**Litterature review**

**PROSPECTS OF APPLICATION OF DRUGS BASED ON GUARIC ACID IN TREATMENT OF PATIENTS WITH OSTEOARTHRITIS AND COMORBID COURSE OF STEATOHEPATITIS AND EXCESSIVE BODY WEIGHT**

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**Key words:** osteoarthritis, nonalcoholic fatty liver disease, guaric acid, guarem, excess body weight, obesity.

**Abstract.** One of the factors of osteoarthritis is obesity, which is now considered to be one of the major health problems around the world. Patients with osteoarthritis have a high comorbidity index. Medicamental therapy of patients with osteoarthritis and comorbid course of steatohepatitis is associated with additional risks such as hepatotoxic effects of drugs that patients take.

**Purpose:** to review scientific articles which cover information on effectiveness of using drugs based on guaric acid to reduce excess body weight.

**Conclusion.** Increased accumulation of visceral adipose tissue is one of the main pathogenetic factors contributing to development of osteoarthritis, steatosis and steatohepatitis. Therefore, drugs aimed at reducing excess body weight should take a leading place in the complex therapy of patients. Such drugs can contribute to reducing early disability of population, optimizing the quality of life indicators, and total life expectancy.

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**Ключові слова:** остеоартроз, неалкогольна жирова хвороба печінки, гуарова кислота, гуarem, надлишкова маса тіла, опасистість.

**Резюме.** Одним із чинників виникнення остеоартрозу є ожиріння, яке на даний час вважається однією з основних проблем охорони здоров'я в усьому світі. У пацієнтів з остеоартрозом відзначається високий індекс коморбідності. При наявності стеатогепатиту медикаментозна терапія остеоартрозу асоціюється з додатковими ризиками, зростає ризик розвитку гепатотоксичних ефектів препаратів, що їх отримує хворий.

**Мета роботи** — провести огляд наукових робіт, в яких висвітлюється інформація про ефективність використання препаратів на основі гуарової кислоти для зниження надмірної маси тіла.

**Висновок.** Підвищене накопичення вісцеральної жирової тканини є одним з основних патогенетичних чинників формування остеоартрозу, стеатозу та стеатогепатиту і тому правідне місце в комплексній терапії даного контингенту хворих повинно посідати препарати, спрямовані на зменшення надлишкової маси тіла, що зможе посприяти зниженню ранньої інвалідизації населення, оптимізації показників якості життя, загальної тривалості життя.
Огляд літератури

Ключеві слова:
остеоартроз,
неалкогольна жирова болезнь печени,
гуаровая кислота,
гуарем,
избыточный вес,
тучность.

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Резюме. Одним из факторов возникновения остеоартроза есть ожирение, которое в настоящее время считается одной из основных проблем здравоохранения во всем мире. У пациентов с остеоартрозом отмечается высокий индекс коморбидности. При наличии стеатогепатита медикаментозная терапия остеоартроза ассоциируется с дополнительными рисками, растет риск развития гепатотоксических эффектов препаратов, получаемых больным.

Цель работы – провести обзор научных работ, в которых освещается информация об эффективности использования препаратов на основе гуаровой кислоты для снижения избыточной массы тела.

Вывод. Повышенное накопление висцеральной жировой ткани является одним из основных патогенетических факторов формирования остеоартроза, стеатоза и стеатогепатита и поэтому ведущее место в комплексной терапии данного контингента больных должны занимать препараты, направленные на уменьшение избыточной массы тела, сможет способствовать снижению ранней инвалидизации населения, оптимизации показателей качества жизни, общей продолжительности жизни.

Introduction. The problem of osteoarthritis (OA) continues to be urgent, due to significant prevalence of the disease, rapid development of functional disorders and early disability of working age people. Among rheumatic diseases, OA is ranked first in the world, and in Europe, it is the second most common disease after ischemic heart disease and cerebrovascular diseases.

