The effectiveness of herbal medicine and acupuncture in patients with metabolic phenotype of osteoarthritis - a pilot study

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Efficacy of phytotherapy and acupuncture in patients with metabolic phenotype of osteoarthritis: a pilot study

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SUMMARY

The relevance of the study is determined by the high prevalence of metabolic syndrome (MS) (from 20 to 35% of the Russian population), the frequent combination of MS with osteoarthritis (OA), and unsatisfactory methods of treatment of this polymorbid pathology.

Objective: To evaluate the efficacy and safety of taking the parapharmaceutical agent Epigenorm antivir (EA) in combination with acupuncture in patients with osteoarthritis in combination with metabolic syndrome (OAMS). For the first time, the analgesic effect of EA and acupuncture in patients with OAMS, a positive effect on indicators of quality of life, physical and mental health has been shown.

For the first time, the multipurpose effect of EA and acupuncture on the manifestations of OA and MS components - systemic anti-inflammatory, lipid-correcting, antiatherogenic - was revealed. The discovered properties make the appointment of EA in combination with acupuncture for patients with OAMS more preferable, since it does not require the appointment of drugs that reduce the content of lipids, antiatherogenic, anti-inflammatory drugs and reduces the direct costs of treatment. The results suggest a synergistic effect of EA and acupuncture and justify the conduct of blind, randomized clinical trials on a larger sample of OAMS patients.

Key words: osteoarthritis, metabolic syndrome, polymorbidity, qualitylife, turmeric, epigenorm antivir, acupuncture, pleiotropy.

RESUME

The rationale for doing this study was based on high prevalence of metabolic syndrome (MS) (from 20 to 35% of the whole population of Russia), frequent cooccurrence of osteoarthritis (OA), and suboptimal treatments of this comorbidity. The aim was to assess the efficacy and safety of parapharmaceutical product Epigenorm Antivir (EA) in combination with acupuncture in patients with OA and MS (OAMS). For the first time we demonstrated analgesic effects of EA and acupuncture in OAMS, improvement in quality of life, physical and mental health. The study showed pleiotropic effects of EA and acupuncture on signs of OA and components of MS - systemic antiinflammatory, lipid modulating and antiatherogenic.

Keywords: osteoarthritis, metabolic syndrome, polymorbidity, quality of life, curcuma, acupuncture, pleiotropic.

INTRODUCTION

Osteoarthritis (OA) is the most common joint disease; the number of patients with clinical and radiological signs of the disease increases significantly from

age. According to epidemiological studies, in the Russian Federation, the number of patients with OA is about 15 million people [1, 2]; over the period 2010–2014, the incidence increased by 12.1%.

The pathogenesis of OA is associated with the action of genetic, epigenetic, biomechanical, metabolic and other factors that lead to the development of sluggish inflammation in all structures of the joint, the involvement of cells of the immune system, adipose tissue, their mediators in the process, and the formation of clinical variants of the disease, heterogeneous in phenotype and pathogenesis [1, 3, 4]. The metabolic phenotype of OA [5] - OA associated with metabolic syndrome (OAMS) occurs as a result of a combination of metabolic disorders - visceral obesity, diabetes mellitus, insulin resistance, dyslipidemia, hyperuricemia with arterial hypertension [2, 5]. The frequency of MS in the population of persons over 18 years old ranges from 10 to 30%, in Russia - from 20 to 35%. [16]. Supposed, that OA and the components of MS are interconnected by one pathophysiological process - systemic low-level inflammation [7]. Treatment of polymorbid diseases is one of the urgent problems of medicine, since the number of such patients is steadily growing with age all over the world, and therapy is characterized by inevitable polypharmacy [8]. Therefore, the development of new drugs with a multipurpose (anti-inflammatory, immunomodulatory, analgesic, lipid-correcting, etc.) action seems to be justified. Some drugs and parapharmaceuticals of herbal origin meet the requirements of pleiotropy [9]. The manufacturer (LLC "Doctor Kornilov", Barnaul, Russia. Www. Dokskor.ru) together with the Federal State Budgetary Scientific Institution "Research Institute of Fundamental and Clinical Immunology" (Novosibirsk, Russia) was developed by an innovative parapharmaceutical "Epigenorm antivir" (EA) multipurpose therapeutic action. Due to the properties of its constituent components and the technology of their processing, it has a pleiotropic effect on cells - targets of various functional systems - immune, nervous and endocrine. "Epigenorm antivir"® (Registration No. RU.77.99.88.003.E.002022.04.17 dated 04/27/2017) contains licorice root extract (source of glycyrrhizic acid), turmeric root extract (source of curcumin), green tea extract (source of catechins), leaf extract sea buckthorn (a source of polyphenols), vitamin C. Clinical trials of EA in patients with metabolic syndrome have shown its effectiveness against all components of the syndrome [10]. The documents of the 67th WHO General Assembly on traditional medicine, in particular Traditional Chinese Medicine (TCM), indicate that the integration of scientific and traditional medicine methods should be based on the results of high-quality clinical trials that comply with the principles of evidence-based medicine [11].

