complex treatment without using hormone replacement therapy.

Individualized treatment and diagnostic algorithm for postmenopausal women



Treatment and prophylactic work



§4.2. Influence of complex therapeutic measures on oral hygiene parameters.

According to the results presented in Table 4.1, normalization of oral hygiene indicators according to Green-Vermillion was revealed in each of the examined patients, which corresponds to a mild form of periodontitis.

Table 4.1

Influence of therapeutic measures on oral hygiene parameters in patients of the main and comparison groups with chronic generalized periodontitis in the postmenopausal period. ($X \pm t$)

Studied parameters	Postmenopausal period											
	MChGP				MChGP2				SChGP			
	Before treatment	After treatment	Comparison	P	Before treatment	After treatment	Comparison	P	Before treatment	After treatment	Comparison	P
Green-Vermilion Hygiene Index, points	1,61±0,16	0,89±0,08	1,09±0,08	<0,002	1,79±0,17	0,97±0,12	1,07±0,12	<0,002	3,21±0,41	1,66±0,18	2,66±0,18	<0,001
KPU Index	7,6±0,89	7,49±0,87	7,59±0,87	>0,004	15,69±1,05	15,09±1,05	15,69±1,05	>0,004	14,28±1,09	14,61±1,09	14,61±1,09	>0,004
KPU-p	7,9±0,89	7,71±0,91	7,81±0,91	<0,001	16,31±1,09	15,89±1,05	15,99±1,05	>0,004	15,06±1,12	14,70±1,12	14,90±1,12	>0,004

Note: P - statistical significance of differences in parameters before and after treatment according to the Wilcoxon T-test.

The results of assessing the parameters of the KPU and KPU_p indices, which

determine the intensity of caries spread to the hard tissues of the teeth (Table 4.1), showed a significant decrease in them in each of the three studied groups of patients. This can be explained by the fact that, at first glance, to a certain extent, the existing damage in the hard tissues of the teeth is irreparable, and on the other hand, the decrease in lost teeth at the stages of treatment can be explained by the persistence of inflammation of periodontal tissues.

Inclusion in the complex of therapeutic measures for chronic generalized periodontitis in postmenopausal women under conditions of significant normalization of oral hygiene indicators contributed to a positive effect on the condition of periodontal tissues.

§4.3. Analysis of changes in the papillary-marginal-alveolar index and Muhlemann's data of complex therapeutic measures

Based on these results, it can be concluded (Fig. 4.1) that a significant decrease compared to the baseline level is considered the result of the papillary-marginal-alveolar index, which indicates the development of inflammation in the gums. In each of the three studied groups of patients, a significant decrease in levels was noted, including 21% for mild periodontitis, 35% for moderate periodontitis, and 27% for severe periodontitis.

