# Influence of local therapy with essential oils on the dynamics of immune and hormonal parameters in patients with osteoarthritis

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Influence of local therapy by essential oils on dynamics of immune effects and hormonal levels in patients with osteoarthrosis

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SUMMARY

The study involved 60 women with OA, divided into 2 comparable groups. In the first group, OA patients were treated with applications of a 5% mixture of essential oils: lavender, ginger, peppermint, rosemary, pine, clove, nutmeg, eucalyptus, thyme, anise, in the control group, diclofenac 100 mg per day was taken. The results of treatment were assessed before and after treatment according to the dynamics of clinical indicators: the Leken index, the Likert scale. The dynamics of laboratory parameters of general analysis and blood biochemistry was assessed before and after treatment. The dynamics of the state of the total number of leukocytes, CD4 +, CD8 +, CD4 + / CD8 +, CD19, IgG, IgA, IgM and the dynamics of indicators of the following hormones were studied before and after treatment: TSH, sT4, sT3, STH, PTH, TKT, OK, KORT, E2 , T, DHEA-s, IRI and the HOMA-IR index.

Before treatment, both groups were found to have CD4 immunodeficiency, an increase in CD8 cytotoxic cells, and a decrease in the CD4 + / CD8 + index. After a course of therapy with EM applications, an increase in CD4, a decrease in CD8, and an increase in the CD4 + / CD8 + index were noted. There was an increase in testosterone ($p < 0.05$), a decrease in the level of insulin, glucose ($p < 0.05$) and the HOMA-IR index ($p < 0.05$). In the control group, the dynamics of the immune and hormonal systems was not observed. The effectiveness of treatment was higher in the group of patients who received treatment with EM applications according to the Likertr index, Likertr scale <0.02, as compared with the control group - Likertr index, Likertr scale <0.05.

Key words: osteoarthritis, essential oils, immune system, hormonal system.

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RESUME

The study involved 60 women patients with OA, divided into 2 comparable groups. In the first group of OA patients treated with applications of 5% mix EM: lavender, ginger, peppermint, rosemary, pine, clove, nutmeg, eucalyptus, thyme, anise., In the control group was received diclofenac 100 mg per day. The results of the treatment were assessed before and after treatment on dynamics of clinical indicators: the index Lekena, the Likert scale. The dynamics of laboratory indicators of the General analysis and blood biochemistry were assessed before and after treatment. Changes in the state of total leukocytes, CD4 +, CD8 +, index CD4 + / CD8 +, CD19, IgG, IgA, IgM.And dynamic performance of the following hormones: STH, PL, cort., TTH, fT4, fT3, PTH, CT, OC, LH, FSH, E2 and T, DHEA-s, AS, PG, INS, C-P, index HOMA-IR were studied before and after treatment.

Before treatment, both groups showed immunodeficiency CD4, increased CD8 cytotoxic cells, reducing the index of CD4 + / CD8 +. After a course of therapy with applications of EM showed an increase of CD4, CD8 decrease, the increase of the CD4 + / CD8 +. The marked increase in testosterone ($p < 0.05$), decreased level of insulin, glucose ($p < 0.05$) and HOMA-IR ($p < 0.05$). In the control group dynamics of the immune and hormonal systems are not marked. The effectiveness of treatment was higher in the group of patients treated with applications of EM according to the index Lekena, Likert scale, $p < 0.02$, compared with the control group index that have been Identified, the Likert scale, $p < 0.05$.

Keywords: essential oils, osteoarthrosis.

## Introduction

Osteoarthritis (OA) occupies a leading place among diseases of the musculoskeletal system, in the world it is found in 20% of the world's population. [12].

The onset of the disease is most often recorded at the age of 40-45 years, and women get sick more often, and they have a more severe course. In people over 50, OA is 27%, in the older age group

60 years old reaches 97%. OA is considered by a number of authors as a disease of age, and changes in the immune and endocrine systems are considered comparable to changes in chronic stress [1, 2].

The choice of methods for treating OA is necessary taking into account its pathogenesis, which has now been largely deciphered. Several factors are involved in the development and progression of OA - immune, hormonal, biochemical, and genetic. OA is characterized by degeneration of the articular (hyaline) cartilage. An important role in the development of OA is played by biomechanical disorders leading to activation of the mechanoreceptor, expression of myogen-activated protein kinase and nuclear factor kappaB (NF-κB) [1, 2].

In this disease, there is an increase in the expression of superoxide radicals and metalloproteinases (MMPs), including collagenase and stromelin, proteinases, reduced synthesis of hyaluronic acid by synoviocytes B, IL-1, IL-6, tumor necrosis factor (TNF alpha), cyclooxygenase-2 (COX-2 ) and nitric oxide. The activation of pro-inflammatory and destructive mediators mediated by the proteins of the nuclear transcription factor NF-κB is triggered. These changes lead to the development of inflammation in the tissues of the joint with the involvement of the immune and hormonal systems. There is a decrease in the expression of growth factors and receptors for them, the content of proteoglycans in hyaline cartilage, collagen, especially type 2, plasminogen-1 inhibitor, as well as a decrease in the concentration of tissue MMP inhibitors. Increased proliferation of chondrocytes into the subchondral bone. All of the above leads to cartilage degeneration. In OA, there is a predominance of catabolic processes not only in cartilaginous tissue, but also in bone and muscle. The course of OA is determined by the degree of imbalance of anabolic and catabolic processes determined by the interaction of the immune and hormonal systems [1, 2].

