The Effect of the Phytocomplex Electrophoresis on the Clinical Symptomatology and Quality of Life of Patients with the Knee Joint Osteoarthritis

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Abstract

BACKGROUND: Improving the effectiveness of rehabilitation of patients with osteoarthritis necessitates the use of drug electrophoresis with sinusal modulated currents (SMC-electrophoresis) in conjunction with drug therapy. The phytocomplex is proposed for electrophoresis composed of the compared, alfalfa and hops dry extract, containing flavonoids, coumestans, polysaccharides, steroids, essential amino acids, vitamins, mineral components and causing its possible use in osteoarthritis.

AIM: The research aims to study the effect of the phytocomplex SMC-electrophoresis on the clinical symptomatology and quality of life of patients with the knee joint osteoarthritis.

METHODS: One hundred and eight patients were randomly distributed into 3 groups (n = 36). The phytocomplex was used in conjunction with drug therapy. The patients were divided into groups according to the applied electrotherapy: electrophoresis, no side effects were registered.

RESULTS: The use of the phytocomplex SMC-electrophoresis had a more pronounced positive effect on pain, knee joint function and quality of life of the patients compared with the treatment with drugs alone or using amplitude therapy. This was especially pronounced immediately after the rehabilitation. The analgesic effect was significant and stably maintained in the patients of the first group for up to 6 months in terms of the level of pain according to the WOMAC and Lequesne indices, VAS, articular and tendon indices, quality of life as per Health Assessment Questionnaire (HAQ).

CONCLUSION: The obtained results give grounds for further research on the evaluation of the effectiveness of using the phytocomplex SMC-electrophoresis in microcirculatory disorders in the affected joint, for correcting connective tissue metabolism and electrolyte metabolism in the patients with the knee joint osteoarthritis.

Introduction

An osteoarthritis is a heterogeneous group of diseases of various etiologies. The basis of osteoarthritis is the damage of all joint components, primarily of cartilage and subchondral bone, synovial membrane, ligaments, and periarticular muscle capsules [1]. The disease has a significant and widespread prevalence in the world [2], [3], [4]. It results from the interaction of multiple genetic and environmental factors, affects mostly people of the older age group, is characterized by a long course with the tendency to recrudescence and progression, deterioration in the quality of life of the patients, and disability [5], [6], [7], [8]. This determines the high social and economic significance of the disease [9], [10].

Traditionally, the treatment of osteoarthritis is comprehensive and includes medical and nonmedical methods, including the physiotherapeutic ones [11], [12], [13]. The low-frequency electrotherapy with SMC, or the amplitude therapy, in osteoarthritis has algiesic, neurostimulation, vasodilator, and trophostimulating effects [14]. To enhance the
therapeutic effect, amplitude therapy is combined with the administration of drugs (SMC-electrophoresis) [15], [16], [17], [18].

The phytocomplex for SMC-electrophoresis offered by the authors is a dry extract from grass and roots of bog strawberry, the alfalfa grass and stems or strobiles of common hop (TU 9375-021-00003938-11 “Bog strawberry, alfalfa and hops dry extract (phytocomplex)”) [19]. It contains a set of biologically active substances, including flavonoids, contestants, polysaccharides, steroids, essential oils, tannins, hydroxycinnamic and phenol carboxylic acids, essential amino acids, vitamins, and mineral components, which stipulates its possible use in medicine for inflammatory-degenerative diseases of the locomotor system, including osteoarthritis.

The scope of the work was to study the effect of the phytocomplex SMC-electrophoresis on the clinical symptoms and quality of life of the patients with the knee joint osteoarthritis.

Material and Methods

The study included 108 patients with a verified diagnosis of the knee joint osteoarthritis. Clinical trials were carried out by the ethical principles of the Helsinki Declaration, good clinical practice (GCP), and applicable regulatory requirements. The clinical trials of the phytocomplex SMC-electrophoresis in the rehabilitation of patients with the knee osteoarthritis were allowed by the Interuniversity Ethics Committee under the Association of Medical and Pharmacy Universities of Russia.