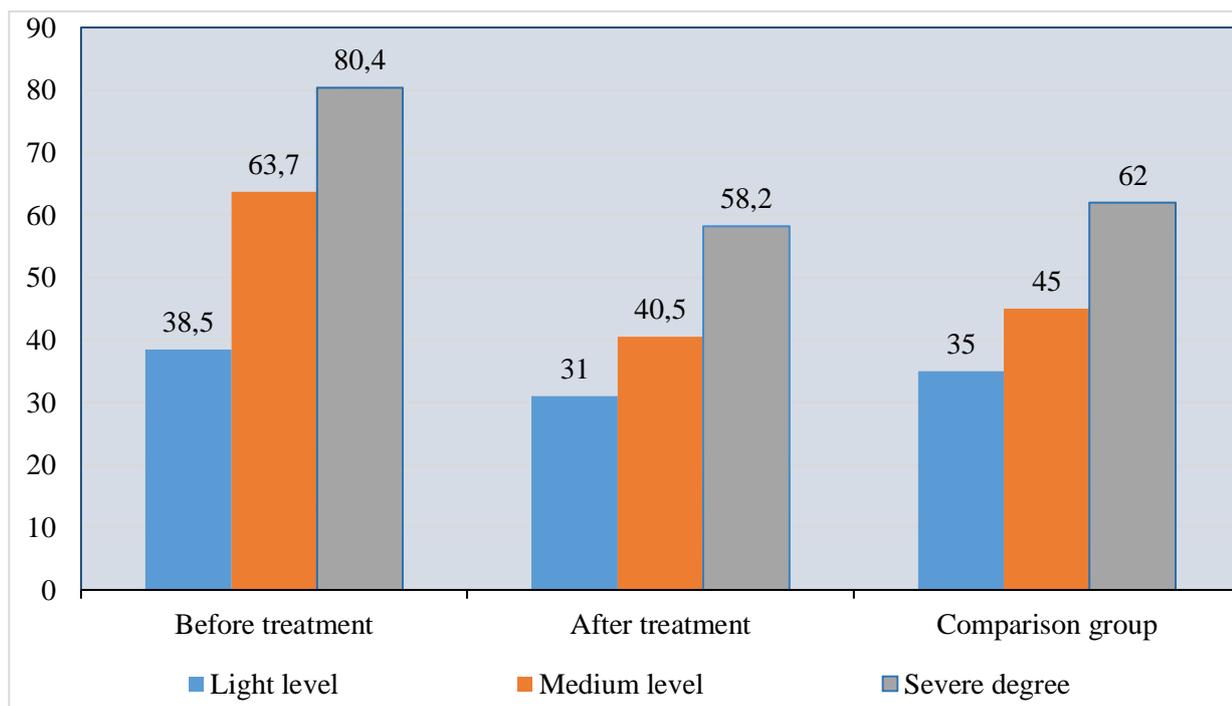


Figure 4.1. Values of the papillary-marginal-alveolar index in women with

chronic generalized periodontitis in the postmenopausal period before and after treatment

According to Muhleman, the positive effect of treatment on periodontal tissues was proven by a significant decrease in gingival bleeding, 1.1 points for mild periodontitis, 1.7 points for moderate periodontitis, and 1.8 points for severe periodontitis in postmenopausal women.

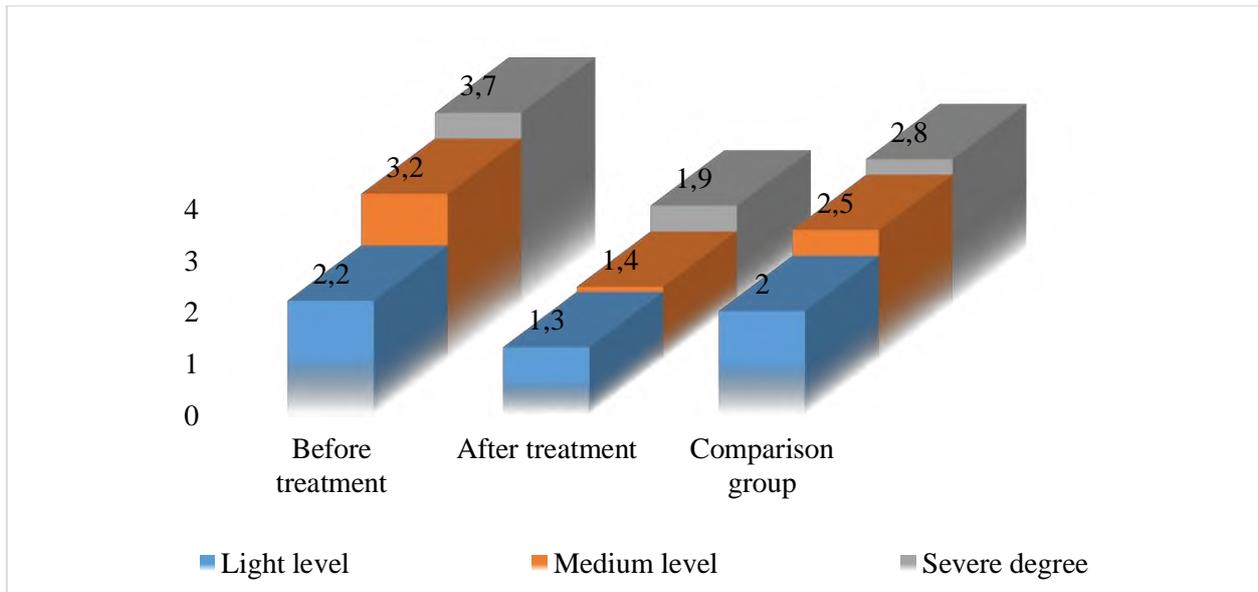


Figure 8. Results of gingival bleeding according to Mulleman in patients of the main and comparison groups with chronic generalized periodontitis in postmenopausal women.

