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ABSTRACT

The article presents an analysis of the literature data on the epidemiology of osteoarticular system injury in diabetes mellitus. Some aspects of the pathogenesis of osteoarticular system disorders in diabetes, as well as the main biochemical diagnostic signs of osteoarticular system disorders in diabetic arthropathy are considered.

Key words: diabetes mellitus, osteoarticular system injury, diabetic arthropathy, diagnosis.

INTRODUCTION

Epidemiology of osteoarticular system injury in diabetes. The general situation with musculoskeletal diseases and diabetes mellitus (DM) in the CIS countries and Uzbekistan is in line with global trends and is characterized by an increasing medical and social burden of these common chronic diseases, especially the aging population [4, 10]. At the same time, diabetes has acquired the character

of a “non-communicable epidemic” affecting nearly 200 million people worldwide, the third most common nosology [4, 17] and a global medical and social problem. maintaining the health of patients in all countries of the world and of all ages. According to experts, by 2030, every 25th inhabitant of the planet will suffer from this disease, 80-90% of whom are patients with type 2 diabetes [4]. In industrialized countries, the prevalence of diabetes is 5-6% and there is a tendency for further growth, primarily in the age group over 40 years [4]. In developed countries, the WHO predicts that by 2025 the number of people with diabetes will increase by 41% (from 51 million to 72 million), in the Russian Federation by 8 million, in Uzbekistan ... and the number is growing. The great social significance of diabetes is that it leads to death due to early disability and late complications.

In diabetes, metabolic disorders, vascular and neurological complications lead to the development of changes in almost all organs and tissues [2, 17, 31]. It plays an important role among themoccupying lesions of connective tissue, leading to changes in the structure of the osteoarticular system [8, 12, 13, 17]. In diabetes, osteopenia is detected in 58% of cases, and osteoporosis in 30% of cases [13, 28, 29]. In diabetes, damage to the osteoarticular system is observed in 0.1–77.8% of cases [5, 7, 9, 18, 23], and the incidence of diabetic osteoarthropathy (DOAP) ranges from 0.7 to 6.8% [8, 18, 19]. This pathology develops 6-10 years after the onset of the disease. However, with type 2 diabetes, when diagnosed, 30 to 50 percent of patients have changes in peripheral sensitivity or atherosclerotic lesions of the arteries of the lower extremities to varying degrees [18]. According to a number of authors [29], the frequency of bone tissue changes in patients with diabetes ranges from 2 to 79%.

Some authors use the term “limited joint mobility syndrome” (OPS) to describe the injury of ODA and diabetes mellitus, because with its long duration not only small but also large joints of the upper and lower extremities are involved in the pathological process. they reach. process [12]. A number of authors use the term “gyarthropathy” to describe all diabetes-related injuries of the upper limbs in their research: in diabetes, frozen shoulder syndrome, rupture of the rotator cuff of the shoulder joint, Dupuytren’s contracture, finger syndrome, and others carpal tunnel syndrome is common [23]. In addition, lesions of the lower extremities are observed, in particular: tendinopathy of the Achilles tendon, plantar fasciitis, limited mobility in the ankle and subtalar joints, which can lead to the appearance of wound defects of the legs along with polyneuropathy. 20]. Changes in the musculoskeletal system (ODA) are common in patients with diabetes mellitus, in particular gyroarthropathy - a specific injury of the connective tissue structures of the hand in the setting of persistent hyperglycemia, in the absence of pain, leads to

limited mobility of the joints [23]]. Some authors use the term “limited joint mobility syndrome” (OPS) to describe an ODA lesion in diabetes because, with its long duration, it affects not only the upper but also the lower and lower limbs. gestures are also involved. pathological process [12]. According to the authors, OPS syndrome is associated with other late complications of diabetes and can significantly impair functional activity, impair self-care and quality of life, and result in accumulation of end products in periarticular tissue and bone is associated with damage to the joints. protein glycation.

Some aspects of the pathogenesis of osteoarticular system disorders in diabetes. Despite significant advances in the study of the pathogenesis of diabetes, its effects on various organs and systems of the body, many aspects of this problem, in particular the development of changes in the development of diabetes, are still insufficiently covered. the osteoarticular system in this pathology. The available literature data on the metabolic properties of bone and cartilage tissue, the frequency and mechanisms of development of osteopenia in diabetes mellitus are highly conflicting. The main links in the pathogenesis of osteoporosis in diabetes are: absolute insulin deficiency → decreased production of collagen and alkaline phosphatase by osteoblasts; direct effect of high glucose concentration due to the final products of glycosylation → increased bone resorption by osteoclasts; decreased insulin secretion → deficiency of active metabolites of vitamin D → decreased intestinal absorption of calcium, increased secretion and activity of parathyroid hormone → negative balance of inorganic elements in the body and increased resorption. bone tissue [27, 33].

