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# Special Changes in the Mineral Composition of Bone Tissue in Rabbits in the Post-Reproduction Period

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**Abstract** Osteoporosis is a systemic metabolic disease of the skeleton, and is considered a severe pathology of the musculoskeletal system, accompanied by a gradual decrease in mineral density and a sharp violation of the microarchitectonics of bone tissue. Depending on the etiology and pathogenesis, primary and secondary osteoporosis is distinguished. Secondary osteoporosis develops as a complication of various diseases. Diseases of the digestive system that cause osteoporosis include chronic pancreatitis, hepatitis of various etiologies, cirrhosis of the liver (LC), biliary dysfunction, malabsorption syndrome, as a result of which the metabolism of vitamin D and calcium is disturbed. These chain processes lead to a decrease in bone mineral density and manifest as osteopenia and osteoporosis. As a result of such changes in the bone tissue, osteoporotic fractures of the skeleton of various localization are observed even with minimal injuries. Our studies have shown that bone tissue in chronic diseases of the digestive system performs the function of a target organ and leaves a mark in the form of biochemical, metabolic and hormonal changes. Therefore, patients with chronic diseases of the hepatobiliary system and gastrointestinal tract are considered a risk group for the development of secondary osteoporosis.

**Keywords** Vitamin D, Hypercalcemia, Hypocalcemia, Bone mineral density, Osteoporosis, Osteopenia, Diseases of the digestive system

## 1. Introduction

There is sufficient data on the development of osteoporosis and bone mineral density disorders in patients with various gastroenterological and Hepatobiliary pathologies.

The spectrum of pathology of the gastrointestinal tract is often pathologies accompanied by the development of bone mineral density disorders (osteoporosis, osteopenia), these are diseases of the liver, intestines, pancreas, and biliary tract. Most of the above diseases can lead to a violation of the absorption process of calcium and, as a result, to a violation of the process of vitamin D metabolism and a deficiency of protein substances. Hypocalcemia leads to activation of the activity of the parathyroid glands and secondary hyperparathyroidism. An absolute or relative deficiency of vitamin D leads to a violation of the mineralization of the organic matrix. As a result of these complex disorders, osteopenia develops in most cases [17].

The fact that osteoporosis can be associated with many somatic diseases, primarily diseases of the digestive tract, has been revered by many scientists. According to the practice guidelines of the world Gastroenterological organization (JGET, 2004), chronic diseases of the digestive system that lead to the development of osteoporosis include chronic inflammatory disease of the intestine (colitis, enterocolitis, enteritis), post-gastroprotection syndrome, celiac disease, cholestatic diseases of the liver, chronic pancreatitis and hepatitis are the main factors in the development of osteoporosis. In addition to a decrease in bone mineral density in patients with chronic pathology of the organs of the digestive system, there is a violation of the functions of vitamin D to be digestion and participate in the processes of metabolism. This, in turn, leads to a decrease in the absorption of calcium, magnesium, and phosphorus substances in the Caspian sea wall and an increase in their excretion through the kidneys. Hypocalcemia leads to activation of the parathyroid glands and an increase in the activity of cytokines against the background of a chronic inflammatory process, in particular, tumor necrosis factor and interleukins-1, -6, which affect bone resorption, leading to secondary hyperparathyroidism. The specificity of the course of diseases of the organs of the digestive system is one of the risk factors directly related to the development of osteoporosis.

Despite the occurrence of unconditional changes in bone tissue in hepatitis, liver cirrhosis (JTS), pancreatitis, biliary dysfunction, malabsorption syndrome, inflammatory bowel disease (chin), etc., no attention is paid by medical personnel to the skeletal system and its mechanisms of continuous re-development.

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Currently, the presence of modern non-invasive methods makes it possible to determine the mineral density, structure of bone tissue, activity of metabolic processes in it, as well as its structural and functional state in chronic diseases of the digestive system [2].

The authors note that in most cases, the pathology of the organs of the digestive system is accompanied by each other as a comorbid disease, and at postreproductive age, as a result of these diseases, a decrease in bone mineral density occurs in patients. The concomitant comorbid course of several diseases harms the clinical manifestations in them, and this condition leads to misdiagnosis cases in elderly people and the post-reproduction period, not receiving sufficient attention from doctors, which in turn leads to misdiagnosis cases at treatment and preventive events. This in turn negatively affects the Prevention of the disease, preventing complications. The rate of decrease in the density of bone tissue increases significantly during the postreproductive period, and in the presence of chronic digestive system diseases, this process is accelerated even more [20,30,38].