The aim of the study was to assess the efficacy and safety of Epigenorm antivir in combination with classical acupuncture in patients with knee osteoarthritis and metabolic syndrome (OAMS).

MATERIAL AND METHODS

The study involved 21 women with MS, clinical and radiological signs of gonarthrosis. The diagnosis of OA of the knee was established according to the 1986 ACR criteria, MS according to the recommendations of the All-Russian Scientific Society of Cardiology [12]. All patients had 2–3 radiological stages of gonarthrosis, according to the Kellgren-Lawrence criteria.

Study design - pilot study before - after.

OAMS patients received Epigenorm antivir at a daily dose of 1000 mg for 12 weeks. In the first month of treatment, patients were prescribed a course of classical acupuncture, based on a syndromic diagnosis, which was established by visiting doctors from the University of Traditional Chinese Medicine (Tianjing, China). The predominant syndrome in the patients was the Kidney Hollow Syndrome (SHENXU), the number of acupuncture sessions was prescribed individually, daily, for a course of 15–20 sessions.

The main inclusion criterion was the VAS scores of pain and health levels of more than 50 mm. The use of non-steroidal anti-inflammatory drugs was not allowed during 12 weeks of treatment. For the treatment of hypertension (HD), patients were constantly taking antihypertensive drugs. Clinical examination and blood sampling were performed prior to EA intake at the first (W0) and last (W12) visits.

The primary endpoint is visual analogue health (VAS). Secondary endpoints - grading quality of life on a scaleShort Form-36 (SF-36) [13], (the Russian-language version is validated by the International Center for Research on the Quality of Life of St. Petersburg) [14], the Russian-language version is PHQ-9 (Patient Health Questionnaire - a scale of depression) [15].

The comorbidity index CIRS-G (Cumulative Illness Rating Scale for Geriatrics) [16] was assessed, the level of systemic inflammation was determined by the content of C-reactive protein (CRP) in the serum of peripheral blood (PC) (Vital Development Corporation, Russia) according to the manufacturer's instructions, the concentration of lipids in serum PC was detected by a standard method.

Statistical analysis. Descriptive statistics presented median and interquartile range, arithmetic mean and standard deviation. The difference between the means was assessed using the paired Student's t-test. Cohen's interpretation of effect size: 0.2 - small, 0.5 - moderate, 0.8 - large.

RESULTS OF THE STUDY

All patients were elderly (interquartile intervals 61.5–70.5 years), with a history of OA disease and hypertension 3–7 years, moderate CIRS-G (interquartile intervals 8–11), obese (interquartile intervals of mass index bodies 32–36.6).

Table 1 presents data on indicators of physical and mental health according to VAS, questionnaires SF-36 and PHQ-9 in patients with OAMS at the beginning and end of observation.

Table 1

Indicators of physical and mental health in patients with OAMS in the dynamics of treatment

Indicators	Before treatment (W0)	After treatment (W12)	R	Effect size (Cohen)
Health Index (YOUR)	57.6 (15.8)	23.7 (20.5)	0.001	1.8
Physical functioning of the SF-36	34.8 (18.5)	48.8 (23.4)	0.013	- 0.66
Role-playing SF-36	12.0 (22.3)	46.1 (33.7)	0.001	- 1.2
Pain severity SF-36	30.3 (19.8)	51.9 (23.8)	0.001	- 0.98
General health SF-36	36.1 (13.8)	53.2 (16.2)	0.007	- 1.13
Mental Health SF-36	52.7 (18.1)	63.1 (13.1)	0.124	- 0.6
Emotional Role Functioning SF-36	9.5 (15.6)	62.3 (34.6)	0.001	- 1.9
Social functioning SF-36	60.4 (23.0)	76.8 (23.0)	0.043	- 0.713
Vital Activity SF-36	42.5 (10.2)	54.0 (16.9)	0.013	- 0.823
Depression level indicator PHQ-9	12.7 (5.7)	7.0 (4.4)	0.001	1.23

Note. Table 1, 2 in columns 2–3 the arithmetic mean and standard deviation.

From table. 1 it follows that in patients with OAMS at the beginning of the observation, indicators were recorded indicating a pronounced decrease in the subjective assessment of the state of physical and mental health. This concerned the assessment by patients of the level of health according to the VAS and most indicators of the SF-36 subscales, the values of which were below 50, with the exception of indicators

subscales "Mental health" and "Social functioning" (52.7 and 60.4, respectively). The mean values of the depression level indicator indicated moderate depression.

It was found that the combination therapy improved the health indicator values according to the VAS, the primary endpoint, 2.4 times.

In addition, most of the indicators of the subscales of physical and mental health components SF-36 underwent positive dynamics by the end of the observation, with the exception of the indicators of the subscale "Mental health". At the end of treatment, the PHQ-9 level of depression almost halved. It is important to note that the size of the listed effects was, according to Cohen's criteria, moderate or high.