The criteria for inclusion of patients in the study were a verified diagnosis of the knee joint osteoarthritis according to the criteria of the American College of Rheumatology (ACR), 1-2 Kellgren-Lawrence grade X-ray stage, without synovitis or with its small manifestations, the intensity of pain in the affected joint on VAS – not less than 40 mm, the administration of Symptomatic Slow Acting Drugs for Osteoarthritis (SYSADOA) as per generally accepted regimens in a stable dosage – at least 3 months before the start of the study, with the possibility of administration of nonsteroidal anti-inflammatory drugs (NSAIDs) in stable, standard daily doses, and the written consent to participate in the test. The exclusion criteria were as follows: secondary knee joint osteoarthritis, intra-articular administration of any drugs within 6 weeks prior to the study, treatment with glucocorticoids during the last month, history of operation on the knee joint tested, pronounced symptoms of synovitis, pregnancy, breastfeeding, contraindications to the use of SMC, individual intolerance to the biologically active substances of the phytocomplex, the presence of other rheumatic diseases, the body mass index above 40 kg/m², and the presence of severe comorbidities.

Among the patients included in the study, 73.1% (79 people) were females, and 26.9% (29 people) were males. The ratio of men and women was approximately 1:3. The age range of the surveyed people ranged from 40 to 78 years. Me (sample median) and IQR (interquartile range, 25th and 75th percentile) of the patients’ age, disease duration and body mass index at the time of the survey were 54.4 (50.0 and 61.5) years, 5.3 (3.0 and 7.5) years, and 30.5 (25.6 and 34.7) kg/m², respectively. The first X-ray stage of the knee joint osteoarthritis was observed in 35.2% of the patients, the second stage – in 64.8%. In the majority of the patients (81%), the pathological process was one-sided, and only in 19%, it was two-sided. A rapidly progressive course of the disease was observed in 3.7% of the patients. A number of the patients included in the study were diagnosed with comorbidities, including hypertension (37 people), diabetes (12 people), and metabolic syndrome (4 people), which were combined in some patients.

All patients with knee osteoarthritis included in the study, along with general clinical examination methods, used special research methods.

The clinical condition of the patients with osteoarthritis was assessed by examining the knee joints and quantifying indicators of clinical symptoms.

The range of motion in the affected joint (Mollier flexion) was evaluated using a Goniometer (ISOM 360°, 6°, Baseline, USA). The principle of D.M. Ritchie et al. were taken as the basis of the articular and tendon indices [20]. The level of pain was determined with moderate pressure of about 4 kg/cm² (before whitening the nail of the main phalanx) on the joint (along with with the joint space) and the place of attachment of tendons and ligaments. The 4-point scale was used as follows: 0 – no pain, 1 – patient states pain, 2 – patient states pain and frowns, 3 – patient withdraws limb. The duration of morning stiffness was estimated in minutes.

For more detailed clinical characteristics of the patients, the parameters recommended by the Osteoarthritis Research Society International (OARSI) were used, namely: the pain level indicator as per VAS (at rest and in motion); WOMAC index (Western Ontario and McMaster Universities Osteoarthritis Index); pain index (PW), stiffness index (SW), daily activity rate (FW); and Lequesne Index.

The quality of life of the patients with knee osteoarthritis was assessed by HQ.

The frequency and nature of adverse events, the dynamics of the pulse, blood pressure, electrocardiography (ECG) were used as safety parameters.

All patients were randomly (by random numbers generated using a computer program)
divided into 3 groups, comparable in clinical and functional characteristics. Patients of the first group (36 people) were on rehabilitation, including the phytocomplex SMC-electrophoresis. The amplitude therapy was prescribed to the patients of the second group (36 people) according to the similar procedure with the first group, without the phytocomplex. The observed patients of the first two groups continued to receive drug therapy, which did not change during the physiotherapy course. Patients of the third group (36 people) received only drug treatment: SYSADOA basic – 36 people (100%), NSAIDs – 8 people (22.2%), general tonic agents, and vitamin preparations. The drug therapy of the patients of the third group was comparable with the drug treatment of the patients in the first two groups.