The regulation of the metabolism of cartilage tissue is provided by periodic pressure and weakening of the load on the cartilaginous tissue, which ensures the diffusion of nutrients dissolved in water, metabolic products and hormonal-humoral regulators from the capillaries of the perichondrium, which has receptors and effectors, or synovial fluid. Chondrocytes also have cytoreceptors for a number of hormones circulating in the blood - growth hormone, thyroxine, triiodothyronine, insulin, glucocorticoids, estrogens and others. In turn, growth hormone and prolactin stimulate the secretory activity of chondrocytes and mitotic activity in the epiphyseal plates. Thyroxine and triiodothyronine accelerate cytodifferentiation, but inhibit growth processes. Estrogens inhibit the biosynthesis of collagen and glucosamingikans in chondrocytes. Testosterone helps to close the pineal glands. Adrenocorticotropic hormone (ACTH) and cortisol inhibit the maturation of cartilage and its replacement by bone tissue at the level of the epiphyseal plates. The reactivity of chondrocytes to hormones depends both on the state of the endocrine status of the body (norm, deficiency or excess of hormones), and on the structural and functional state of chondrocytes. This can explain the very contradictory data on the effects of hormone therapy and their influence on the course of OA [2, 4]. The question of the relationship between low concentrations of estradiol and the activation of monocytic IL-1 and TNF-alpha, which have a depressive effect under the condition of weakening the influence of other hormones, is discussed. It has been established that androgens are extremely necessary for the synthesis of estrogens in postmenopausal women. The transformation of hormones occurs under the influence of enzymes such as aromatase, 5-alpha reductase and others. A balanced local influence of androgens (TS and DHEA) and estrogens is important for the metabolism of bone and cartilage tissue in men and women. Men and women have receptors for these hormones, both in bone and cartilage tissue. During local synthesis and metabolism in bone tissue, they are not released into the circulatory bed and into the intercellular space [5]. The positive effect of testosterone on the improvement of bone tissue metabolism and metabolic processes in the liver by the correlation increase in the level of alkaline phosphatase and TS, which do not exceed the physiological norm, has been established [6]. During local synthesis and metabolism in bone tissue, they are not released into the circulatory bed and into the intercellular space [5]. The positive effect of testosterone on the improvement of bone tissue metabolism and metabolic processes in the liver by the correlation increase in the level of alkaline phosphatase and TS, which do not exceed the physiological norm, has been established [6]. During local synthesis and metabolism in bone tissue, they are not released into the circulatory bed and into the intercellular space [5]. The positive effect of testosterone on the improvement of bone tissue metabolism and metabolic processes in the liver by the correlation increase in the level of alkaline phosphatase and TS, which do not exceed the physiological norm, has been established [6].

In connection with the above, at present, in the pathogenesis of OA, special attention is paid to the role of the immune system with the search for adequate therapy. In this regard, pharmacological effects are associated with the effect on NF-κB, with a decrease in the expression of IL-1beta by synoviocytes and chondrocytes and the concentration of IL-6, inhibition of chemotaxis and phagocytosis. According to a number of studies, the use of hormone therapy is ambiguous and highly controversial [1, 2].

At present, no pathognomonic laboratory signs of OA have been found [1, 2, 6]. The diagnosis of OA is based on the diagnostic criteria of the American College of Rheumatology (ACR, 1987). Pain is the main and persistent symptom of OA that is the immediate cause of seeking medical attention. The level of the latter often does not correspond to the severity of its manifestations on radiographs, but it affects the prognosis of the disease and is decisive in the criteria for the effectiveness of OA therapy. Local inflammation in the tissues of the joint and subchondral bone can be considered the predominant cause of pain in OA. According to modern concepts [7], in the pathogenesis of various pain syndromes, the leading role is assigned to violations of the mechanisms of neuroendocrine-immune interaction.

Currently, the central place in the treatment of OA is given to a group of non-steroidal anti-inflammatory drugs (NSAIDs) aimed at combating pain. However, the appointment of NSAIDs apriory is impossible in the presence of polyprogasia of comorbid diseases, and frequent side effects induced by the intake of NSAIDs that cause gastropathy from the gastrointestinal tract, from the side of the cardiovascular system - various "vascular catastrophes", from the side of the kidneys - drug nephropathy and possible damage to other organs and systems, require the abolition of NSAIDs and dictate the need to search for alternative treatments for OA [1, 2].