One of the factors of osteoarthritis is obesity, which is now considered to be one of the major health problems around the world. Patients with osteoarthritis have a high comorbidity index. Medicamental therapy of patients with osteoarthritis and comorbid course of steatohepatitis is associated with additional risks such as hepatotoxic effects of drugs that patients take.

Purpose: to review scientific articles which cover information on effectiveness of using drugs based on guaric acid to reduce excess body weight.

Discussion. According to state statistical reporting in 1997, the prevalence of OA in Ukraine was 1212 cases per 100,000 people, the incidence was 254 cases per 100,000 people. In 2008, they were 3172.6 and 607.3 cases per 100,000 people respectively (V. M. Kovalenko, V. M. Kornatskyi, 2008). The prevalence of OA will continue to increase due to population aging in Ukraine, significant urbanization, development of vehicles, which has led to a decrease in physical activity and an increase in body weight [1]. The disease leads to degeneration of articular cartilage and is ranked first among all disorders of the bone and muscular system that cause disability. Medical and social indices in Europe and the United States show the continuation of population aging and an increase in the number of persons over the age of 60.

P. Creamer, M. C. Hochberg (1997) highlighted the main risk factors for the disease, including genetic ones (gender (female), inherited pathology of type II collagen gene, mutation of type II collagen gene, other hereditary diseases of bones and joints, race/ethnicity), non-genetic ones (old age, excess body weight, decrease in the level of female hormones, developmental abnormalities of bones and joints, a history of surgeries on joints), and exogenous ones (professional activity, joint injuries, sports activities). Despite the fact that it is mostly elderly people who are affected by OA and its prevalence in the age group younger than 45-50 is extremely low, it cannot be called the inevitable consequence of aging [2]. Quite often, this nosology occurs in patients with excess body weight and steatohepatitis.

One of the causes of OA is obesity which is now considered to be one of the major health problems around the world. According to recent WHO data, over 1.6
billion adults are overweight, and 400 million are obese. In Ukraine, obesity is detected in almost 30% of cases among the working age population, and every fourth person has excess body weight. The Clifford study has shown that with each two units of the body mass index (BMI) increase (about 5 kg), the probability of development of X-ray knee joint osteoarthritis increases by 1.36 times [3, 4]. Population studies have shown that a higher risk of development of gonarthrosis is recorded in persons with excess body weight. The greatest risk of OA is reported in individuals with BMI > 25 kg/m². In the Framingham study, patients have been examined once every 2 years for 40 years. It was found that weight gain is a risk factor for manifest OA of knee joints in women, and a 5 kg body weight loss in women with a body mass index of 25 kg/m² reduced the risk of developing OA by 50%. In the studies of recent years, due to the application of new diagnostic methods, including magnetic resonance imaging (MRI), which is more sensitive than conventional X-rays, the importance of obesity in the development of OA of knee and/or hip joints has been proved [5].

Obesity as a risk factor for OA is not limited to emergence of OA in the bearing joints which are directly overloaded by weight. Development of OA in nonbearing joints suggests there might be other mechanisms associated with obesity which affect metabolism of cartilage and bone tissues [6].

Adipose tissue is considered to be an endocrine organ that secretes many factors, including proinflammatory cytokines and adipokines (leptin, adiponectin, resistin, visfatin etc.). Adipokines exhibit pleiotropic functions indirectly through hemostasis system, lipid and carbohydrate metabolism, regulation of blood pressure, insulin sensitivity, bone formation and angiogenesis [7]. Thus, recent data suggest that lipid dysregulation may also be one of the pathophysiological mechanisms of OA [8].

It is well-known that patients with osteoarthritis (OA) have a high comorbidity index. Recent epidemiological studies have shown that the metabolic syndrome (MS) has a major impact on the severity of OA, since concentration of adipokines with proinflammatory effects in plasma is associated with the MS [9]. Non-alcoholic fatty liver disease (NAFLD) is considered within the framework of the hepatic component of the MS [10]. In the presence of NAFLD, drug therapy of OA is associated with additional risks. NAFLD increases the risk of developing hepatotoxic effects of drugs, especially in cases of polypharmacy or administration of drugs for a long period of time in cases when these drugs cannot be prescribed (e.g. in case of OA) [11]. Therefore, urgency of the problem of effective and safe therapy choice for patients with OA with underlying NAFLD is evident.

