

THE USE OF ANTIPROTEASE DRUGS IN ACUTE PANCREATITIS

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<https://doi.org/10.5281/zenodo.23019259>

Annotation. *This thesis examines the use of antiprotease preparations in the management of acute pancreatitis. The study focuses on the pathogenetic role of premature activation of pancreatic enzymes, particularly trypsin, and the theoretical rationale for inhibiting proteolytic activity. The clinical characteristics and therapeutic potential of gabexate mesilate, nafamostat, and ulinastatin are discussed. Current evidence indicates that although antiprotease agents may influence certain inflammatory and biochemical parameters, their ability to consistently reduce mortality and severe complications has not been clearly established. Therefore, antiprotease therapy should be considered cautiously and primarily within evidence-based treatment strategies.*

Keywords: *Acute pancreatitis, antiprotease therapy, protease inhibitors, pancreatic enzymes, trypsin, gabexate mesilate, nafamostat, ulinastatin, pancreatic inflammation, pancreatic necrosis.*

Introduction

Acute pancreatitis is a sudden inflammatory disease of the pancreas that may progress to local complications, systemic inflammatory responses, and organ failure in severe cases.

Premature activation of pancreatic enzymes, particularly the conversion of trypsinogen to trypsin within pancreatic tissue, plays a key role in the pathogenesis of the disease. Therefore, the use of antiprotease agents aimed at suppressing pancreatic enzyme activity has been investigated as a pathogenetic therapeutic approach. Protease inhibitors such as gabexate mesilate, nafamostat, and ulinastatin have been studied in different forms of acute pancreatitis; however, their clinical efficacy remains inconsistent. Current international recommendations indicate that no pharmacological targeted therapy with clearly established efficacy is currently available for acute pancreatitis, while the clinical role of protease inhibitors requires further high-quality investigation. Therefore, studying the pathogenetic rationale, clinical efficacy, and contemporary role of antiprotease agents in acute pancreatitis remains an important scientific and practical issue.

Relevance

Acute pancreatitis can develop severe local and systemic complications, making effective pathogenetic treatment an important clinical issue. Because premature activation of pancreatic enzymes plays a key role in disease development, the use of antiprotease agents has attracted considerable scientific interest.

Main part

Acute pancreatitis is associated with premature activation of pancreatic digestive enzymes within the pancreatic tissue. Trypsinogen activation to trypsin is considered one of the important mechanisms initiating the enzymatic cascade. Activated trypsin promotes the activation of other proteolytic enzymes and contributes to pancreatic autodigestion. This process causes cellular injury, edema, inflammation, and damage to the pancreatic microcirculation.

Severe enzymatic activation may also stimulate the release of inflammatory mediators and contribute to systemic inflammatory response. Antiprotease preparations have therefore been developed to inhibit proteolytic enzymes and reduce enzymatic tissue injury. Gabexate mesilate, nafamostat, and ulinastatin are among the agents that have been investigated in acute pancreatitis.

Their proposed therapeutic effect is associated with inhibition of protease activity and limitation of pancreatic tissue damage. However, the pathogenesis of acute pancreatitis involves multiple mechanisms beyond enzyme activation. Microcirculatory disorders, immune activation, endothelial dysfunction, and inflammatory mediator release may also contribute to disease progression.

Therefore, suppression of proteolytic enzymes alone may not completely prevent severe pancreatic injury. The theoretical basis of antiprotease therapy remains important for understanding the pathophysiology of acute pancreatitis.

The use of antiprotease preparations in acute pancreatitis depends on the clinical severity, underlying cause, and general condition of the patient. Before treatment, patients should undergo clinical assessment, laboratory investigations, and appropriate imaging studies. Serum lipase, amylase, C-reactive protein, hematocrit, renal function, and other parameters may help assess disease activity and severity. The effectiveness of antiprotease therapy should not be determined only by a decrease in pancreatic enzyme levels. Important clinical outcomes include pain reduction, improvement of inflammatory parameters, prevention of organ failure, reduction of local complications, and duration of hospitalization. Clinical studies of gabexate, nafamostat, and ulinastatin have produced inconsistent results. Some studies have reported beneficial effects on selected inflammatory or clinical parameters, whereas others have failed to demonstrate significant reductions in mortality or severe complications. Therefore, antiprotease treatment cannot currently be considered a universal therapy for all patients with acute pancreatitis. When used according to local clinical protocols, it should be considered together with standard supportive treatment.

Adequate fluid management, pain control, nutritional support, and monitoring of organ function remain essential components of treatment. Careful observation is also necessary to identify potential adverse drug reactions.

Modern management of acute pancreatitis is mainly based on early severity assessment, supportive treatment, nutritional therapy, and prevention of complications. Antiprotease preparations do not replace these fundamental therapeutic measures. Current international evidence has not established a consistent clinical benefit of routine antiprotease therapy in acute pancreatitis. Nevertheless, protease inhibition remains an important research direction because enzyme activation plays a significant role in the early pathogenesis of the disease. Future studies should identify patient groups that may benefit from targeted antiprotease treatment. Disease severity, etiology, inflammatory biomarkers, and the presence of organ dysfunction should be considered when selecting patients for clinical trials. Randomized controlled studies with large patient populations are needed to determine whether specific antiprotease agents can improve clinically relevant outcomes. Mortality, persistent organ failure, pancreatic necrosis, complications, and hospital stay should be assessed rather than relying only on biochemical changes. The safety profile and cost-effectiveness of these medicines should also be evaluated.

Personalized treatment approaches may help determine whether protease inhibitors are beneficial in specific forms of acute pancreatitis. Further investigation of new selective protease inhibitors may provide additional therapeutic possibilities. At present, however, antiprotease preparations should be interpreted as an investigational or selectively used treatment rather than a universally established standard. Their future role will depend on the results of high-quality clinical research and stronger evidence of meaningful patient benefit.

Conclusion

Antiprotease preparations in acute pancreatitis are aimed at reducing the activity of pancreatic proteolytic enzymes and limiting enzymatic tissue injury. Their theoretical use is based on the important role of premature enzyme activation in the pathogenesis of acute pancreatitis.

However, current clinical evidence does not demonstrate a consistent reduction in mortality or severe complications with routine antiprotease therapy. Therefore, the main treatment approach should remain based on adequate supportive therapy, pain control, fluid management, nutritional support, and careful monitoring of organ function. Antiprotease preparations may be considered only in accordance with clinical indications and established treatment protocols. Further well-designed clinical studies are required to determine their effectiveness and identify patients who may benefit from targeted antiprotease therapy.

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