The electrotherapy was performed on the knee joint region using a transverse technique in a straightened SMC mode with the first and fourth type of work, 5 min each. The modulation frequency was equal to 100 Hz, the modulation depth – to 75%, the half-periods’ duration was 2 and 3 sec, the current strength – 5 mA, and the duration of exposure – 10 min, with 10 daily procedures per course. The procedures were performed on an Amplipulse-6 apparatus (Elektroapparat, Russia).

A working solution of the electrophoresis phytocomplex was prepared ex tempore by dissolving the dry extract (10 parts) in dimethyl sulfoxide (15 parts) and then adding warm (40°C) distilled water (up to 100 parts). 20 ml of the working solution was applied to pads, which were placed on the medial and lateral surfaces of the affected knee joint. The content of flavonoids in the working solution was 0.7% (in terms of quercetin – the predominant flavonoid of the phytocomplex) or 4% (in terms of the absolute dry residue of flavonoids). The phytocomplex concentration in the working solution was chosen experimentally as a result of the study of transdermal delivery of the phytocomplex biologically active substances under the SMC action in model experiments [21]. It had been previously found that SMC electrophoresis did not destroy the main active substances of the phytocomplex, introduced from two poles.

The results were statistically processed using the SPSS.Statistics.v17.Multilingual-EQUINOX (SPSS Inc) software.

Results

The main clinical symptoms in the examined patients are presented in Figure 1. Central to the clinical picture was the pain in the joint (100 %), both in the patients with the first and the second disease stage. The overwhelming majority of the patients with the second stage osteoarthritis also had morning stiffness (98 %), limited movement in the joint (79 %), and a crunch in the joint (66 %). It should be noted that all clinical symptoms occurred approximately two times more often in the patients with the second stage of the disease than with the first one and were more pronounced.

The clinical condition of the patients with the knee joint osteoarthritis was assessed by the JROM, the duration of morning stiffness (MS), the articular (AI) and the tendon (TI) indexes (Table 1). The use of the method of the phytocomplex SMC-electrophoresis (first group) had a beneficial and significant effect on these parameters in the patients with the knee osteoarthritis. Thus, the MS index decreased 2.5 times, palpation pain decreased by 60% (AI) and 55% (TI), and the JROM increased by almost 14%.

A comparative analysis of the investigated rehabilitation methods showed that the phytocomplex SMC-electrophoresis method (first group) was more effective than drug therapy (third group) immediately after the physiotherapy and 3 – 6 months after that according to the values of MS, CI and TI (P < 0.05). When analysing two physiotherapeutic rehabilitation methods, it has been established that immediately after the physiotherapy, the phytocomplex SMC-electrophoresis (first group) was significantly better than the amplipulse therapy (second group) in terms of AI and TI (P < 0.05). The effect persisted for up to 3 months after the course of treatment in terms of TI (P = 0.044). In terms of MS, the phytocomplex SMC-electrophoresis method (first group) was better than the effects of SMC (second group) 3 months after the physiotherapy (P = 0.020). The effect persisted for up to 6 months (P = 0.038).

Pain in the joint is one of the most important clinical signs of osteoarthritis. Therefore, the pain level, as per VAS is the most significant indicator for assessing the effectiveness of patient rehabilitation. It was found that the studied physiotherapy rehabilitation methods reliably reduced the VAS indicators by the end of the treatment by 59% (at rest) and 51% (in motion) using the phytocomplex SMC-
electrophoresis (first group), 54% (at rest) and 43% (in motion) for the amplitude therapy (second group) (Figure 2).