The search for alternative methods of treatment is supported by a number of international medical organizations: EULAR (EuropeanLeagueAgainstReumatism), OARSI (OstheoarthritisResearchSosietyIntenational), ACR (AmericanCollegeofRheumatology) [1, 2].

One of the alternative treatments for OA is the aromatherapy method based on the use of essential oils (EM) of plant origin. This method of treating diseases of the musculoskeletal system has been used since time immemorial, but in modern medicine it is unfairly limited due to a weak evidence base. EM are substances of an isoprene nature, terpinoids, multicomponent systems that have a genetic affinity for animal and human cells. The studied EO substances are alpha- and beta-pinenes, eugenol, polyphenolic compounds, linalol acetate, cineole, camphor, methyl salicylate, levomenthol, safrole, myristin, emelin. These substances are synergistic towards each other, precursors of vitamins and peptides. With different molecular weights, EOs penetrate well into subcutaneous structures at various speeds from 15 to 120 minutes [2, 6, 8]. Recently, thanks to the achievements of fundamental science in medicine, biology and genetics associated with the discovery of the superfamily of olfactory genes in animals and humans, interest in the use of EM in the treatment of various diseases has renewed. Olfactory genes are located at 51 different loci of almost the entire human genome, with the exception of chromosome 21 and Y. Studies of the late 20th century have shown that olfactory genes are much more associated with the skin than with the olfactory analyzer and genes encoding the function of the immune and hormonal systems. The activation of olfactory genes by EM components leads to the synthesis of specific transmembrane peptides capable of improving the function of various cells / tissues according to the principle of one activated gene - one specific protein. Transmembrane proteins affect the activation of G-proteins, and the latter affect the flow of Ca + and Na + ions, improve membrane activity, increase the accumulation of energy by the cell, lead to inhibition of cell lipid peroxidation, which is reflected in the improvement of cell / tissue function as a whole. The described effects of the influence of EM on cells / tissues were discovered long before the discovery of olfactory genes and explained with the discovery of transmembrane peptides [2, 6, 8, 9]. lead to inhibition of cell lipid peroxidation, which is reflected in the improvement of cell / tissue function as a whole. The described effects of the influence of EM on cells / tissues were discovered long before the discovery of olfactory genes and explained with the discovery of transmembrane peptides [2, 6, 8, 9]. lead to inhibition of cell lipid peroxidation, which is reflected in the improvement of cell / tissue function as a whole. The described effects of the influence of EM on cells / tissues were discovered long before the discovery of olfactory genes and explained with the discovery of transmembrane peptides [2, 6, 8, 9].

The multicomponent nature of each EO and the multifunctionality of the individual component provide a multivalent therapeutic effect. The positive effect of EM on the expansion of the adaptive capabilities of a person in general and the immunohormonal status of patients with various diseases in particular is noted. The studied effects of EM allowed us to include the EM composition in the treatment of patients with OA.

## Purpose of the study

To study in patients with idiopathic OA before and after treatment the dynamics of the state of the total number of leukocytes, CD4 +, CD8 +, CD4 + / CD8 + index, CD19, IgG, IgA, IgM and the dynamics of indicators of the following hormones: STH, sT4, sT3, PTH, TKT, OK, KORT , E2, T, DHEA-s, IRI and the HOMA-IR index and the effectiveness of four-week therapy with 5% applications of essential oils.

## Materials and methods

The study involved 60 women aged 49 to 72 years, patients with primary osteoarthritis of the knee and hip joints, with minor synovitis (Table 1). The main inclusion criteria were the presence of osteoarthritis with pain and inflammatory syndrome. The exclusion criteria were the presence of diabetes mellitus or other endocrine pathology, the presence or suspicion of cancer. The diagnosis of OA was established on the basis of the ACR criteria, 1987. The patients had II-III-IV radiological stage of the disease according to Kellgren-Laurence. The presence of algo-functional disorders of more than 7 points (according to the Lequesne / Lequesne index) in patients with OA was the basis for starting therapy. To assess the effectiveness of treatment, patients with OA were divided into 2 comparable groups of 30 women. Randomization was carried out by random sampling. In the first group of OA patients, treatment was carried out with EM applications, in the control group, OA patients took only diclofenac. All patients before treatment took regularly chondroprotectors in a stable dose for the last 3 months and for the last 2 weeks before treatment - diclofenac 100 mg per day. Body mass index was calculated before and after treatment. Within 28

days of treatment, patients underwent clinical observation on an outpatient basis. In both groups, the state of health was assessed according to the Likert scale, which included 5 answer options, each of which was assigned a certain number of points (very good - 1, good - 2, satisfactory - 3, poor - 4, very bad - 5). Before inclusion, all patients underwent the following examination: clinical examination, X-ray of the joints, ultrasound of the joints, MRI of the affected joint and ultrasound of the abdominal cavity. Before and after treatment in the morning on an empty stomach and before taking medications, blood sugar, prothrombin, general analysis of urine and peripheral blood were determined in patients (Table 2).