Table 2 presents data on the effect of therapy on the content of C-reactive protein and indicators of the content of lipids (laboratory components of MS) in the serum of PC.

From table. 2 it follows that the combined intervention led to a twofold decrease in the level of CRP, as well as a statistically significant decrease in total cholesterol, LDL cholesterol, triglycerides and atherogenic index.

table 2

The content of lipids and CRP in the serum of PC in patients with OAMS before and after combined treatment

Indicators	Before treatment (W0)	After treatment (W12)	R
C-reactive protein	6.05 (1.3)	3.2 (0.7)	0.022
Total cholesterol, mmol / l	6.33 (0.35)	5.0 (0.24)	0.024
LDL cholesterol, mmol / l	3.26 (0.26)	2.43 (0.2)	0.001
HDL cholesterol, mmol / l	1.27 (0.1)	1.35 (0.12)	0.260
Triglycerides, mmol / l	2.02 (0.16)	1.31 (0.1)	0.005
Atherogenic index	3.52 (0.27)	3.06 (2.3)	0.001

It should be noted that not a single episode of hypertensive crisis was recorded in all observed patients for 12 weeks of treatment, and therapy with antihypertensive drugs did not undergo any changes.

In two patients, a week after the start of the acupuncture session, there was a short-term (2-3 days) increase in pain in the knee joints, which did not require the appointment of analgesics.

DISCUSSION

The urgency and complexity of the problem of polymorbidity is due to the fact that it is not considered as a simple combination of several diseases. The combination of phenotypes of individual diseases, their pathogenesis is a new whole with poorly studied, emergent properties and other possibilities of therapy [8]. There are special forms of polymorbidity - syntropy, which, according to Academician V.P. Puzyrev, the presence of common ("syntropic") genes of predisposition and the similarity of the pathogenesis of those diseases that are part of polypathy and form a specific syntropy phenotype [17]. It is assumed that the frequent combination of OA and MS is due to their pathogenetic similarity, which is based on sluggish inflammation, and the OAMC phenotype belongs to the syntropy group [17, 4, 7].

Previously, we hypothesized that the use of drugs aimed at the central nodes of the network of intercellular interactions in patients with syntropias can cause a pleiotropic effect [18], contributing to the treatment of not only the main, but also concomitant diseases. An alternative to "nodal therapy" is the use of herbal preparations with multipurpose action, in particular, compounds obtained from

rhizomes of Curcuma longa [19, 20]. The pleiotropic effect of turmeric has been shown in a number of studies [19, 20, 21]. The complexity of the composition of herbal extracts in the composition of EA, the lack of data on pharmacodynamics, the pronounced clinical effect of the intake does not exclude the possibility of a synergistic action of turmeric, other components of EA and acupuncture in the implementation of the pleiotropic effect in patients with OAMS.

The deterioration in mental health indicators is probably due to the presence of signs of moderate depression identified at screening using the PHQ-9 questionnaire. Depression in patients with OA is an element of the pathogenetic link: "pain - depression - disturbances in the sleep - wakefulness cycle", contributes to a decrease in the physical and mental capabilities of the patient and, as a consequence, the quality of life [22]. It is noteworthy that the use of EA and the course of acupuncture halved the signs of depression, while the indicators of the SF-36 “Mental health” subscale did not undergo any changes.

The results of the study revealed dyslipidemia in patients with OAMS, which is a criterion for the diagnosis of MS and a biomarker for the development of atherosclerosis and its dire consequences. At the end of treatment, a statistically significant decrease in the serum content of total cholesterol, low-density lipoprotein cholesterol, triglycerides is recorded, which suggests an antiatherogenic effect, primarily of EA. This assumption is also supported by a twofold decrease in the serum of PC in the content of C-reactive protein, a marker of systemic inflammation and the development of atherosclerosis [23].

CONCLUSION

The results of evaluating the effectiveness and safety of the use of EA in combination with acupuncture in patients with OAMS indicate the multipurpose effect of the complex intervention: improvement of indicators of general health and quality of life, reduction of signs of depression. Clinical findings are associated with decreased lipid content, anti-inflammatory and anti-atherogenic effects. The established properties provide grounds for conducting larger-scale, controlled, blind, randomized clinical trials. The purpose of such studies is to obtain evidence on the efficacy and safety of taking EA parapharmaceuticals in combination with classical acupuncture in patients with OAMS, information on the possibility of reducing over-treatment and reducing direct costs of therapy.

Conflict of interests. The authors declare the absence of obvious and potential conflicts interests related to the publication of this article.

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Compliance with the principles of ethics. Clinical Study Protocol Formpatient information sheet, registration card were approved at a meeting of the local Ethics Committee of NIIFKI on June 29, 2018 (protocol No. 108).

Registration of the protocol. The research protocol is registered in the database ClinicalTrials.gov registration number NCT03540186.

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