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Calcidiol (25-OH-D) Level in Serum of Patients with Chronic Pancreatitis

Aripova N. N., Khamraev A. A., Inoyatova F. Kh.

Tashkent Medical Academy, Uzbekistan

Abstract Chronic pancreatitis (CP) remains one of the most urgent problems in modern gastroenterology. In developed countries, the incidence of CP is 100 cases per 4000-8000 people per year. At the same time, the primary disability of patients reaches 15% and covers the population of working age. In specialized gastroenterology hospitals, patients with CP account for approximately 10% of hospital admissions.

Keywords Chronic pancreatitis, Pancreatic insufficiency, Immunoenzyme, Vitamin D

1. Introduction

It is mentioned in the scientific literature that CP is common among diseases of the digestive system and causes severe complications and death in most cases [1,4]. Absorption of dietary fats and fat-soluble vitamins is impaired and causes nutrient deficiencies in patients with chronic pancreatitis due to pancreatic insufficiency (PI). In patients with CP, the risk of vitamin D deficiency is on average 60%, and this condition, in turn, increases the risk of osteoporosis, muscle weakness, depression, and cardiovascular diseases [7].

In recent years, cases of vitamin D deficiency have been observed to increase significantly in all regions of the globe, and this situation is associated with an increase in the incidence of chronic diseases, which necessitates the need to reconsider the approach to this issue. The widespread prevalence of conditions associated with vitamin D deficiency makes it necessary for scientists to carry out extensive research and research of patients [8]. To date, the role of some therapeutic diseases in the development of vitamin D deficiency has been shown [4]. This condition may be associated with reduced intestinal absorption of fats and fat-soluble vitamins, gluten enteropathy, and chronic pancreatitis or liver cirrhosis [4,6]. At the same time, increased catabolism or decreased synthesis of vitamin D and its metabolites can also lead to its deficiency. The purpose of the study: to determine the amount of vitamin D in chronic pancreatitis and to determine its effect on the course of the disease.

2. Materials and Methods of Research

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Researches were conducted in 94 (31 men and 63 women) patients aged 31 to 83 years (mean age 58.40±1.29 years) and 15 healthy subjects (mean age 39.73± 39.73) who were treated at the gastroenterology department of the multidisciplinary clinic of the Tashkent Medical Academy. 4.92 years) was conducted in humans. Patients were divided into the following groups according to the amount of calcidiol (25-OH-D), a metabolite of vitamin D in blood serum: group 1 those with 25-OH-D 30 ng/ml and above (normal), group 2 those with 25-OH-D 20- 30 ng/ml (deficiency), 3rd group - 10-20 ng/ml (deficiency), 4th group consisted of patients with 25-OH-D 10 ng/ml (obvious deficiency) and control group. According to the etiological factor of patients CP, biliary in 73 (77.7%), idiopathic in 8 (5.2%) and mixed etiology in 13 (13.8%) patients. Patients were subjected to clinical and anamnestic, instrumental, coprological and biochemical examinations. In order to determine the state of PI, UT examination was carried out on the "MINDRAY DC-60" device (manufactured in China). Osteopenia and osteoporosis are detected by ultrasound densitometer SONOST-3000 OsteoSys (South Korea). Deficiency of pancreatic exocrine secretory function was assessed by elastase 1 activity in feces, and the amount of 25-OH-D in blood serum was determined by immunoenzyme method in "ELIZA" immunoenzyme analyzer with special reagents of this company. The amount of calcium in the blood serum was determined in a biochemical analyzer using special biotests. Statistical analysis of the obtained results was performed using Microsoft Office Excel 2010 (Microsoft Corp., USA) and Portable Statistica 8 (StatSoft, Inc., USA). The description of categorical data was carried out in the form of degree indicators expressed in percentages. Given that most of the analyzed characteristics have a non-normal distribution, non-parametric statistical tests were used for statistical analysis of the obtained results. Correlation between the

studied characteristics was evaluated using Spearman's rank correlation method (r – correlation coefficient). A significance level of 0.05 was assumed for statistical hypothesis testing.