Table 1: The results of the comparative analysis of the effectiveness of various methods of rehabilitation of the patients with the knee osteoarthritis in terms of JROM, MS, AI and TI

| Examination period | Group | JROM, degree | MS, minute | AI, points | TI, points |
|--------------------|-------|--------------|------------|------------|------------|
| Before treatment   | 1 (n = 36) | 116.5 ± 19.2 | 18.2 ± 3.6 | 3.8 ± 0.36 | 1.34 ± 0.26 |
|                    | 2 (n = 36) | 124.6 ± 16.8 | 17.1 ± 3.4 | 1.79 ± 0.40 | 1.26 ± 0.22 |
| After treatment    | 1 (n = 36) | 123.2 ± 25.6 | 7.3 ± 1.8  | 0.74 ± 0.30 | 0.60 ± 0.18 |
|                    | 2 (n = 36) | 126.5 ± 19.5 | 7.0 ± 2.4  | 0.93 ± 0.42 | 0.79 ± 0.15 |

The results of the comparative analysis of the effectiveness of various methods of rehabilitation of the patients with the knee osteoarthritis in terms of pain level as per VAS (in motion). The significance of differences between the groups (**) and in the group (***) before and after treatment as per the Student's t-test (numbers indicated in parentheses).

The WOMAC index can also be used for a comparative evaluation of the effectiveness of various rehabilitation methods for patients with osteoarthritis. The significant decrease in the PW, SW and FW indicators of the WOMAC index was observed by the end of the physiotherapy course using the phytocomplex SMC-electrophoresis (first group) by 40%, and by the end of the amplitude therapy (second group) – by 30% (Table 2).

The phytocomplex electrophoresis method (first group) immediately after the physiotherapy course was not significantly better than the phosphamide therapy method (second group) (P > 0.05). When assessing the analgesic action stability after 3 – 12 months, it was assumed that the effect had been stable at the pain level as per VAS of no more than 40 mm. Three months after the rehabilitation, the VAS indicators in the first group of the patients were at a level of less than 40 mm. In the subsequent periods, the analgesic effect persisted and was significantly better than the pain level indicators in the patients of the second and third groups (P < 0.05). When exposed to SMC (second group), the analgesic effect persisted for up to 6 months after the physiotherapy; at subsequent follow-up periods, the VAS indicators did not significantly differ from the pain level data in the patients of the third group who had received only drug treatment (P > 0.05). The proportion of the patients with VAS ≤ 40 mm during the rehabilitation by

The WOAMC index can also be used for a comparative evaluation of the effectiveness of various rehabilitation methods for patients with osteoarthritis. The significant decrease in the PW, SW and FW indicators of the WOMAC index was observed by the end of the physiotherapy course using the phytocomplex SMC-electrophoresis (first group) by 40%, and by the end of the amplitude therapy (second group) – by 30% (Table 2).

Table 2: The results of the comparative analysis of the effectiveness of various methods of rehabilitation of the patients with the knee osteoarthritis as per the WOMAC index

| Examination period | Group | WOMAC index, score | M ± σ* |
|--------------------|-------|---------------------|--------|
| Before treatment   | 1st (n = 36) | 38.9 ± 23.4 | 116.3 ± 20.4 |
|                    | 2nd (n = 36) | 33.6 ± 18.4 | 115.2 ± 26.6 |
| After treatment    | 1st (n = 36) | 31.5 ± 18.4 | 113.5 ± 25.6 |
|                    | 2nd (n = 36) | 28.6 ± 21.6 | 112.5 ± 26.4 |

The experimental, empirical distribution of JROM, MS, AI, TI variables did not differ much from the normal distribution (the Kolmogorov-Smirnov criterion and the schedule of the normal distribution in SPSS). The significance of differences between the groups in the group before and after treatment as per the Student's t-test (numbers indicate the numbers of the groups).
A comparative analysis of various methods of treating knee osteoarthritis has shown that when using the phytocomplex SMC-electrophoresis (first group) immediately after the rehabilitation, the WOMAC indicators were significantly better than with the amplipulse therapy (second group) ($P < 0.05$) and with drug treatment (third group) ($P < 0.05$). This picture persisted for 3 – 12 months after the rehabilitation. The WOMAC indices, when exposed to SMC (second group) 6 months after the course of treatment did not significantly differ from the drug treatment data (third group) ($P > 0.05$).