Table 1

Characteristics and clinical data of patients participating in the study

| Indicator | EM applications, n = 30 | NSAID therapy, n = 30 |
|---|---|---|
| Age (years) | 67 [58.7; 70.2] | 68 [58.8; 70.1] |
| Duration of illness (years) | 6.1 [3.9; 10.2] | 6.3 [3.7; 10.3] |
| X-ray stage | | |
| 2 | 12 | eleven |
| 3 | 12 | thirteen |
| 4 | 6 | 6 |
| Body mass index [Q1; Q3] | | 28 [25.4; 29.3] |
| before treatment | 28 [25.3; 29.4] | 28 [25.4; 29.3] |
| after treatment | 28 [25.3; 29.4] | |
| Accompanying illnesses: | | |
| arterial hypertension | thirty | thirty |
| chronic gastritis | thirty | thirty |
| peptic ulcer 12-duodenum | 10 | 9 |
| xp. cholecystitis | 15 | 17 |
| Lequin index [Q1; Q3] | | 12 [10.1; 13.5] |
| before treatment | 12 [10.2; 13.7] | 8.4 [8; 9.2] * |
| after treatment | 6.5 [6; 7.7] ** | |
| Likert doctor [Q1; Q3] | | 3 [3; 3] |
| before treatment | 3 [3; 3] | 2 [3; 2] * |
| after treatment | 1 [1; one]** | |
| Likert Sick [Q1; Q3] | | 3 [3; 3] |
| before treatment | 3 [3; 3] | 2 [3; 2] * |
| after treatment | 1 [1; 1.75] ** | |

Note: comparison of doubly linked samples (before and after treatment) was carried out according to the Wilcoxon test, ** - p <0.02, * - p <0.05. Data are presented as median (Me) and quartiles (lower - Q1 and upper - Q3).

table 2

Dynamics of indicators of general blood analysis before and after treatment with EM applications and NSAID therapy groups

| Patient group | | Treated with EM applications, n = 30 | | Treated with applications of NSAIDs, n = 30 | | Norm |
|---|---|---|---|---|---|---|
| No. p.p | General analysis blood | before treatment | after | before treatment | after | |
| | | Me [Q1; Q3] | Me [Q1; Q3] | Me [Q1; Q3] | Me [Q1; Q3] | |
| one | Hemoglobin (g / l) | 127 [121; 138] | 122 [121; 136] | 130 [122; 138] | 121 [120; 135] | 120-140 |
| 2 | Erythrocytes | 4.0 [3.8; 4.3] | 4.0 [3.8; 4.4] | 4.0 [3.9; 4.7] | 4.0 [3.8; 4.4] | 3.9-4.7 h 1012 l |
| 3 | Color indicator | 0.93 [0.88; 0.98] | 0.93 [0.9; 0.98] | 0.97 [0.89; 0.98] | 0.93 [0.88; 0.98] | 0.85-1.05 |
| 4 | Leukocytes | 5 [4.2; 6.2] | 4.6 [3.5; 5.1] | 5.4 [4.3; 6.4] | 4.9 [4.0; 5.2] | 4.0-9.0 h 109 l |
| 5 | Pal. cores | 1 [1.0; 1.7] | 1 [1.0; 1.0] | 1 [1.0; 1.5] | 1 [1.0; 1.5] | 1-6 |
| 6 | Eosinophils | 1 [0.5; 1.0] | 1 [0.5; 3.5] | 1 [0.5; 1.0] | 1 [0.5; 1.0] | 0.5-5.0 |
| 7 | Seg. cores | 55 [21; 61] | 55 [43; 58] | 56 [22; 61] | 55 [28; 59] | 47-72 |
| eight | Lymphocytes | 29 [23; 34] | 35 [27; 40] | 29 [21; 36] | 29 [23; 34] | 19–37 |
| 9 | Monocytes | 6 [5; 10] | 4.5 [3; 6] | 6 [5; 9] | 5.5 [4.2; 6] | 3-11 |
| 10 | ESR (mm / hour) | 14 [12; 17] | 9.5 [5.8; 15] | 13 [12; sixteen] | 12 [10; 15] | 17 < |

Note: comparison of doubly linked samples (before and after treatment) was carried out according to the Wilcoxon test, p <0.05. Data are presented as median (Me) and quartiles (lower - Q1 and upper - Q3).

Patients with OA before and after treatment underwent an assessment of the immunological status, endocrine system, biochemical parameters of venous blood and the HOMA-IR (HOMA) index (Tables 3, 4, 5). The latter was assessed to reveal latent insulin tolerance, which, with normal blood sugar and fasting insulin levels, are not informative. The HOMA-IR index evaluates the activity of pancreatic B-cells and is calculated using the formula: fasting glucose (mmol / l) x fasting insulin (μU / ml) / 22.5.