An analysis of the literature on this issue showed that patients with type 1 diabetes with absolute insulin deficiency are more prone to osteoporosis. A number of studies have shown the development of osteopenia in patients with type 1 diabetes and type 2 diabetes, but its onset and severity were more common in type 1 diabetes [14, 15]. According to the authors, absolute or relative deficiency of insulin, which has an anabolic effect on osteoblasts, is accompanied by a decrease in osteoporosis bone formation in patients with type 1 diabetes. Thus, when examining 94 patients with type 1 diabetes, the authors found no decrease in bone mineral density (BMD) in the spine, but increased biochemical parameters reflecting bone resorption and significantly lower osteocalcin levels. control group [16]. In another study, on scintigraphy with technical pyrophosphate 99-t in 32 children [6], 34.4% showed absorption of the drug in the leg bones, indicating an increase in metabolic activity. According to the authors, the increased repositioning detected in the leg bones does not lead to complete formation of bone mass and probably increases the risk of developing DOAP.

It should be noted that the development and progression of diabetic polyneuropathy leads to the opening of arteriovenous shunts in the microvasculature of bone tissue not only in somatic but also in vegetative axons [8]. This leads to increased blood flow in the form of arterio-venous outflow, which reduces the microcirculatory perfusion of the leg tissue, especially its skeleton [2, 11]. According to the authors, with the development of neuropathy, the tone of microtubules decreases, which increases inefficient blood flow in bone tissue, resulting in the development of aseptic destruction of bones due to their hypervascularization. However, unlike “diabetic foot syndrome,” DOAP persists in a less aggressive course of purulent-necrotic processes, which, according to the authors, is a consequence of a type of immuno-autoaggression. Given the decline in collagen synthesis, impaired calcium metabolism, and impaired bone remodeling in diabetes, the target of autoimmune aggression in DOAP is the bone and synovial structures of the hind and middle leg, unlike conventional forms of osteoporosis. damage to articular tissue [2].

Although DOAP was described more than a hundred years ago, its pathogenesis is still unclear. There are currently three main theories of its development:

• neurotraumatic, i.e. the sensory form of distal neuropathy leads to a decrease in sensitivity and an increase in the likelihood of pathological expansion of the range of motion in the invisible leg injury and joints. In contrast, motor neuropathy is the cause of interosseous muscle atrophy: gait impairment and the development of foot deformity are associated with the formation of abnormally loaded areas of the foot and are prone to injury [21];

• Neurovascular: According to this theory, when the autonomic nerve fibers are damaged, the innervation of the vascular system is disrupted, the number of arteriovenous shunts increases with an increase in local volumetric blood flow in the bone tissue of the leg, and as a result, subsequently destroyed against the background of its demineralization trauma [11, 19, 21];

• group combined: it combines the above two hypotheses with the theory of inflammation1. An integrated theory of DOAP development. Other authors follow the same idea, viz. DOAP occurs in patients with the above risk factors and is an uncontrolled inflammation in the skeletal system of the foot, leading to osteolysis with subsequent destruction and dislocation of the bones of the foot. It is known that an increase in anti-inflammatory cytokines from damaged tissue occurs during bone fracture, leading to expression of the receptor activator of the nuclear factor-kbligand (RAnKl) receptor polypeptide from local cells [30]. RAnKl activates nuclear factor-kb (nuclear factor - nF-kb) transcription, which in turn stimulates

the maturation of osteoclasts from progenitor cells and increases bone resorption and loss. According to the authors, nF-kb simultaneously stimulates the synthesis of osteoprotein glycopeptide (osteoprotegerin - oPG) from osteoblasts. It is an effective antagonist of RanKl. Jeffcoate W.J., Game F.L. Genetic studies in patients with DOAP have identified single polymorphisms in the oPG gene that contribute to changes in the oPG / RAnKl ratio and, consequently, an imbalance in bone remodeling toward increased resorption [27]. In addition, peptides released from nerve nodes play an important role in the pathogenesis of DOAP, in particular, peptides associated with the calcitonin gene (cocalcigenin, a calcitonin gene-related peptide - CGRP) that is an antagonist of RAnKl [26]. According to the authors, against the background of chronic hyperglycemia, end products of glycation, reactive oxygen species, and increased lipid oxidation may also enhance RAnKl expression.