3. Research Results and Discussion

The conducted studies showed that the amount of 25-OH-D in 22 (23.4%) patients was within normal values (32.57±1.32 ng/ml), 17 (18.1%) - partial deficiency (23.84±0.83 ng/ml), 39 (41.5%) - deficiency (15.55±0.61 ng/ml) and 16 (17%) - severe deficiency (7.00±0.75 ng/ml) were observed (1 see the table). In healthy people, the average amount of 25-OH-D was 25.90±1.53 ng/ml. When we analyzed the changes in the amount of 25-OH-D in the blood serum according to the etiological factor of SP, a tendency to decrease (20.72±1.07 ng/ml) was observed in the biliary form compared to the indicators of the conditionally healthy group, while in the idiopathic and mixed forms it was statistically reliable 1.63 (P <0.01) and 2.18 (P<0.001) were low and were 15.87±3.39 and 12.32±1.28 ng/ml. The obtained results showed that 19.4% of patients with CP biliary had normal 25-OH-D, 25% - partial deficiency, 44.4% - deficiency and 11.2% - obvious deficiency; in the idiopathic form, 75% of patients have a deficiency, and 25% have a severe deficiency; In the mixed form, 50% of patients have deficiency and 50% - severe deficiency. The obtained results substantiated that the strongest changes are observed in the mixed form of CP.

It is worth mentioning that the amount of calcium in the blood serum of patients with CP also changed in parallel with the amount of 25-OH-D: in patients with a normal amount of 25-OH-D, its amount tended to increase compared to the indicators of a conditionally healthy group, while a deficiency of 25-OH-D was observed. and in patients with a tendency to decrease, in the groups of patients with deficiency and extreme deficiency, statistically significant 1.13 (P<0.05) and 1.31 (P<0.05) times decrease was observed. When we analyzed the changes in the amount of calcium in blood serum according to the etiological factor of SP, a tendency to decrease (1.85±0.03 mmol/l) was observed in the biliary form compared to the parameters of the conditionally healthy group, while in the idiopathic and mixed forms it was statistically reliable 1.19 (P<0.05) and 1.24 (P<0.05) times lower and amounted to 1.67±0.16 and 1.60±0.03 mmol/l. The obtained results showed that the changes in calcium metabolism are more specific in the mixed form of CP.

At the same time, we performed ultrasound densitometry in patients suffering from CP. The obtained results showed that osteopenia and osteoporosis developed monad to 25-OH-D and calcium levels. Osteopenia symptoms were observed in 26.7% of the conditionally healthy group of tubular bone ultrasound examinations. 50 (53.2%) and 18 (19.1%) patients with CP showed osteopenia and osteoporosis. Among them, 9.1 and 9.1% of 25-OH-D were normal, 35.3 and 23.5% were deficient, 25.6 and 66.7% were deficient, and 25 and 75% of patients with severe deficiency. osteopenia and osteoporosis were observed. When we analyzed the results of ultrasound examinations according to the etiological factor of SP, 46.6% of osteopenia and 19.2% of osteoporosis were observed in the biliary form, 25 and 50% of these indicators were observed in the idiopathic form, and osteopenia was observed in all patients of the mixed form group (100%).

It is known that the extrinsic secretory function of PI decreases in CP, and elastase activity in feces is considered as a criterion for its detection. Studies have shown that when serum vitamin D levels of patients with CP were normal, elastase activity in feces was 1.22 (P<0.05) times higher than that of the healthy group, while its activity was 1.25 (P<0.05) in patients with deficiency, deficiency, and marked deficiency 0.05); 1.45 (P<0.01) and 1.79 (P<0.001) times lower (Table 1). The obtained results proved that 25-OH-D deficiency in CP patients can be caused by the external secretory function of MOB. When we analyze the activity of elastase in feces by etiological factor, it is statistically reliable 1.18 (P<0.05) in biliary, idiopathic and mixed forms of CP; We observed a decrease of 1.23 (P<0.05) and 1.67 (P<0.01) times. The obtained results showed a sharp decrease in the external secretory function of PI in the mixed form of CP.