Table 3

Dynamics of biochemical parameters before and after treatment with applications of essential oils and control groups

| Patient group | | Treated with EM applications, n = 30 | | Treated with applications NSAIDs, n = 30 | | Norm |
|---|---|---|---|---|---|---|
| No. p.p. | Biochemical parameters | before treatment | after | before treatment | after | |
| | | Me [Q1; Q3] | Me [Q1; Q3] | Me [Q1; Q3] | Me [Q1; Q3] | |
| one | Alkaline f-for (unit / l) | 79.0 [62.0; 96.5] | 100 [84.5; 116.5] ↑ * | 76.0 [62.0; 96.5] | 78.0 [56.5; 95.5] | 53-141 |
| 2 | Fibrinogen (g / L) | 4.5 [3.7; 5.3] | 3.9 [3.3; 4.7] | 4.5 [3.6; 5.2] | 4.0 [3.5; 4.7] | 3.4-5.3 |
| 3 | Potassium (mmol / L) | 4.3 [3.9; 4.5] | 4.4 [4.1; 4.6] | 4.3 [3.9; 4.5] | 4.3 [3.9; 4.5] | 3.5-5.1 |
| 4 | Sodium (mmol / L) | 140 [133; 141] | 143 [140; 145] ↑ * | 140 [133; 141] | 140 [130; 141] | 136-145 |
| 5 | Calcium ionization. (mmol / l) | 1.24 [1.2; 1.25] | 1.25 [1.20; 1.27] | 1.24 [1.21; 1.26] | 1.25 [1.2; 1.27] | 1.12-1.32 |
| 6 | Calcium total (mmol / l) | 2.4 [2.19; 2.50] | 2.4 [2.29; 2.6] | 2.4 [2.19; 2.55] | 2.4 [2.19; 2.52] | 2.1-2.6 |
| 7 | Sugar blood (mmol / l) | 4.0 [3.9; 5.0] | 3.6 [3.1; 4.0] ↓ * | 4.0 [4.8; 4.9] | 4.1 [4.5; 4.9] | 3.3-5.5 |

Note: comparison of doubly linked samples (before and after treatment) was carried out according to the Wilcoxon test, * - p <0.05. Data are presented as median (Me) and quartiles (lower - Q1 and upper - Q3).

Table 4

Dynamics of immunological parameters before and after treatment with applications of essential oils, NSAIDs and the healthy group

| Patient group | | Treated with applications EM, n = 30 | | Treated with applications NSAIDs, n = 30 | | Group healthy |
|---|---|---|---|---|---|---|
| No. p.p. | Immunological indicators | before treatment | after | before treatment | after | |
| | | Me [Q1; Q3] | Me [Q1; Q3] | Me [Q1; Q3] | Me [Q1; Q3] | |
| one | Leukocytes 106 / l | 6300 [4700; 8850] | 5500 [4600; 9050] | 63500 [4750; 8900] | 6300 [4600; 950] | 6400 [4800; 8000] |
| 2 | CD4 + cells% (T-helpers) | 21 [20; 28] * ↓ | 25 [18; 30] * ↑ | 21 [20; 27] * ↓ | 221 [19; 28] * ↓ | 28.5 [21.38; 35.62] |
| 3 | CD4 + abs cells (T-helpers) 106 / l | 171 [103; 242] * ↓ | 182 [137; 288] * ↑ | 170 [101; 244] * ↓ | 175 [116; 232] * ↓ | 335 [251.25; 418.75] |
| 4 | CD8 + cells% (Cytotoxic-eTkl T-suppressors) | 25 [15; 32] * ↑ | 22 [11; 26] * ↓ | 25 [16; 33] * ↑ | 25 [14; 32] * ↑ | 16 [12; twenty] |
| 5 | CD8 + abs cells (Cytotoxic-eTcl. T-suppressors) 106 / l | 188 [117; 246] * ↑ | 174 [89; 229] * ↓ | 190 [118; 246] * ↑ | 184 [102; 239] * ↑ | 180 [135; 225] |
| 6 | CD19 cells% (B-lymphocytes) | 19 [13; 25] * ↑ | 18 [13; 22] | 19 [16; 25] * ↑ | 19 [14; 24] * ↑ | 16.5 [12.40; 20.60] |
| 7 | CD19 cells abs. (B-lymphocytes) 106 / l | 337 [91; 630] | 315 [236; 480] | 337 [91; 630] | 315 [236; 480] | 460 [345; 575] |
| eight | CD4 + / CD8 + (IR) | 0.87 [0.31; 1.12] * ↓ | 1.08 [0.77; 1.34] * ↑ | 0.87 [0.37; 1.10] * ↓ | 0.88 [0.97; 1.09] * ↓ | 1.72 [1.290; 2,150] |
| 9 | IgG | 11.8 [4.8; 12.3] | 12 [12; 13] ** ↑ | 11.7 [5.1; 12.0] | 11.2 [6.0; 12.1] | 15 [13.13; 16.87] |
| 10 | IgA | 1.7 [0.5; 2.1] | 2.0 [1.5; 2.0] | 1.7 [0.5; 2.2] | 2.0 [1.6; 2.0] | 1.62 [1.58; 1.80] |
| eleven | IgM | 0.9 [0.5; 1.20] | 1 [0.9; 1,2] | 0.9 [0.35; 1.25] | 0.9 [0.5; 1,2] | 1.39 [1.32; 1.50] |

Note: comparison of two related samples (before and after treatment) was carried out according to the Wilcoxon test (* - comparison with the control group, ** - dynamics after treatment), p <0.05. Data are presented as median (Me) and quartiles (lower - Q1 and upper - Q3).

