

Metabolic acidosis as an important factor of pathogenesis of chronic pancreatitis

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Key words: chronic pancreatitis, metabolic acidosis, pathogenesis, trophic insufficiency, treatment programme

Introduction. Metabolic acidosis is the accumulation of acids due to their increased formation or consumption, reduced excretion or loss of HCO_3^- through the gastrointestinal tract or kidneys. Chronic metabolic acidosis mainly affects two alkaline digestive glands — liver and pancreas, which produce alkaline bile and pancreatic juice with a lot of bicarbonate. Even small changes in pH in these secretions can lead to serious biochemical and biomechanical changes. When acidification of the juice of the pancreas decreases the antimicrobial activity, which can lead to intestinal dysbiosis. Reducing the pH of pancreatic juice can lead to premature activation of protease in the pancreas with the possible development of pancreatitis. Restoration of the usual acid-base homeostasis can be a useful tool in pathophysiological therapeutic method.

The cause of persistent metabolic acidosis in chronic pancreatitis is the following: chronic inflammation of the tissue of the pancreas with the development of edema and a violation of microcirculation and perfusion and hypoxia; oxidative stress of tissues with predominantly acidic metabolites; activity of the intestinal microflora in the event of dysbiosis (*Candida* fungus or excessive colonization of the small intestine bacterial overgrowth, SIBO); decrease in the capacity of the buffer systems of blood [2].

The main buffer system of the organism is the bicarbonate-hemoglobin buffer ($\text{CO}_2^- / \text{HCO}_3^-$), which occupies more than 70% of the total buffer capacity of the organism. The secretion of bicarbonate in the pathway of CP is reduced with chronic systemic metabolic acidosis. We give data on the concentration of bicarbonates in plasma compared with pancreatic juice (Table 1) [7].

Table 1

The content of bicarbonates in human body environments

Compartment	Bicarbonate content (mEq/Liter)
Blood (Plasma)	27
Pancreatic juice	92-145

In diseases of the pancreas there is a decrease of bicarbonate in pancreatic juice and bile of patients [8-9]. Such a reduction in the amount of bicarbonate in the pancreatic secretion has a practical clinical significance [10]. Duodenal acidity mainly depends on the amount of bicarbonate in pancreatic secretion and bile. CP-patients have very low the pH of the duodenum [11, 12]. Low pH in the duodenum is the most significant factor determining the activity of all pancreatic enzymes [13]. For example, pancreatic lipase stops working if the duodenal pH is <4.5 [14]. Exocrine insufficiency of the pancreas is unfavorable for the enzymatic activity of the digestive system and has a direct negative impact on the quality of life of patients [15].

At the same time, the lowered level of bicarbonates may act as a trigger for the formation of chronic calcifying pancreatitis, which is most often diagnosed (appropriately in 70-80% of patients) and characterized by tissue damage pancreas with the formation of intracerebral protein casts and stones, atrophy and stenosis of the duct system. [16]

As is known, in the pathogenesis of chronic calcifying pancreatitis has three main mechanisms: a) when stimulating acinus in the secretion, the proportion of water and bicarbonate HCO_3^- decreases, which increases the concentration of protein in pancreatic juice. This leads to the precipitation of protein in the duct with the formation of protein crust; b) calcium is deposited on the precipitated protein. There is a formation of stones in the lumen of small ducts and concentric deposits of calcium on the walls of the duct system. The reason for this is the exhaustion of the natural mechanisms for preventing the precipitation of calcium salts, in particular, the lack of secrecy in the pancreas of two components —

citrate, which normally binds calcium, and in the conditions of acidosis it begins to waste on the needs of buffer systems, and lithostatin (a protein with a mass of 14 kDa), which keeps calcium salts in solution at physiological hypersaturation; c) sometimes intraperitoneal activation of trypsin, as in case of acute pancreatitis.

Regarding the prognosis of CP, there is evidence that exocrine insufficiency of the pancreas combined with a low pH of the duodenum the risk of carcinoma increases [12]. In general, the risk of appearance cancer with CP is 5 times higher than in the general population. [20]

The severity of metabolic acidosis defines the clinical picture. Light acedemia goes asymptomatic. However, with more severe acidemia (pH <7,10), nausea, vomiting and general malaise may occur. [17]

Severe acidemia can provoke cardiac dysfunction with the fall of blood pressure and the development of ventricular arrhythmia. Chronic acidemia also causes demineralization of bones (rickets, osteomalacia, osteopenia). [18] The formation of osteodyne deficiency is also significantly affected by malabsorption syndrome. [21]

Conclusion. Metabolic acidosis becomes an important predictor of the formation and deepening of trophic insufficiency, which further reduces the quality of life of patients with CP. All of the above suggests the need to take into account the presence of metabolic acidosis in the development of a comprehensive treatment program for such patients.

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Article presents the results of the analysis of scientific literature on the role of metabolic acidosis in the pathogenesis of chronic pancreatitis. It is stated that metabolic acidosis is an important predictive factor in the formation and deepening of trophic insufficiency, which further reduces the quality of life of patients with

chronic pancreatitis and worsens the prognosis. This motivates the need to take into account the presence of metabolic acidosis during the development of a complex treatment program for such patients.