A number of researchers discuss the role of osteopenia in the development of OOP and the high frequency of osteopenia in patients with type 1 diabetes, although the incidence of OOA is the same in type 1 and type 2 diabetes [33]. According to the authors, systemic manifestations of osteopenia in patients with type 1 diabetes, especially in the femoral neck, are more common than in the local condition in the legs. Factors in the development of DOAP also include osteopenia on the background of insulin deficiency, vitamin D deficiency with and / or non-renal insufficiency, and secondary hyperparathyroidism, thiazolidinediones for type 2 diabetes, and glucocorticoids as immunosuppressants in people undergoing kidney transplantation. and / or pancreas.

There are indications of a correlation between the frequency of DOAP and the presence of macro- and microangiopathies, neuropathies. Such changes lead to increased bone blood flow, which is a key link in the pathogenesis of DOAP, especially in the foot area (Charcot’s foot) [27, 33]. According to the authors, the leading pathogenetic factor is insulin deficiency, which has an anabolic effect. It has a direct stimulating effect on bone tissue metabolism and collagen and hyaluronate synthesis. Insulin deficiency leads to the formation and accumulation of atypical mucopolysaccharides in the body of patients with diabetes with impaired bone matrix [22]. Histologically, bone resorption, proliferation of connective tissue, aseptic necrosis, mainly localized in the metatarsal bones are identified. Impairment of hematolymphatic balance adversely affects the microtomules and adversely affects cell remnants, protein detritus, triglycerides, complete drainage of glycosaminoglycans and their accumulation in the interstitial space and microcirculatory bed, which contributes to changes in osteoarthritis. [182]. Some researchers have linked the underlying processes of connective tissue

damage to chemical modification of collagen structure due to glycosylation and oxidation [3]. Changes in connective tissue in diabetes mainly affect oxidative stress, sorbitol pathway activation, and the development of microangiopathy. DOAP is accompanied by an increase in the oxidative modification of broad-spectrum proteins, a significant increase in the concentration of calcium-regulating hormones, and a significant increase in oxidative metabolism with an increase in the release of free oxyproline. There is a clear correlation and correlation between oxidative metabolism disorders, changes in immune status, and the degree of degenerative processes in the soft tissues of the lower extremities in patients with DOAP.

Given that glucose is the only energy substrate for chondrocytes, it can be assumed that with only the anaerobic nature of the metabolism of these tissues, synthetic processes in cartilage, bone and connective tissue are disrupted in diabetes. By activating the polyol pathway of glucose metabolism and non-enzymatic glycosylation of proteins, hyperglycemia can detect damage to muscle and periarticular tissue. Clinical research Markova N.G. (2007) showed more pronounced degenerative changes in osteoarthritis of the knee joints associated with type 2 diabetes, which is determined by the development of late macro- and microvascular complications in patients with rheumatic diseases with diabetes mellitus [10]. According to the authors, diabetes mellitus in rheumatoid arthritis does not affect the severity of articular syndrome, the nature and frequency of extravascular manifestations, clinical and laboratory indicators of the inflammatory process. The authors found that the nature and frequency of arthralgia and joint mobility restriction syndrome depended on the type of diabetes mellitus, the presence of neuropathic and ischemic complications.

The main biochemical diagnostic signs of disorders of the osteoarticular system. Diagnosis is based on a comprehensive assessment of clinical appearance, history, and examination. It is necessary to consult an endocrinologist, vascular surgeon, neurologist, traumatologist. In the majority of patients with DOAP using neurological instruments and Doppler ultrasound, the development of distal sensory-motor neuropathy, hyperthermia, in which arterial blood flow in the legs is preserved or increased (difference of more than 2 ° C compared with the opposite limb). The acute phase of DOAP) is defined. Determining the nature of bone destruction is a bone biopsy. X-rays can visualize the structure and extent of bone mineralization. "D": elongation of joints, dislocation, debris (fragments), disorganization (destruction with loss of function), increase in density (increase in density) [20]. Densitometry reliably detects local and systemic decline in bone mass. MRI allows you. DOAP is already diagnosed at the stage of bone marrow