Table 5

Dynamics of hormone indices in patients with OA before and after the course of treatment with ether applications oils and control groups

| Patient group | | Treated with EM applications, n = 30 | | Treated with applications NSAIDs, n = 30 | | Group healthy |
|---|---|---|---|---|---|---|
| No. p.p. | Hormones | before treatment | after | before treatment | after | |
| | | Me [Q1; Q3] | Me [Q1; Q3] | Me [Q1; Q3] | Me [Q1; Q3] | |
| one | TSH, mIU / l | 1.76 [1.18; 3.12] | 1.98 [0.67; 4.15] | 1.88 [1.24; 3.8] | 1.90 [1.27; 4.15] | 0.15-5.0 |
| 2 | svT4, nmol / l | 14.7 [13.0; 15.5] | 15.4 [12.7; 18.0] | 14.7 [13.2; 15.5] | 14.4 [12.0; 17.7] | 11.5-23 |
| 3 | svT3, nmol / l | 4.2 [3.9; 4.7] | 4.5 [3.8; 4.8] | 4.4 [4.0; 4.8] | 4.5 [3.8; 4.7] | 2.5-5.8 |
| 4 | COURT, nmol / l | 289 [255; 396] | 300 [263; 429] | 326 [239; 447] | 329 [240; 429] | 170-720 |
| 5 | E2, nmol / l | 94.7 [80.2; 139.4] | 100.0 [64.2; 127.5] | 96.3 [66.2; 106.4] | 96.4 [64.2; 109.5] | Up to 500 |
| 6 | T, nmol / l | 0.65 [0.52; 1.0] | 0.86 [0.58; 1.19] ↑ * | 0.63 [0.52; 0.9] | 0.65 [0.55; 1.0] | Up to 5.0 |
| 7 | DHEA-S, μmol / l | 2.37 [1.7; 3.63] | 2.40 [1.79; 3.53] | 2.39 [1.3; 3.73] | 2.35 [1.40; 3.53] | 0.9-5.5 |
| eight | IRI, mME / l | 10.09 [7.07; 13.35] | 8.72 [4.62; 13.2] ↓ * | 9.90 [6.37; 13.32] | 9.72 [6.62; 13.4] | 2.1-22 |
| 9 | NOMA index | 2.3 [1.8; 3.6] | 1.7 [1.39; 2.4] ↓ * | 2.3 [1.8; 3.5] | 2.3 [1.7; 3.6] | 2.5 < |
| 10 | STH mIU / l | 2.0 [0.64; 3.3] | 3.6 [1.16; 5.6] | 1.9 [0.84; 3.7] | 2.0 [0.82; 3.6] | Up to 20 |
| eleven | TKT, ng / l | 3.2 [1.79; 5.60] | 2.56 [1.16; 5.63] | 3.1 [2.01; 5.60] | 3.2 [1.76; 5.17] | Up to 20 |
| 12 | PTH, ng / l | 26.4 [21.2; 41.5] | 28.7 [21.4; 43.1] | 26.8 [21.20; 47.5] | 28.7 [21.4; 44.1] | 16-62 |
| thirteen | OK, mcg / l | 25.1 [22.0; 31.3] | 21.3 [22.2; 31.3] | 24.1 [21.0; 32.3] | 24.3 [21.1; 31.9] | 9.5-48.3 |

Note: comparison of two related samples (before and after treatment) was carried out according to the Wilcoxon test, * - p <0.05. Data are presented as median (Me) and quartiles (lower - Q1 and upper - Q3).

The level of alkaline phosphatase (ALP), fibrinogen, potassium ($K^+$), sodium ($Na^+$), ionized calcium ($Ca^{++}$), total calcium ($Ca_{total}$).

The following indicators of immunological status were studied: total number of leukocytes; T-helpers (CD4 +), T-cytotoxic cells (CD8 +), indicators of the immunoregulatory index CD4 + / CD8 + (IR), the number of B-lymphocytes (CD19), immunoglobulins IgM, IgG, IgA.

The analysis of indicators of somatotropic hormone (STG), cortisol (COURT), thyroid-stimulating hormone (TSH), free thyroxine (fT4), free triiodothyronine (fT3), parathyroid hormone (PTH), calcitonin (TKT), osteocalcin (OC), estradiol (E2) and total

testosterone (T), dehydroepiandrosterone sulfate (DHEA-S), aldosterone (ALD), progesterone (PG), insulin (IRI), C-peptide (C-p).