The study of the dynamics of the Lequesne index in the 3 research groups has shown that the largest decrease in this indicator was observed in the first group after using the phytocomplex SMC-electrophoresis (45%) (Figure 3). This method of rehabilitation of the patients with knee osteoarthritis was significantly better by the Lequesne index compared with the amplitude therapy (second group) and drug treatment (third group) immediately after the physiotherapy and 6 months after ($P < 0.05$). The arithmetic means values of the Lequesne index 12 months after the rehabilitation were in the range of 10 – 11 points and did not differ significantly in all research groups ($P > 0.05$).

The quality of life of the patients with knee osteoarthritis was assessed using the HAQ index. A significant decrease in HAQ indices was observed immediately after the rehabilitation using the phytocomplex SMC-electrophoresis (first group – by 34%; $P = 0.003$) and the amplitude therapy (second group – by 28%, $P = 0.015$) (Figure 4). These indicators were significantly better than those of HAQ obtained using only the drug therapy (third group) ($P < 0.05$). After 3 – 12 months of observation, the HAQ values in the first and second groups did not differ significantly ($P > 0.05$). HAQ parameters ≤ 20 points were taken as satisfactory (the functional state of the joint was not impaired). In the groups under study, the predominant proportion of HAQ parameters before the treatment was lower than 20. Therefore, the HAQ values after the rehabilitation and 3 – 12 months after were satisfactory.

Currently, there are no systematic works on the effect of flavonoids on the clinical symptoms and quality of life of patients with osteoarthritis during electrophoresis. The only reliable results concern the relief of clinical manifestations of osteoarthritis of the knee joint according to the WOMAC index (in 64% of cases) when using sodium salicylate sodium phosphate electrophoresis [17], pain relief (according to VAS) and the functional disability index decrease immediately after treatment and for the next six weeks when using sodium salicylate electrophoresis [16], increasing the effectiveness of degenerative osteoarthropathy treatment (by 19%) when using electrophoresis of a Chinese drug compared to electric current monotherapy [18], which is consistent with the results of our research.

**Figure 3: The results of the comparative analysis of the effectiveness of various methods of rehabilitation of the patients with the knee osteoarthritis as per the Lequesne index. The significance of differences between the groups (*) and in the group (**) before and after treatment as per the Student’s t-test (group numbers are indicated in numbers)**

**Figure 4: The results of the comparative analysis of the effectiveness of various methods of rehabilitation of the patients with the knee osteoarthritis as per the HAQ index. The significance of differences between the groups (*) and in the group (**) before and after treatment as per the Student’s t-test (group numbers are indicated in numbers)**

**Discussion**

The study has shown that the use of the phytocomplex SMC-electrophoresis in conjunction with the drug therapy has a more pronounced effect on the clinical symptoms of the patients with the knee joint osteoarthritis compared with the drug therapy or shared use of drugs with the amplipulse therapy. This was especially pronounced immediately after the rehabilitation. The analgesic effect was consistently maintained using the phytocomplex SMC-electrophoresis for 6 – 12 months, with the amplitude therapy for 3 – 6 months in terms of the pain syndrome (PW) of the WOMAC index, as well as VAS, Lequesne index, articular and tendon indices. Stable results have been obtained in improving the functions of the knee joint during the rehabilitation using the phytocomplex SMC-electrophoresis in terms of stiffness (SW) and daily activity (FW) of the WOMAC index. It should be noted that when using the phytocomplex SMC-electrophoresis, no side effects
were recorded.

The obtained results give grounds for further research on the assessment of the effectiveness of using the phytocomplex SMG-electrophoresis in microcirculatory disorders in the affected joint, to correct the connective tissue metabolism and electrolyte metabolism in the patients with the knee osteoarthritis.

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