ORIGINAL RESEARCH

Clinical Analysis of Atorvastatin Calcium, Fenofibrate, and Acipimox in the Treatment of Hypertriglyceridemia-induced Acute Pancreatitis

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ABSTRACT

Background • Hypertriglyceridemia-induced acute pancreatitis (HTG-AP) is an increasingly recognized and potentially severe form of acute pancreatitis. The effective management of HTG-AP is critical due to its association with significant morbidity and mortality. HTG-AP poses a considerable burden on affected individuals and healthcare systems. It can result in persistent upper abdominal pain, nausea, vomiting, abdominal distension, fever, and in severe cases, hypotension or shock and multiple organ dysfunction. Standard treatment strategies often involve lipid-lowering agents, but the optimal therapeutic approach remains a subject of ongoing research. This study aims to evaluate the efficacy of atorvastatin calcium, fenofibrate, and acipimox, either individually or in combination, in the treatment of HTG-AP, providing insights into more effective management strategies.

Methods • 150 HTG-AP patients admitted to the first hospital of Putian from June 2020 to December 2022 were selected. The age range of the patients included in the study was between 30 and 70 years, with an average age of approximately 48 years. The cohort consisted of 90 males and 60 females, resulting in a male-to-female ratio of 3:2. The patients were grouped: atorvastatin calcium, acipimox, fenofibrate, fenofibrate + Atorvastatin calcium, fenofibrate + acipimox, and no drug. The therapeutic effects and clinical indicators of the six groups were compared.

Results • Patients in the fenofibrate + acipimox and fenofibrate groups experienced significantly reduced hospitalization duration compared to the other groups. They also had shorter abdominal pain relief time and gastrointestinal function relief time. Additionally, these groups had lower peak levels of amylase (an enzyme) and cholesterol compared to the other groups. In terms of neutrophil (NEUT) increase, the fenofibrate + acipimox, atorvastatin calcium, and fenofibrate groups had significantly lower peak levels compared to the other groups, indicating a less pronounced increase in NEUT. Furthermore, the fenofibrate and acipimox groups exhibited significantly lower peak levels of C-reactive protein (CRP) compared to the other groups. CRP is an indicator of inflammation. On the other hand, the atorvastatin calcium group had higher levels of procalcitonin (a marker of infection) and a higher peak score on the acute physiology and chronic health evaluation II (APACHE II) scale, which assesses the severity of acute pancreatitis, compared to the other groups (all $P < .05$).

Conclusion • The findings of this study highlight the effectiveness of combining fenofibrate and acipimox in the treatment of HTG-AP, leading to rapid disease recovery and significant improvement in clinical symptoms. These results have important implications for clinical practice, as the combination therapy can be widely adopted as an effective treatment strategy for HTG-AP patients. Moreover, this study provides valuable insights into the management of HTG-AP and suggests that lipid-lowering agents, such as atorvastatin calcium and fenofibrate, play a crucial role in the treatment of this condition. However, further research is needed to explore the optimal dosages, treatment durations, and potential side effects of these medications in HTG-AP patients. (*Altern Ther Health Med.* 2024;30(12):200-207).

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INTRODUCTION

Acute pancreatitis (AP) is a common acute abdomen in clinical work, with high incidence, high mortality, and great pain in severe AP, which seriously affects the quality of life of patients.[1] With the development of China's economy, the improvement of people's living standards, the changes in people's eating habits, and the impact of various problems of environmental pollution and food safety, the number of AP cases in China has increased sharply in recent years.[2,3] AP is considered a common gastrointestinal disorder worldwide. It has been reported that the global incidence of AP ranges from 13 to 45 cases per 100 000 population per year. Factors contributing to the rising prevalence of AP include changes in lifestyle, dietary habits, and the impact of environmental factors. Furthermore, the burden of AP on healthcare systems is substantial, with significant healthcare costs and implications for patient well-being and quality of life. Cholelithiasis (It is believed that gallstones can obstruct the common bile duct, impairing the flow of pancreatic enzymes into the duodenum. Consequently, the accumulation of these enzymes within the pancreatic ducts can lead to autodigestion and inflammation of the pancreas, initiating an episode of AP), alcoholism (Alcohol abuse and chronic alcoholism are recognized as major causes of AP. The exact mechanisms by which alcohol induces pancreatitis are not completely understood, but several hypotheses have been proposed. One prevailing theory suggests that chronic alcohol consumption leads to the formation of toxic metabolites and oxidative stress within pancreatic acinar cells. This, in turn, triggers intracellular activation of digestive enzymes, premature

activation of trypsinogen, and subsequent pancreatic autodigestion and inflammation), and hypertriglyceridemia (Hypertriglyceridemia, defined as elevated levels of triglycerides in the blood, is another important cause of AP. Excess triglycerides can accumulate within the pancreas, resulting in increased production of free fatty acids. These free fatty acids cause direct injury to pancreatic cells, leading to inflammation and tissue damage. Additionally, elevated triglyceride levels can impair the clearance of pancreatic enzymes, further exacerbating pancreatic injury and the development of AP) are the main causes of AP.