The results of treatment of patients with OA were assessed according to the dynamics of clinical indicators: the Leken index, the Likert scale; and dynamics of laboratory indicators of general analysis and blood biochemistry, immune and hormonal statuses (Tables 1-5).

To carry out applications to patients with OA, a 5% composition of EOs was prepared, permitted for use in Russia as a therapeutic or health-improving agent and corresponding to OST, GOST or ISO 9001: 2000 standards. The composition of the composition included the following essential oils: cloves, lavender, nutmeg, peppermint, sage, thyme, eucalyptus, rosemary, geranium, in the following ratio 3: 6: 6: 4: 3: 3: 1: 3: 3, s subsequent mixing with base (transport) sweet almond oil.

For the application of EM, we have developed the following technique: in the supine or half-sitting position, 5% EM composition in the amount of 5 ml (1 teaspoon) is rubbed alternately into the skin of the lower extremities from the proximal part of the feet with the grip of the soles towards the lower legs (front and back surfaces ), then - in the area of the knee joints (front and back surfaces) for 8-10 minutes (one limb) - "high boots". After that, it was recommended to wear light trousers made of light-colored cotton fabric and lie on the couch or in bed for at least 30 minutes, not rinse for 2 hours. The procedure was carried out 3 times a day. The course of treatment is 28 days. In the control group, patients continued to receive diclofenac.

Statistical data processing was carried out using the software package SPSS 19. Quantitative characteristics with distributions different from the normal law were described by medians (Me) and quartiles [Q1; Q3]. To compare related groups (analysis of dynamics), the Wilcoxon method was used for dependent samples; $p < 0.05$ was considered a statistically significant level of difference.

## results

Before treatment, in patients with OA, the indicators of the Leken algo-functional index corresponded to a significant manifestation of the disease and averaged 12 points, the indicators of well-being on the Likert scale, on average = 3, which corresponded to a satisfactory state, the body mass index, on average, was within the normal range for the groups. In all patients with OA, concomitant diseases were recorded in the form of exacerbation of arterial hypertension and / or gastrointestinal diseases, which required the withdrawal of NSAIDs and / or the appointment of additional therapy.

In the group of patients who received therapy with EM applications, after treatment, the Leken index values averaged 6.5 points ($p < 0.02$), the Likert scores of well-being, on average = 1 ($p < 0.02$), which corresponded to significant improvement in condition. In this group, patients with OA by the end of the observation stopped taking NSAIDs and noted regression of exacerbation of arterial hypertension and gastrointestinal diseases.

In the group of patients who received NSAID therapy, after treatment, the Leken index values averaged 8.4 points ($p < 0.05$), the indicators of well-being on the Likert scale = 2 ($p < 0.05$), which corresponded to an improvement in the condition. Against the background of NSAID therapy, an exacerbation of concomitant diseases was recorded, which required an addition or intensification of therapy for arterial hypertension and gastrointestinal diseases. The body mass index of patients with OA in both groups remained stable. Table 1 presents the demographic and clinical data of patients with OA.

Evaluation of indicators of the general analysis before and after treatment showed the lack of dynamics, which coincides with the literature data on the non-pathognomonicity of signs of indicators of peripheral blood [1, 2, 8].

When assessing the dynamics of blood biochemical parameters in the group of patients treated with EM applications, there was an increase in WF ($p < 0.05$) and sodium ($p < 0.05$), a decrease in sugar level ($p < 0.05$), which did not go beyond the normal range. , and the lack of dynamics of biochemical parameters in the NSAID treatment group.

On the part of the immune system in patients with OA before treatment, signs of metabolic immunosuppression were revealed in both study groups compared with the group of healthy patients: the mean CD4 + counts, the mean CD8 + counts (cytotoxic cells) were higher than normal values, the CD4 + / CD8 + IR ratios were on average less than 1, that is, below normal values, the indices of immunoglobulins did not differ from the healthy group (Table 4).

After treatment with EM applications, there was a tendency to an increase in CD4 + and RI CD4 + / CD8 +, a decrease in the number of CD8 + cells, confirmed by the absence of differences with the healthy group and an increase in IgG ($p < 0.05$), which did not exceed the physiological norm. In the group of patients treated with NSAIDs, the dynamics were not observed (Table 4).

Evaluation of the hormonal status of patients with OA in both study groups before treatment showed that the levels of growth hormone, cortisol, total testosterone, dehydroepiandrosterone sulfate corresponded to the lower limit of the norm. In all patients, regardless of age and stage of the disease, sugar indicators

blood and insulin levels were normal. However, the HOMA-IR index in most patients approached or was higher than 2.5, which, according to the literature, may indicate the initial onset of insulin resistance, tissue consumption of glucose, leading to impaired energy metabolism and the likelihood of developing oxidative stress [5, 6] ...

After treatment with EM applications, patients with OA showed an increase in total TS ($p < 0.05$), a decrease in insulin levels ($p < 0.05$) and HOMA index ($p < 0.05$). In the group of patients treated with NSAIDs, no dynamics was observed (Table 5).