Studies conducted to determine the depth of pathological pockets showed that the implementation of a complex of therapeutic measures for generalized periodontitis in the studied patients contributed to a significant reduction in the studied value in each examined area of occlusion (Table 4.2). At the same time, in comparable studies, a significant improvement in the depth of pathological pockets was revealed, especially in severe periodontitis (on average 1.2 mm), in mild periodontitis (on average 0.2 mm), to a lesser extent.

In turn, the conducted treatment contributed to a reliable decrease in the indicators of the complex periodontal index in mild periodontitis, in addition, in women in the postmenopausal period, there was a stable and a certain tendency to decrease in

periodontitis with moderate and severe lesions of the surrounding tissues of the tooth. (Table 4.3).

Table 4.2

Indicators of periodontal pocket depth in patients of the main and comparison groups with chronic generalized periodontitis in the postmenopausal period.

Studied parameters	Postmenopausal period											
	MChGP				MChGP2				MChGP			
	Before treatment	After treatment	Comparison	P	Before treatment	After treatment	Comparison	P	Before treatment	After treatment	Comparison	P
Upper side sextant	3,29± 0,04	3,03± 0,01	3,13± 0,01	<0,01	4,21± 0,07	3,49± 0,08	3,99± 0,08	<0,02	6,28± 0,19	5,39± 0,19	5,89± 0,19	<0, 01
Previous sextant	3,20± 0,05	3,1±0, 01	3,11± 0,01	<0,02	3,59± 0,09	3,19± 0,06	3,39± 0,06	<0,01	5,80± 0,15	4,70± 0,180	4,90± 0,180	<0, 01
Lower side sextant	3,39± 0,05	3,05± 0,04	3,15± 0,04	<0,02	4,67± 0,07	3,90± 0,07	3,99± 0,07	<0,02	6,79± 0,23	5,59± 0,194	5,99± 0,194	<0, 01

Note: P - statistical significance of differences in parameters before and after treatment according to the Wilcoxon T-test.

Table 4.3

Parodontal index (PI) values in patients with chronic generalized periodontitis in the postmenopausal period ($X \pm m$)

Studied parameters	Postmenopausal period									
	MChGP			MChGP2			MChGP			
	Before treatment	After treatment	Comparison n	P	Before treatment	After treatment	Comparison n	P	Before treatment	

PI index, points	2,50 ±0,04	2,33 ±0,04	<0,002	4,70 ±0,07	4,69 ±0,07	>0,04	6,33 ±0,07	6,230 ±0,083	>0,04
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Note: P - statistical significance of differences in parameters before and after treatment according to the Wilcoxon T-test.

For a better study of the effect of a complex of therapeutic measures on the organs and tissues of the oral cavity in the examined patients, a complete analysis of the known qualities and structure of oral saliva was conducted. The results of this study showed (Fig. 4.4) that the conducted treatment had a positive effect on the mineral structure of oral saliva, which was manifested by a significant decrease in the level of potassium ions, total calcium, and phosphates. At the same time, no significant improvement in the level of sodium ions in saliva was observed in the examined patients.

