



**CLINICAL FEATURES AND PHARMACOTHERAPY OF CHRONIC PANCREATITIS
IN THE ELDERLY**

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Abstract: Chronic pancreatitis – it is disease, prevalence of which has been steadily increasing during the last 30 years among the elderly people. Physiological, agespecific changes invariably influence the course of chronic pancreatitis, modifying clinical characteristics and treatment approaches to this disease in elderly people. Main etiologial factors, developing mechanisms, clinical course options and basic approaches to medical therapy of chronic pancreatitis in elderly patients are described in the article.

Key words: chronic pancreatitis, ageing, elderly, clinical picture, treatment

As an independent disease, chronic pancreatitis is rare in the elderly and is a continuation and progression of an early process that persists after the cessation of the etiologic factor [3]. In 60% of patients, chronic pancreatitis is caused by alcohol [2]. It should be noted that the pancreas in most people is more sensitive to alcohol than the liver. However, for the elderly, alcoholic genesis is not a determining factor in the development of chronic pancreatitis. In 75% of cases, the etiologic factor for the development of pancreatic diseases in the elderly is bile duct stones, and in patients over 80 years of age, the development of pancreatitis is associated with increasing pancreatic ischemia due to vascular atherosclerosis [5]. Changes occurring in the pancreas with age can be considered a risk factor for the development of chronic pancreatitis. In 10% of cases, chronic pancreatitis can be caused by hyperparathyroidism, long-term diabetes mellitus, and medications. The most common association between recurrent pancreatitis and the use of cytostatics and glucocorticoids, which cause toxic damage to acinar cells and increased viscosity of pancreatic secretions, is reported. Cases of chronic pancreatitis developing during treatment with sulfonamides, nonsteroidal anti-inflammatory drugs (NSAIDs), thiazide diuretics, and tetracycline have been described. As a rule, the etiologic factor for chronic pancreatitis in elderly patients can only be identified in 60-80% of cases. Most often, patients over 60 years of age experience a combination of risk factors (age, alcohol, smoking, medication use, comorbidities such as diabetes, hyperlipidemia, autoimmune diseases, etc.) [5]. In other cases, the underlying cause cannot be determined. In this case, the disease is referred to as idiopathic chronic pancreatitis. The idiopathic variant is more common with late onset of the disease (onset after 60 years). Among the idiopathic variants of chronic pancreatitis in the elderly, idiopathic senile pancreatitis is distinguished—a variant of nonalcoholic chronic pancreatitis that develops predominantly in men over 50 years of age [6].

Pathogenesis

The mechanism of development of chronic pancreatitis is not fully understood. Some researchers place the primary role in the obstruction of ducts and tubules due to the formation of so-called "protein plugs." Protein precipitates are insoluble fibrillar protein (lithostatin) combined with calcium carbonate deposits, which can subsequently lead to their calcification.



Pancreatic calcification occurs in both alcoholic and non-alcoholic chronic pancreatitis. According to other studies, the most important factor in the development of chronic pancreatitis is the premature activation of pancreatic enzymes within the pancreatic duct. Under conditions of oxidative stress, pancreatic cells are damaged, the activity of lysosomal enzymes increases, and limited self-digestion of the pancreas begins. Gradual cell death leads to parenchymal atrophy and stromal sclerosis. In some cases, necrosis of parenchymal areas during an exacerbation may result in cyst formation.

Altered tone of the sphincter of the hepatopancreatic ampulla (sphincter of Oddi) can negatively impact the development of chronic pancreatitis. Spasm of the sphincter causes intraductal hypertension, and relaxation causes reflux of duodenal contents and bile. Reflux often occurs with increased pressure in the duodenum and common bile duct. All of the above-described pathways for the development of chronic pancreatitis are believed to be valid, but depending on the etiologic factor, one or another variant predominates [2].

Clinical Features of Chronic Pancreatitis in the Elderly

Age-related changes in functional systems in general and the pancreas in particular modify the clinical picture, prognosis, and treatment of chronic pancreatitis in the elderly.

The clinical manifestations of the disease at this age are individual and multifaceted. The duration of exposure to etiologic factors leads to the fact that the onset of the disease after 60 years is significantly less common. An atypical, and in most cases, latent or even asymptomatic course of chronic pancreatitis is observed [5]. However, it is necessary to distinguish an asymptomatic course from a pseudo-asymptomatic course of the disease, which is determined due to the inability to fully interview and examine the patient. In most patients, with age, chronic pancreatitis is characterized by an increase in the frequency of exacerbations, occurring under the guise of ulcer or gallstone disease [5]. Pain is the leading and most persistent symptom of chronic pancreatitis, occurring in no more than 5% of patients and is more moderate in those over 60 years of age [1,12]. Pain localization depends on the predominant lesion of the head, body, or tail of the pancreas. However, with age, clearly defining the projection of pain in chronic pancreatitis in elderly patients becomes less informative due to the presence of a large number of concomitant lesions in adjacent organs. In such cases, the physician must deal with a diffuse abdominal pain syndrome. According to studies conducted in 2002, recurrent or persistent abdominal pain in the elderly was severe but lacked a typical localization in 20% of cases, and was mild or absent in 40% of cases [11]. The disappearance of pain is associated with the progression of acinar cell atrophy in the gland. This situation is accompanied by dysfunction of the gland and the formation of calcifications in its tissue [10]. A painless course of chronic pancreatitis is more typical of late-onset chronic pancreatitis and idiopathic senile pancreatitis. Dyspeptic disorders, inherent and characteristic of all patients with chronic pancreatitis, are less pronounced in old age. The intensity of dyspeptic disorders in old age does not always correspond to the degree of organ and tissue damage. To a greater extent, they are caused by age-related changes and previously developed gastrointestinal diseases [5]. The presence of symptoms associated with other gastrointestinal diseases (esophageal lesions, gastric motility disorders, etc.) for many years leads to the perception of existing symptoms as normal for their age and the absence of complaints from elderly patients.