Table 1. Serum 25-OH-D and calcium levels in patients with chronic pancreatitis, as well as elastase activity in feces, M±m

Groups	25-OH-D,ng/ml	Calcium, mmol/l	Elastase,
Conditionally healthy	25,90±1,53	1,98±0,03	208,27±10,83
According to the amount of 25-OH-D in patients with chronic pancreatitis			
the norm, n=22	32,57±1,32[a]	2,12±0,08	254,45±25,01[a]
deficiency, n=17	23,84±0,83	1,95±0,07	166,37±19,01[a]
scarcity, n=39	15,55±0,61[a]	1,75±0,05[a]	143,50±9,39[a]
obvious shortage, n=16	7,00±0,75[a]	1,51±0,07[a]	116,37±11,73[a]
According to the etiological factor of chronic pancreatitis			
biliary, n=73	20,72±1,07	1,85±0,03	176,69±7,12
idiopathic, n=8	15,87±3,39	1,67±0,16	169,75±25,88
mixed, n=13	12,32±1,28	1,60±0,03	125,00±5,44

Note: * is statistically significant (r<0.05) compared to the indicators of a conditionally healthy group.

It is known that obesity-related diseases are associated with obesity. In our conditionally healthy group, the body mass index was 26.82±1.03, but we observed a statistically significant increase in TVI in patients with CP, but these changes were not related to 25-OH-D deficiency and etiological factor. In particular, 31.70±0.75 in the 25-OH-D norm, deficiency, deficiency and extreme deficiency groups; 31.48±0.91; 32.84±0.62 and 31.39±1.11, and 32.06±0.46 in biliary, idiopathic and mixed forms; 31.42±1.00; externalized 32.01±1.35.

Table 2. Correlation of clinical symptoms in patients with chronic pancreatitis depending on the amount of 25-OH-D

Signs	Conditionally healthy group, n=15	Grouping according to the amount of 25-OH-D in patients with chronic pancreatitis, n=94			
		standard n=22	deficiency, n=17	scarcity, n=39	obvious shortage, n=16
Hepatogenic steatorrhea,%	0,0	0,0	13	15	25
Enterogenic steatorrhea, %	0,0	27,3	13	10	25
Mixed steatorrhea, %	0,0	27,3	37,5	30	37,5
Amylorrhoea,%	0,0	18,2	37,5	30	50,0
Creator, %	0,0	36,4	50,0	30	37,5
Presence of bile acid salts, %	0,0	27,3	50	35	25

Table 3. The results of ultrasound examinations of the pancreas in the course of changes in the amount of 25-OH-D in chronic pancreatitis, %

Indicators	Conditionally healthy group, n=15	Grouping according to the amount of 25-OH-D in patients with chronic pancreatitis, n=94			
		the norm, n=22	deficiency, n=17	scarcity, n=39	obvious shortage n=16
Diffuse increase in parenchyma echogenicity, preservation of the image	40,0%	72,7%	70,6%	71,8%	81,3%
View of "Stone Bridge".	0,0%	45,0%	100,0%	64,1%	62,5%
Medium and dense types of echosignals, uneven distribution on the normal background	26,7%	54,0%	88,2%	74,4%	87,5%
Inhomogeneous distribution of echo signals, alternating dense and cystic areas	-	45,5%	58,8%	61,5%	62,5%
Extreme variability of the amplitude and duration of echo signals	20,0%	54,5%	76,5%	77,0%	93,8%
Increase PI	-	77,3%	88,3%	89,7%	81,3%
PI tissue calcification	-	31,8%	23,5%	48,7%	50,0%
Determination of concretions in the pancreatic tract	-	18,2%	5,9%	7,7%	37,5%
Presence of cysts	-	9,1%	0,0%	5,1%	12,5%
PI road widening(>2,5 mm)	-	0,0%	23,5%	7,7%	12,5%
Increase PI density	33,3%	45,5%	41,2%	49,0%	43,8%

At the same time, we compared the clinical symptoms of the disease according to the amount of 25-OH-D in patients with CP (Table 2). As can be seen from the table, CP patients with 25-OH-D deficiency had a higher incidence of mixed steatorrhea, amylorrhea, creatorrhea, and the presence of bile acid salts compared to the group of CP patients with normal 25-OH-D. This was especially evident in severe 25-OH-D deficiency.