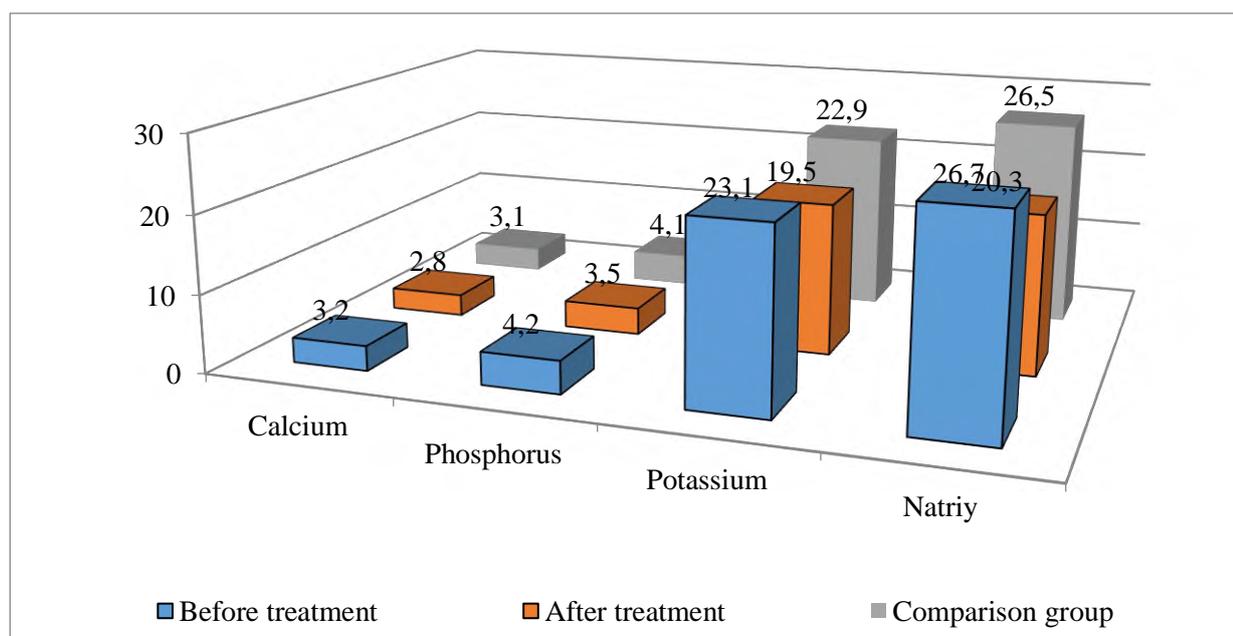


Figure 4.4. Parameters of oral fluid composition in patients of the main and comparison groups with chronic generalized periodontitis before and after treatment in the postmenopausal period.

The conducted analyses should be considered as a sufficient basis for reducing the level of the inflammatory process and, as a consequence, reducing the level of cellular elements of damage, thereby reducing the level of specified ions in the oral fluid.

When assessing the pH values of saliva, as well as the value of the acid-base

balance of the oral cavity, its average value was 6.69 ± 0.04 in women with chronic generalized periodontitis in the postmenopausal period. At the end of the treatment, no significant improvement in the studied value was observed.

In the studied category of patients, there was also no significant improvement in the rate of oral fluid flow and was equal to 2.09 ± 0.24 ml/min.

As can be seen from the data presented above, the results presented in Figure 4.5 led to a significant decrease in the concentration of interleukin-6 in dentogingival fissures due to complex treatment of generalized periodontitis in a significant part of the patients we studied. At the same time, an improvement in indicators was more pronounced in moderate periodontitis (by 1.5 pg/ml), and less pronounced in severe periodontitis (by 0.4 pg/ml).

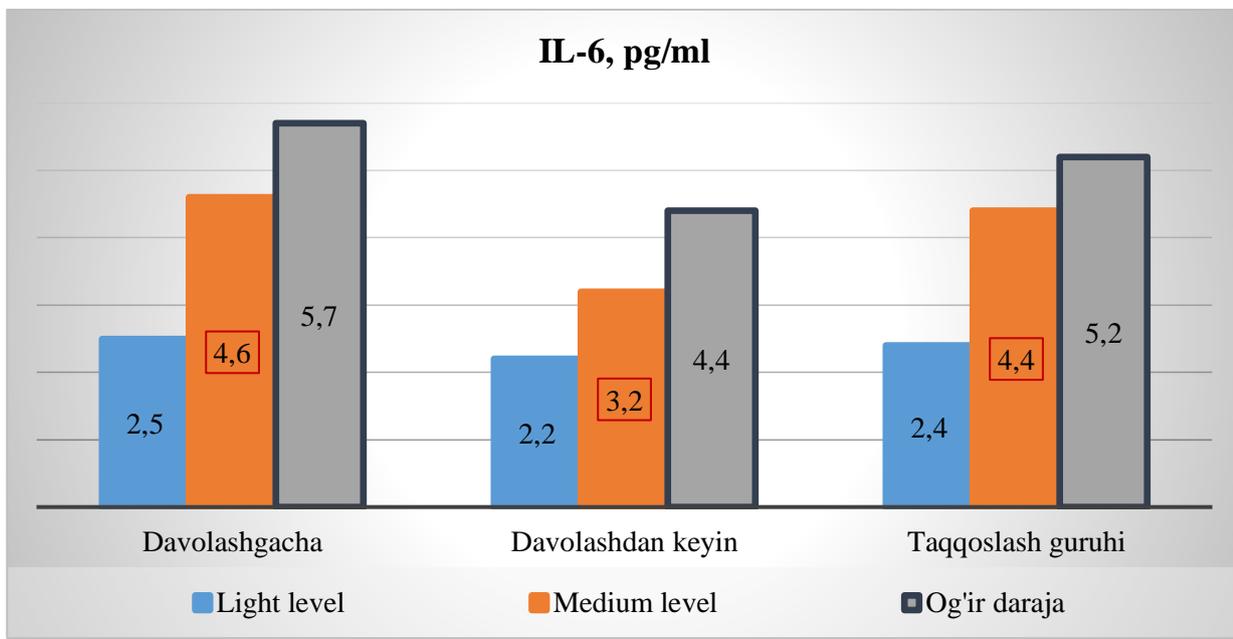


Figure 4.5. Concentration of interleukin-6 in the periodontal contents of patients with chronic generalized periodontitis in the postmenopausal period in the main and comparison groups.