## 2. Materials and Methods

The relevance of the problem of osteodephesitis in the pathology of the digestive organs is primarily due to a violation of the absorption of mineral and organic substances in the intestines, namely, maldigestion (violation of the absorption of microelements, nutrients, and vitamins) and malabsorption (violation of the absorption and transport of minerals in the small intestine) syndromes. In addition, such patients are forced to strictly follow the diet, which also leads to a deficiency of vitamins and microelements necessary for the organism and forced dysbalance. Also, in cases associated with the increased secretory activity of the stomach, prescribing proton pump inhibitors, the secretory activity of the stomach is reduced, on the second hand, it also relieves the absorption of microelements in the intestines as a result of the action of proton pump inhibitors [27,43]. Calcium absorption disorders can also occur as a result of surgical interventions (in resections) [15].

Given its etiology and pathogenesis, primary and secondary osteoporosis are differentiated. Secondary osteoporosis develops as a complication of various diseases. One of the chronic diseases of digestive nei organs that leads to a decrease in bone mineral density (in the form of osteopenia and osteoporosis)is chronic pancreatitis, which is accompanied by a lack of exocrine function [17]. The cause of osteoporosis is pancreatic diseases, especially chronic pancreatitis (SP), which is accompanied by a violation of the function of its exocrine Part [3]. Chronic pancreatitis is an inflammatory process in which diffuse or segmental fibrosis of the glandular parenchyma and functional insufficiency of the gland are observed. [1]. Pancreatic insufficiency is a disease accompanied by a deficiency in the production of all enzymes or certain enzymes, and this enzyme deficiency is a factor affecting the rate of rejection of chronic pancreatitis and the quality of life of the patient [16]. Disorders of the exocrine function of the pancreas are observed in most cases in the late stages of the disease, leading to a change in fibrosis of the organ and a decrease in enzyme production, which manifests clinical manifestations of malabsorption. Sometimes exocrine deficiency of the organ can also be observed in the early stages of the disease due to a decrease in the functional parenchyma of the organ. Some authors suggest that a 5-10% reduction in exocrine secretion results in significant steatorrhea I steatorrhea [5,11]. Clinically, the importance of steatorrhea is important. It leads to malabsorption, especially impaired absorption of fat-soluble vitamins A, D, E, and K.

In patients with chronic pancreatitis (CP), various pathogenetic processes lie at the base of the decrease in bone mineral density in the form of osteopenia. The first is a violation of vitamin D absorption and hypocalcemia, while the next is a violation of stool formation in the large intestine and malabsorption syndrome. This results in increased excretion of calcium from the body [34]. Lack of fat-soluble vitamins in the body can lead to pain in the bones, their fragility, a decrease in bone tissue elasticity and atypical muscle contraction, and disruption of the blood clotting system in the form of bleeding. In addition to decreased vision in the dark, cases of increased skin dryness can also be manifested [1]. Vitamin D deficiency leads to a decrease in calcium absorption, and an increase in the secretion of parathyroid hormone (PTG), and this leads to a decrease in bone mineralization. There are also other risk factors for osteopenia in patients with CP, such as the increased activity of anti-inflammatory cytokines, smoking, alcohol consumption, as well as limiting rational nutrition due to constant pain [25]. Chronic inflammation of the pancreas has been found to activate bone resorption by increasing the functional activity of osteoclasts along with the production of anti-inflammatory cytokines (interleukin (IL)-1, IL - 6, tumor necrosis factor - a-TNF-a).

Many factors of the external and internal environment are involved in the regulation of the process of pancreatic secretion. There is no doubt that the regulation and management of this complex process are carried out directly using a neuroendocrine system. Sa2 + ions are a universal means of transmitting extracellular signals into the cell and their response to hormones and neurotransmitters [1,15,23]. In evidence-based medicine today, calcium ions have been shown to play a key role in triggering and coordinating enzyme excretion by digestive gland cells [4,31,33]. The results of most studies have shown that loss of extracellular calcium leads to decreased excretion of amylase in pancreatic exocrine cells [4,39]. The production of secretin, pancreozymine, and pancreatic enzymes is a calcium-dependent process according to data. Thus, calcium contributes to the release of pancreozymin by the duodenal mucosa by acting on pancreocytes. In addition, calcium is involved in regulating the contractile activity of the Oddi sphincter [40,44]. The substance calcium enhances the