As the amount of 25-OH-D decreases in the US examination of the pituitary gland, the frequency of diffuse increase of echogenicity of the parenchyma of the gland, preservation of the image, extreme variability of the amplitude and duration of echosignals, calcification of the PI tissue increases (Table 3). In particular, the extreme variability of the amplitude and duration of echosignals increased with the decrease in the amount of 25-OH-D and was detected in 77 and 93.8% of patients in cases of deficiency and extreme deficiency, while only 54.5% of patients with normal levels of 25-OH-D % observed. Enlargement and calcification of the pancreas was detected in 31.8% of patients with normal 25-OH-D, and in 50.0% of patients in the group with severe deficiency. Concretions in the pancreatic tract were detected in 37.5% of patients in the group with obvious deficiency of vitamin D. It should be noted that the increase in the size of the PI and the calcification of its tissue were characteristic of the mixed form of CP. Sometimes, in the biliary etiology of CP, an increase in the size of the organ, an increase in the pancreatic ducts, the presence of concretions and cysts, and a thickening of the glandular tissue were observed.

At the same time, in patients with vitamin D deficiency, non-calculous and calculous cholecystitis, post-cholecystectomy condition and reactive hepatitis were often detected. Coprological examinations showed the development of hepatogenic steatorrhoea, malabsorption of fat-soluble vitamins and calcium, creatorrhoea, amylorrhoea.

According to many authors, vitamin D deficiency is observed in most inflammatory diseases, including

inflammatory bowel diseases, severe tuberculosis, pancreatitis, etc. [3]. According to the literature, the absorption of dietary fats and fat-soluble vitamins due to impaired exocrine function of PI in CP patients exacerbates the malabsorption syndrome observed in this disease, and vitamin D deficiency is high compared to the general population (57.6%; 95%). DI 43.9–70.4) [7,10,12]. Clinical studies show that 40% of patients with acute and chronic pancreatitis develop a severe form of vitamin D deficiency [13], and the administration of this vitamin to such patients leads to its normalization [2]. Therefore, according to the Russian and pan-European recommendations, it is necessary to provide replacement therapy to patients with CP, as well as when there is a violation of the external secretory function of the PI [5].

It is known that vitamin D participates in many biochemical processes in the body. In particular, it enhances calcium absorption in enterocytes, increases calcium reabsorption in renal tubules, activates the cellular immune system, and enhances cell growth and development [9]. Some scientists believe that the anti-inflammatory effect of this vitamin blocks the synthesis of inflammatory cytokines in monocytes and T-lymphocytes [14]. This is evidenced by the decrease in serum 25(OH)D3 in patients with acute pancreatitis, which coincides with the increase in S-reactive protein [11]. Our research also showed that it is consistent with the above-mentioned points, that is, it was found that vitamin D deficiency increases the activity of elastase, accelerates the development of osteopenia and osteoporosis, and increases the changes of various forms of PI in patients with CP.

4. Conclusions

Based on the obtained results, we can make the following conclusions:

1. In the majority of patients with chronic pancreatitis, a deficiency of 25-OH-D, as well as a pronounced deficiency, was found, which led to a decrease in the amount of calcium in these patients, which led to the development of osteopenia and osteoporosis.
2. The degree of 25-OH-D deficiency coincided with a decrease in the exocrine secretory function of the pancreas.
3. In patients with 25-OH-D deficiency, ultrasound examinations reveal fibrosis and calcification of the pancreas parenchyma, and stool examinations record hepatogenic steatorrhea and malabsorption of fat-soluble vitamins.

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