§4.4. Analysis of changes in the content of homocysteine, CRP, and IL-6 in the blood of complex therapeutic measures

The studied significant improvement in blood flow in the alveolar gingival tissues can be explained by the dependence of the blood flow velocity in the capillaries of small vessels, primarily on the ability of formed elements to accumulate.

Homocysteine increases the activity of platelet aggregation, reduces the activity of natural anticoagulants, and as a result, disrupts blood circulation in periodontal tissues. Consequently, a decrease in the concentration of homocysteine in blood serum leads to the normalization of its properties and an increase in the efficiency of blood flow velocity.

Increasing the effectiveness of complex treatment showed a significant improvement in the concentration of serum homocysteine levels in postmenopausal women (Fig. 4.6).

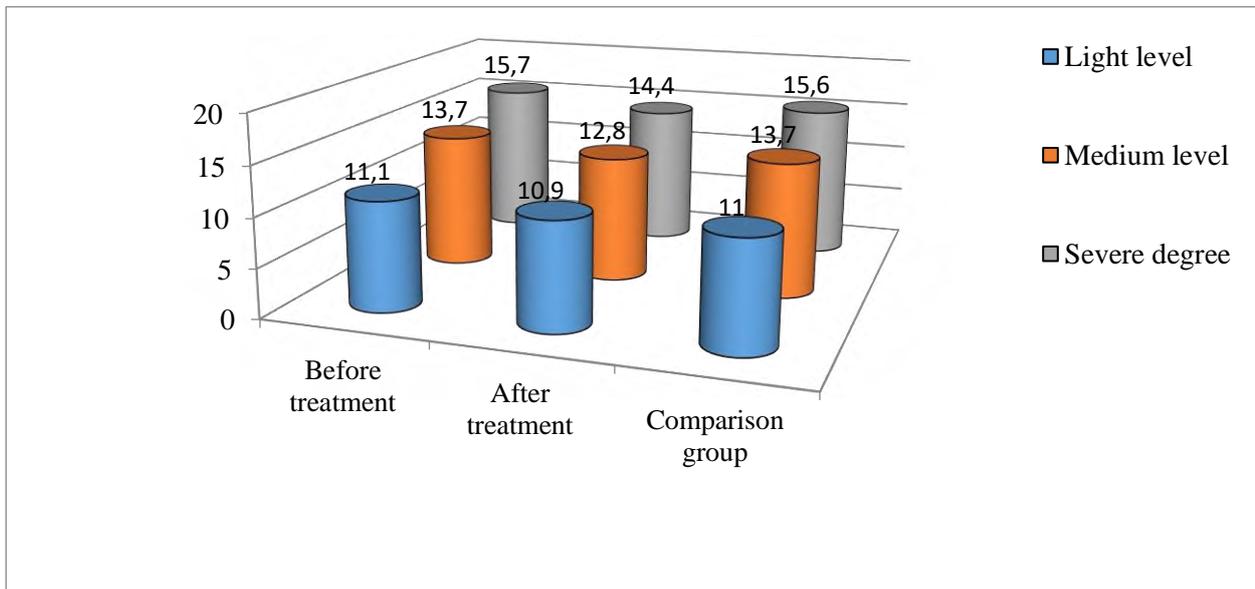


Figure 4.6. Concentration of homocysteine in blood serum in patients with chronic generalized periodontitis in the postmenopausal period in the main and comparison groups.

In each of the studied groups, a reliable decrease in the considered parameter was revealed, which in severe periodontitis was a significant decrease in the level of homocysteine from the baseline value, i.e., by 16%. In moderate periodontitis, this change was 13%, in mild periodontitis - 8%.

Such improvements can be explained by the fact that the metabolism of this homocysteine is carried out through the sequence of biochemical processes, the coenzymes of which are vitamins B12, B6, and folic acid, which are present in the drug "Angiovit."