tumor, intraosseous cysts and micro fracture formation, as well as differential diagnosis between osteomyelitis m and osteoarthropathy. Computed tomography allows to observe the healing process and accurately determine the degree of displacement of the bones relative to each other, which may be required in the planning of reconstructive surgery on the foot [17]. Ultrasound examination in patients with DOAP reveals a clear pathology of the soft tissues of the lower extremities with a decrease in blood flow, which manifests itself in the form of irreversible fibrosis of the dermis and atrophy of muscle tissue, which is associated with its duration. and the severity of diabetes mellitus. Ultrasound tomography in patients with DOAP records a progressive increase in changes in the soft tissues of the lower extremities in the distal direction. however, leukocytosis and an increase in ESR may also occur in patients with Charcot's disease. a sign of inflammation. The main diagnostic signs for the timely diagnosis of bone metabolism disorders in patients with type 1 diabetes are osteocalcin (OC), bone resorption - C-terminal telopeptide (CTx). In the research of Z.A Adamkhanova. and others. (2016) showed a significant decrease in TC content in patients with type 1 diabetes, especially with the onset of the disease in childhood and adolescence [1]. However, CTx, a marker of bone tissue destruction, was significantly increased, especially with the long duration of the disease. According to the author, absolute insulin deficiency reduces the production of collagen and alkaline phosphatase by osteoblasts, which are necessary for the formation of the bone matrix and its mineralization, and reduces the stimulation of osteoblasts mediated by insulin-like and other growth factors. The authors note that hyperglycemia may increase bone resorption by osteoclasts, firstly due to protein glycation, and secondly due to decreased insulin secretion and the development of nephropathy, which leads to a lack of active metabolites of vitamin D, which reduces Ca absorption. an increase in its secretion in the intestine and a change in the activity of the parathyroid hormone (PTH).

In S.S.'s research. Safarova (2018) showed a decrease in ionized calcium levels at a normal concentration of total calcium in 41% of patients with diabetes mellitus, especially in patients with type 2 diabetes [14, 15]. Apparently, a significant decrease in the value of ionized calcium in people with T2DM is associated with insulin resistance, as insulin secretion is a Ca2 +-dependent process in response to increased plasma glucose concentrations [24]. However, serum phosphorus levels in the examined patients have an increasing tendency, i. the development of hyperphosphatemia activates the parathyroid gland and accelerates the decline in renal function [32]. There was a downward trend in albumin levels, which is associated with a decrease in glomerular filtration rate, the

development of hypercreatinemia. A correlation was found between an increase in the sign of bone resorption and a progressive decrease in GFR [34]. In T2DM, a correlation was found between PTH and vitamin D values and GFR. Vitamin D deficiency was detected in 30% of patients with diabetes depending on the duration of the disease.The results of the analysis showed that the studied signs of bone formation (ALP, P1NP) decreased depending on the duration of the disease. However, despite the clinical presence of alkaline phosphatase, its use as a bone marker is not very informative. However, P1NP levels were statistically significantly reduced in patients with type 1 diabetes and did not differ from control in patients with type 2 diabetes. A decrease in P1NP in type 1 diabetes indicates a slowing of bone formation. The mean values of the b-CTx bone resorption marker in patients with type 1 and type 2 diabetes did not go beyond the reference range, but were higher than in the control group, indicating an increase in bone resorption in these groups. 36]. A positive correlation was found between P1NP and GFR levels; Negative correlation between b-CTx and GFR.

The same dynamics was found in children with type 1 diabetes [5]. Thus, in the early stages of the development of type 1 diabetes, an increase in the ratio of total Ca / P and Ca2 + / P in the serum of children, alkaline phosphatase activity, gradients of calcitonin, osteocalcin levels is observed. , b-CrossLaps with a decrease in parathyroid hormone, calcium (total, ionized) and 25-hydroxyvitamin D, this indicates an increase in the rate of bone remodeling, which is associated with an increase in bone formation intensity. In the late stages of endocrinopathy, with a decrease in calcium concentration, alkaline phosphatase activity, osteocalcin, parathyroid hormone, b-CrossLaps concentration, a total increase in Ca / P and Ca2 + / P ratio, a further increase in calcitonin level gradients, calcium (total, ionized) with a decrease in the amount, this indicates a slowing of bone resorption processes with the predominance of bone resorption processes over bone formation processes.

Thus, the analysis of the literature data showed that insulin deficiency and hyperglycemia are the main link in the formation of many pathological conditions in the body, in particular, in the formation of disorders of the osteoarticular system. The study of molecular mechanisms of their development, early diagnosis of diabetes and connective tissue dysplasia, and improvement of therapy is a very topical and socially important problem.

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