release of enzymes by pancreatocytes, activates enzymes, and stabilizes the state of cell molecules [4,15,22]. The role of calcium in the secretory activity of the pancreas is confirmed by studies, according to which the concentration of calcium in pancreatic juice in SP decreases in parallel with a decrease in the number of enzymes [8]. Since the excretion of enzymes is a calcium-dependent process, hypocalcemia leads to a weakening of the activity of the exocrine part of the pancreas and leads to impaired excretory function of the organ. Based on the above data, it can be concluded that calcium ions play an important role in the development of pancreatic pathology. Hypocalcemia leads to a decrease in the secretory function of the gland, and this condition causes malabsorption syndrome and, consequently, hypocalcemia. Thus, not only exocrine pancreatic insufficiency leads to the development of the related sac, which is the basis of a violation of bone metabolism [15,18].

Calcium ions also enhance the secretion of hydrochloric acid, an indirect stimulant of pancreatic secretion. Calcium is directly involved in the regulation of muscle contraction. This exchange of calcium substances can lead to dysfunction of the Oddi sphincter, and this is the impetus to consider as the main pathogenetic factor in the development of pathology. The functional state of the sphincter apparatus also affects calcium metabolism, which increases the loss of microelement with bile in cases of decreased sphincter tone, and vice versa during high peristaltic dyskinesias, absorption processes are disrupted in the intestine due to decreased bile acid excretion [36].

Thus, SP and exocrine pancreatic insufficiency are one of the main risk factors that lead to a decrease in bone mineral density within diseases of the digestive tract.

It is known that vitamin D, which affects the state of bone mineral density, belongs to fat-soluble vitamins, and normal lipolysis processes are provided by a sufficient amount of bile acids. In this regard, it is logical to assume that a lack of bile acids can affect the absorption of vitamin D and lead to a violation of bone mineral density. 90% of vitamin D is produced in the liver, and in this place, the first stage of the reaction of hydroxylation of cholecalciferol and calciferol gives ruy [19]. The functional significance of bile acids is the emulsification of fats contained in food bites and the formation of lipoid-bile compounds. In addition, bile acids activate the enzyme lipase of the pancreas and therefore facilitate the absorption of fat-soluble vitamins, in particular vitamin D [6]. Bile deficiency is found in more than 87% of cases following gallstone disease and postholesistectomic syndrome (PXS) [7]. In turn, insufficient and timely access to grass to the duodenum can lead to malabsorption not only of lipids but also of fat-soluble vitamins. So, herb deficiency can negatively affect bone mineral density, being considered one of the causes of malabsorption of calcium and vitamin D, that is, impaired absorption [6].

It is known that gallbladder disease is often accompanied by biliary insufficiency, which can affect a significant violation of digestive processes. Therefore, insufficient or timely access of grass to the duodenum can lead to a violation of the absorption of not only lipids but also fat-soluble vitamins. Thus, bile deficiency is one of the causes of impaired absorption of calcium and vitamin D, which can negatively affect bone mineral density [17].

However, to date, it is not entirely clear how much the combination of various risk factors affects the decrease in mineral density in the pathology of the bile ducts. Russian scientists have noted that 42.6% of patients with gallstone disease have a norm of bone mineral density, while 57.4% have been diagnosed with osteopenia or osteoporosis [10]. Vitamin D deficiency has also been observed in 69% of patients with gallstone disease.

One of the main causes of calcium metabolism disorders in cases of biliary system pathologies is lower than normal levels of vitamin D in the blood [32]. This is observed in patients with gallbladder disease and postholesistectomic syndrome with cases of gallbladder failure, in people of this category, accompanied by an increased risk of developing osteopenia. It has been found that the risk of developing osteopenia directly depends on the degree of biliary system deficiency [9]. The development of grass deficiency in gallstone disease and postholecystectomy syndrome leads to an increase in the activity of hormones that regulate the calcium substance as a result of a violation of phosphorus-calcium constancy. This increases parathormone activity and results in decreased bone mineral density and the development of osteopenia and osteoporosis. This certainly increases the risk of osteoporotic fractures.

Various disorders of bone tissue in liver diseases are commonly referred to as liver (hepatogenic) osteodystrophy. In such a situation scientists say that members of the biliary system occur in 40-75% of patients with chronic pathology. The development of osteopenia and osteoporosis in liver diseases depends on most factors, and the pathogenetic mechanism of this process is complex [13].