During treatment, a significant improvement in the concentration of homocysteine in blood serum in postmenopausal women was accompanied by a significant decrease in

the level of endothelin-1, a sign of vascular endothelial damage (Fig. 4.7). In mild periodontitis, it was 13%, in moderate periodontitis 22%, and in severe periodontitis 31%.

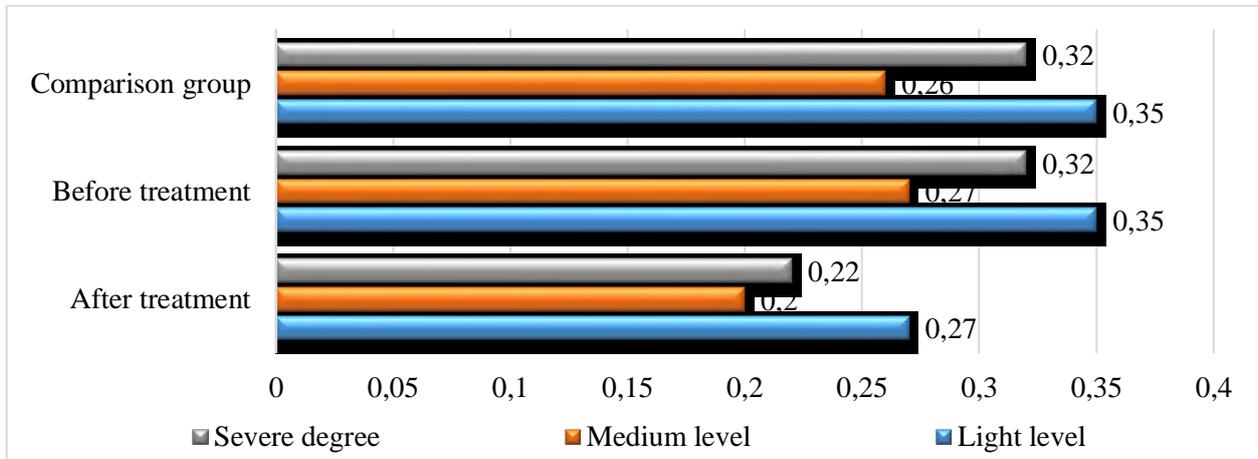


Figure 4.7. Endothelin-1 values in patients with chronic generalized periodontitis in the postmenopausal period in the main and comparison groups. A significant decrease in the level of chronic generalized inflammation in blood plasma (Table 4.5) - C-reactive protein and interleukin-6, found in the studied patients under the influence of treatment, manifested as a completely natural state. At the same time, significant changes were noted in the group of women with severe periodontitis - 1.50 mg/ml and 2.28 pg/ml, respectively.

Table 4.6.

Blood serum levels of CRP and IL-6 in patients of the main and comparison groups with chronic generalized periodontitis in the postmenopausal period.

Studied parameters	Postmenopausal period								
	MChGP			MChGP2			MChGP		
	Before treatment	After treatment	Comparison	Before treatment	After treatment	Comparison	Before treatment	After treatment	Comparison
C-reactive protein, mg/ml	4,49 ±0,06	3,93 ±0,03	4,39 ±0,06	6,39 ±0,11	4,10 ±0,06	6,19 ±0,11	7,89 ±0,11	6,40 ±0,11	7,79 ±0,11

IL-6, pg/ml	2,53	2,30	2,43	4,25	3,50	4,15	6,89	4,62	6,79
	±0,05	±0,05	±0,05	±0,13	±0,07	±0,13	±0,25	±0,11	±0,25

From the foregoing, we can conclude that the use of a folic acid complex, consisting of vitamins, osteotropic drugs, anti-inflammatory and antimicrobial agents, in the complex treatment of chronic generalized periodontitis in postmenopausal women contributed to the improvement of inflammatory processes. In this case, a reliable decrease in the depth of periodontal tissues (PMA index, Schiller-Pisarev test, Muhlemann gingival bleeding), a normalization of blood flow in the tissues of the alveolar part of the gingival tissue, an improvement in the structure and quality of mixed saliva were observed. These positive changes in teeth led to a significant decrease in the concentration of homocysteine, interleukin-6, endothelin-1, and C-reactive protein in blood serum, which confirms the influence of these signs on the development of chronic generalized periodontitis.

The normalization of the process after the completion of the improved complex treatment and its influence on the main parameters of the pathological state of periodontal tissues in postmenopausal women has been reliably proven by clinical examples.

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