## Conclusion

The data obtained indicate that the course of treatment of patients with OA with EM applications leads to a more pronounced regression of the clinical picture of the disease compared with the group of patients taking NSAIDs, according to the Leken algo-functional index - the dynamics of pain reduction and improvement of joint function. The effectiveness of treatment, according to the Likert scale, was also higher in the group of patients treated with EM applications, compared with the group of patients treated with NSAIDs, and corresponded to a significant positive shift in the health status of patients. Improvement of clinical data occurred against the background of positive dynamics of indicators of the immune and hormonal systems and biochemical parameters of blood. There was also an improvement in the state of concomitant cardiovascular pathology and diseases of the gastrointestinal tract.

The positive effect of EM applications on the clinical course of OA and the absence of side effects made it possible to consider the obtained dynamics of the parameters of the immune, hormonal systems and blood biochemical parameters as positive. The obtained results of the treatment confirm the possibility of essential oils to exert a general biological effect on the human body, in general, and suggest an anti-inflammatory and improving musculoskeletal metabolism effect in patients with OA, in particular. This gives grounds to recommend this method of treatment for use in health resort and general medical practice.

conclusions

Before treatment, patients with OA were found to have:

1. Immunosuppression of the T-link of immunity, expressed in a decrease in the number of CD4 +, IRCD4 + / CD8 +, increased CD8 +.

2. Levels of growth hormone, cortisol, estradiol, testosterone, dehydro-epiandrosterone - sulfate, corresponded to the lower limit of the norm.

3. Indicators of energy metabolism index HOMA corresponded to the upper limit of the norm. In patients with OA after treatment, it was noted:

1. The effectiveness of the treatment of patients with OA according to the Leken index and the Likert scale was higher in the group treated with EM applications compared with the NSAID treatment group.

2. A decrease in the signs of T-link immunosuppression was noted after treatment with EM applications. immunity according to the trend of growth of CD4 +, IR CD4 + / CD8 +, a decrease in CD8 + indices, an increase in IgG indices and the lack of dynamics of these indices in the group of patients who received NSAID therapy.

3. An increase in the level of testosterone in the blood, a decrease in insulin and the lack of dynamics of indicators hormones in the NSAID treatment group.

4. Decrease in blood glucose and HOMA index after treatment with EM applications and lack of their dynamics in the NSAID treatment group.

5. After treatment with EM applications, an increase in the level of alkaline phosphatase and sodium in within the physiological norm and the lack of dynamics in the NSAID treatment group.

## Literature

1. Rheumatology: Clinical guidelines / Ed. acad. RAMS E. L. Nasonova. 2nd ed., Rev. and add. - M .: GEOTAR-Media, 2010 .-- 752 p.

2. Dashina T.A., Derevnina N.A., Bobkova A.S., Agasarov L.G. "Study of the effect of local therapy applications of essential oils on the dynamics of immune and hormonal parameters and the effectiveness of optimization of rehabilitation treatment of patients with osteoarthritis "// Bulletin of new medical technologies. Electronic edition. - 2015. - No. 1. - P.6-5.

3. Fingers M.A., Kvetnoy I.M. Guide to neuroimmune endocrinology. - M .: JSC "Publishing house" Medicine ", 2006. - 384 p., With ill.

4. Kristich R.V. Illustrated Encyclopedia of Human Histology. - SPb .: SOTIS, 2001 .-- 536 p., 1576 ill.

5. Burduli A.G., Smetnik V.P. Androgens and bone tissue // Problems of reproduction. - 2011. - No. 5. -

Pp. 110-115.

6. Dashina T.A., Derevnina N.A., Bobkova A.S., Agasarov L.G., Krikorova S.A., Yakovlev M.Yu. "The dynamics of the relationship of indicators of immune and hormonal status and the effectiveness of optimization of rehabilitation treatment of patients with osteoarthritis as a result of local therapy with applications of essential oils" // Bulletin of new medical technologies. Electronic edition. - 2015. - No. 1. - P.6.

7. Vasilenko A.M., Zakharova L.A. Neuroimmunology of Pain: Biological and Clinical Aspects. In the book. Actual problems of neuroimmunopathology / Guide under. Ed. G.N. Kryzhanovsky, S.V. Magaeva, S.G. Morozov. - M .: Genius Media, 2012. - pp. 236–284.

8. Nikolaevsky V.V. Aromatherapy: A Handbook. - M: Medicine, 2000 .-- 336 p.

9. Buck, LB, and Axel, R. A novel multigene family may encode odorant receptors: a molecular basis for odor recognition. 1991. Cell 65, 175-187.

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Dashina, T.A. Influence of local therapy with essential oils on the dynamics of immune and hormonal parameters in patients with osteoarthritis / T.A. Dashina, N.A. Derevnina, L.G. Agasarov // Traditional medicine. - 2016. - No. 2 (45). - pp. 29-36.

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