Along with classic signs of pancreatitis such as pain and dyspeptic disorders, manifestations of exocrine pancreatic insufficiency become prominent in elderly patients with chronic pancreatitis. However, late-onset chronic pancreatitis is characterized by rapid progression of both exocrine



and endocrine functions [11]. In one pilot study conducted in 21 elderly patients with chronic pancreatitis and 26 healthy volunteers, a 55% reduction in exocrine function was recorded, indicating moderate to severe exocrine pancreatic insufficiency in 19% of the elderly [9]. Morphologically, exocrine pancreatic insufficiency in the elderly develops as a result of diffuse disruption of the structure of the functioning pancreatic tissue. Clinically, increasing exocrine insufficiency is manifested by steatorrhea and significant weight loss (cachexia). In all forms of the natural course of chronic pancreatitis, carbohydrate metabolism disorders in the form of diabetes mellitus of varying severity are often observed in the late stages of the disease [1,5]. The development of diabetes in patients with chronic pancreatitis depends on the presence of a genetic predisposition.

Basic approaches to pharmacotherapy

When prescribing medications to elderly patients with chronic pancreatitis, a number of factors must be taken into account, as taking a large number of medications is only part of the problem. Even a single drug can have a more pronounced effect on the elderly due to age-related physiological characteristics that affect drug metabolism. Furthermore, previous and concomitant diseases must be taken into account.

The primary goals of treatment for patients with chronic pancreatitis are pain relief and correction of pancreatic exocrine insufficiency. The best method for pain relief is to attempt to eliminate the underlying cause. However, for patients with chronic pancreatitis, pain control is more appropriate. Non-narcotic and narcotic analgesics are used as symptomatic pain relievers. All NSAIDs, especially those with a prolonged half-life, should be used with caution in the elderly, given the frequent development of adverse reactions (upper gastrointestinal tract damage, bleeding, worsening of arterial hypertension, heart failure, etc.) [5, 8]. Therefore, it is advisable to initiate therapy with low starting doses to avoid the development of adverse reactions. When prescribing narcotic analgesics, it is necessary to take into account that many opiates cause spasm of the sphincter of Oddi, leading to increased pain.

The use of somatostatin analogs, the most potent inhibitors of pancreatic secretion, in individuals over 60 years of age is limited and insignificant due to the mild severity of pain in this age group [1]. In the last decade, enzyme preparations have been used to relieve pain during exacerbations of chronic pancreatitis. The analgesic effect of these drugs is due to a decrease in the activity of regulatory proteins (secretin and cholecystokinin releasing peptides) when exogenous enzymes are administered. This leads to a cessation of the release of the corresponding hormones, a reduction in pancreatic secretion, and thus a decrease in pressure in the ducts and parenchyma of the pancreas, pain relief, and the creation of the necessary conditions for functional rest for the pancreas.

Despite the emergence of new applications for enzymes, the main indication for enzyme use is the regulation of exocrine insufficiency. To achieve this goal, preparations containing only pancreatic enzymes without bile components are used. Currently, minimicrospherical enzyme preparations are recognized as the gold standard for the treatment of chronic pancreatitis.

Their effectiveness for replacement therapy in exocrine pancreatic insufficiency corresponds to the highest level of evidence. However, there are studies questioning their use in patients with polycystic pancreas, as they can lead to increased strictures. However, their use in patients with other forms of chronic pancreatitis is considered justified [5].

Anticholinergics are often used in combination treatment for patients with chronic pancreatitis. Considering the cholinergic mechanism of pancreatic secretion, the use of drugs in this group is appropriate from both a physiological and pathogenetic perspective. In patients with chronic



pancreatitis, the use of M3-anticholinergic agents is more justified, since the effect of acetylcholine on pancreatic enzyme synthesis is mediated through M3-cholinergic receptors on acinar cells [1,4]. A particular feature of the use of these drugs in the elderly is the possible change in sensitivity to the drug, due to changes in the number and sensitivity of the receptors with which the drug interacts. As a result, the elderly may experience an inadequate response to standard (therapeutic) doses, requiring careful titration of doses with monitoring of the clinical effect. Platyphylline is widely used for this purpose in clinical practice. However, when prescribing these drugs, it should be taken into account that non-selective M-anticholinergics have a significant number of side effects and should not be used in patients with tachyarrhythmia, glaucoma, prostate adenoma, etc. Side effects that develop in the elderly when taking anticholinergic drugs include confusion, difficulty urinating, dry mouth, and numbness in the legs [5].

Conclusion

Management of elderly patients with chronic pancreatitis remains a complex task due to age-related changes in physiological systems, the individual nature of the disease, the presence of comorbidities, and the specifics of pharmacotherapy. The main principles of pharmacotherapy include knowledge of the pharmacokinetics of the drugs used, the use of low starting doses, and careful titration of doses due to the potential risk of adverse reactions in the elderly.

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