Treatment of excess body weight and obesity in combination with osteoarthritis is a multi-stage process that involves a change in lifestyle and medication. Reducing body weight should be achieved by reducing caloric content and streamlining food composition. Together with correction of nutrition, patients with obesity should do special physical exercises aimed at overcoming hypodynamia [12]. On one hand, medicinal methods of treating obesity in patients with underlying osteoarthritis are limited by means aimed at overcoming excess body weight, in particular, central action drugs, thermogenic sympathomimetics, as they cause side effects, which are dangerous to the digestive system, and the emergence of allergic reactions. On the other hand, the use of a large number of drugs often leads to polypharmacy. So, during development of therapeutic tactics for this group of patients, it is advisable to select drugs that affect the various pathogenesis links carefully.

According to the American Gastroenterological Association data on the problem of obesity, when reducing body weight the risk of developing symptoms of gallstone disease increases because of an increase in the saturation of bile cholesterol and formation of its crystals and decrease in the contractile function of the gallbladder. An important factor complicating the implementation of these algorithms and programs is poor compliance, which is determined not only by the unwillingness of patients to adhere to recommendations of a doctor, but also their psychological peculiarities caused by the underlying disease [13, 14]. Proper evaluation of the main mechanisms of the pathogenesis of comorbid conditions in each particular patient, as well as adequate pathogenetic therapy, contribute to correction of disorders and rapid and effective elimination of manifestations of the disease.

It is known that non-drug therapy for obesity includes a change of lifestyle and a decrease in daily caloric intake. Unfortunately, only fewer than half of patients with excess body weight follow dietary recommendations. In this regard, using drug therapy for obesity should first and foremost be effective and safe for this type of patients. Today, it is particularly important to include dietary fibers in the diet of patients with excess body weight. According to recommendations of the American Dietetic Association, daily requirement is 25-30 g. Data from a number of studies indicate that adding 15 g of soluble dietary fiber to a daily ration reduces blood cholesterol by 15-21%, improves carbohydrate metabolism, and provides a sense of satiety [15].

Guarem (guar gum) is a typical representative of this group. It can be used to control and reduce body weight, lipid levels and is the source of dietary fiber. Guarem (guar gum) is in the form of granules to be used to prepare a solution. It is a dietary fiber that is obtained from seeds of tropical guar tree Cyamopsis tetragonolobus. Guarem reduces the feeling of hunger and accelerates saturation which leads to a decrease in the amount of food consumed and body weight. Since Guarem is a fiber substance, it has additional properties, e.g. normalizes the stools, intestinal microflora, binds toxins. The drug acts only in the digestive tract and is excreted in an unchanged form. Since guar gum is not absorbed, there are no contraindications for taking it during pregnancy and lactation. Guar fibers of the drug form a viscous jelly in contact with water. The drug is not absorbed in the
dDigestive tract and breaks down into short chains of fatty acids under the influence of intestinal bacteria. It is safe, since guar gum is not absorbed, it has no systemic action, acting only in the digestive tract, and is combined with the usual diet. Works of a number of scientists have shown that adding this drug to the prescribed hypocaloric diet significantly optimized the effectiveness of measures aimed at reducing excess body weight [16]. While taking Guare at a stable dose of antihypertensive therapy, there has been reported a decrease in systolic blood pressure by 8.13% and diastolic blood pressure by 10.5%, which may be due to a decrease in body weight and waist volume and leads to a decrease in the activity of sympathetic nervous system [17].

**Conclusion.** Increased accumulation of visceral adipose tissue is one of the main pathogenetic factors contributing to development of osteoarthritis, steatosis and steatohepatitis. Therefore, drugs aimed at reducing excess body weight should take a leading place in the complex therapy of patients. Such drugs can contribute to reducing early disability of population, optimizing the quality of life indicators, and total life expectancy.

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