The study of the state of bone tissue and the pathogenesis of changes in bone mineral density in it in connection with diseases of the hepatobiliary system has a long history of tar. In the 60s of the Twenty-First Century, chronic diseases of the hepatobiliary system and especially liver osteodystrophy were said to cause types of osteomalacia, osteoporosis, and periosteal reactions [35]. In modern times, osteomalacia has been rapidly occurring in chronic pathologies of the hepatobiliary system, and osteoporosis of bone tissue is common in chronic hepatitis and cirrhosis of the liver. Scientists note that 39% of patients with liver cirrhosis are diagnosed with osteoporosis [24].

Autoimmune hepatitis, autoimmune cirrhosis, and primary biliary cirrhosis of the liver are diseases accompanied by a rapid and intensive decrease in bone mineral density [21,26]. Osteopenia and osteoporosis hepatobiliary the development of the system as a complication in pathologies accompanied by cholestasis have been clarified by scientists [37]. Disorders of bone mineral density are 4 times more common in patients with

primary manifestations of hepatic biliary cirrhosis than in the norm. This disease is more common to be accompanied by osteopenia compared to cholangitis and cholestatic hepatobiliary diseases such as hemochromatosis, which are complicated by primary sclerosis of the biliary tract.

The pathogenesis of osteoporosis rejection in chronic liver diseases is complex and multifaceted. The causes of the origin of the disease, the degree of course, the state of functional failure of the liver, and the level of cholestasis are considered the main factors affecting the metabolite state of bone tissue [12,13,28,42]. Among the additional factors that lead to a decrease in bone mineral density: the period of postmenopause in women, a low index of body mass (obesity), and constant intake of glucocorticosteroid drugs are the reasons.

Currently, the main risk causes for the development of osteopenia and osteoporosis have been identified in diseases of the chronic hepatobiliary system. It has been found that the development of Osteopathy in diseases of the hepatobiliary system is inextricably linked with chronic hepatitis and the degree of liver cirrhosis rejection, in which osteopathy is an integral part of the symptom complex. In patients with chronic alcoholic hepatitis, an X-ray densitometry examination of the spine and thigh was found in 12.6% and 7.8%, respectively, with osteoporosis, and osteopenia in 72.8% and 71.8% [13].

## 3. Conclusions

In hepatic cirrhosis with HCV and HBS viral etiology, there is an increase in parathormone concentration with the formation of secondary hyperparathyroidism syndrome, which determines the pathogenetic properties of remodeling processes. Active vitamin D compounds are lacking during the decompensation of chronic diseases of the hepatobiliary system and especially in alcoholic hepatitis [41]. Liver cirrhosis in men is explained by a decrease in testosterone concentration in the blood, as a result of which hepatocellular insufficiency develops [29]. Of the potential mechanisms for the development of osteoporosis in chronic liver diseases, this is also explained as the consequence of the toxic effects of bilirubin and steamed bile acids on osteoblasts [29].

Chronic alcoholic hepatitis and the course of liver cirrhosis are directly related to an imbalance in the production of cytokines, which is manifested by an increase in the concentration of anti-inflammatory cytokines (il-f, il-6, TNF-a). Anti-inflammatory (il-4, il-10) is due to a decrease in the content of interleukins and the activity of the pathological process and hepatocellular insufficiency [14]. Due to insufficient cleansing by the liver, hypercytokinemia negatively affects bone metabolism, which leads to the activation of osteoclastic resorption.

In chronic liver diseases, mineral substance disorders have been found to depend on the causes of the origin of the pathology and the severity of the disease. In these cases, a violation of mineral metabolism is characterized by a decrease in calcium, and magnesium substances in the blood and a tendency to an increase in the outflow of calcium through the urine, while in patients with liver cirrhosis – the loss of calcium, phosphates through the urine and a decrease in the amount of calcium in the blood. It can be argued that impaired Mineral metabolism is another pathognomonic symptom of SJK. Hypocalcemia is a trigger factor for the development of secondary hyperparathyroidism typical of cirrhosis, especially in the terminal stages [19].

Thus, the assumption of our research has shown that bone tissue is a tissue that exhibits reactive changes among the first in chronic concomitant diseases of members of the digestive system, occurring in the form of changes in Endocrine, biological, and substance metabolism, which means that patients with chronic diseases of the hepatobiliary system and digestive system organs are the main risk.

Our research sees the need to form control groups from within patients with chronic pathologies of the digestive system and develop special rehabilitation measures aimed at this. This guru presupposes when carrying out patients not only knowledge of the main Gastroenterological diseases, but also the narrowness of early diagnosis of osteopenia and osteoporosis and the appointment of the necessary therapeutic, orthopedic, and preventive measures.

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