Long-term intake of food with high-fat content is an important factor causing obesity and hyperlipidemia. The occurrence of hyperlipidemia is closely related to cholesterol intake, and excessive intake of animal fat will increase the secretion of bile acids in the intestine, promote the absorption of cholesterol, and increase the incidence of AP.[4,5] Excessive intake of a high-fat diet will make the pancreas secrete digestive enzymes with a high load, which aggravates the inflammatory response and oxidative stress of the pancreas. The clinical manifestations of AP patients are sudden onset of persistent upper abdominal pain, which may be accompanied by nausea, vomiting, abdominal distension, fever, etc. Severe AP may be accompanied by hypotension or shock and multiple organ dysfunction.[6,7] The severity of AP can be assessed using the most commonly used being the Revised Atlanta Classification. This classification system categorizes AP into three severity grades: Mild: Patients with mild AP typically experience self-limited inflammation of the pancreas without organ failure or local complications. They may have mild to moderate abdominal pain, minimal systemic symptoms, and no evidence of organ dysfunction. Moderate: Moderate AP is characterized by the presence of transient organ failure or local complications that resolve within 48 hours. Organ failure refers to the dysfunction of one or more organs, such as the lungs, kidneys, or cardiovascular system. Local complications can include fluid collections, such as pseudocysts or necrosis, within or around the pancreas. Severe: Severe AP is associated with persistent organ failure that lasts for more than 48 hours. It can involve multiple organs and is often accompanied by significant systemic inflammation. Severe AP is also characterized by the presence of persistent local complications, such as infected necrosis or abscesses.

Accurate and timely diagnosis of AP is essential for effective management. Several diagnostic methods play a crucial role in confirming the diagnosis of AP. These include laboratory tests: Blood tests, such as serum amylase and lipase levels, are commonly used to assess pancreatic enzyme activity. Elevated levels of these enzymes are often observed in patients with AP. Other laboratory markers, such as C-reactive protein (CRP) and complete blood count (CBC), may also be measured to evaluate the severity of inflammation and monitor the patient's condition.

Imaging techniques: Various imaging modalities aid in the diagnosis and assessment of AP. Abdominal ultrasound is often the initial imaging test of choice, as it can detect gallstones and assess biliary obstruction. Computed tomography (CT) scans provide detailed anatomical information and can identify complications of AP, such as pancreatic necrosis or fluid collections. Magnetic resonance imaging (MRI) and endoscopic retrograde cholangiopancreatography (ERCP) may be utilized in specific cases to further evaluate the pancreas and its ductal system.[8-10]

The management of acute pancreatitis involves a multidisciplinary approach and may include various treatment modalities. In addition to pharmacological interventions, other treatment modalities may be employed: Fluid resuscitation: Adequate fluid replacement is crucial to maintain hydration and prevent complications associated with fluid loss, such as hypovolemia and organ failure. Nutritional support: In severe cases of AP, enteral or parenteral nutrition may be necessary to meet the patient's nutritional needs and support the healing process. Endoscopic or surgical interventions: In cases of complications, such as infected fluid collections or biliary obstruction, endoscopic or surgical interventions may be required to drain the collections or alleviate the obstruction.[11,12]

Given the global prevalence of AP and its potential complications, effective management strategies are of utmost importance. AP patients are generally intervened by drug therapy.[13] Drug therapy mainly uses statins, hydrochloric acid derivatives, and fenofibrate drugs.[14,15] Atorvastatin calcium can protect blood vessels and prevent the occurrence of inflammatory reactions, thereby protecting pancreatic tissue and preventing the development of severe pancreatitis.[16] Atorvastatin calcium can also regulate the level of CRP and has a better anti-infection effect. Fenofibrate is widely adopted in cardiovascular diseases and can significantly reduce patients' cholesterol levels.[17] Fenofibrate is often adopted in combination with statins, which has a good effect on hypercholesterolemia and hypertriglyceridemia and has a positive application value in the treatment of HTG-AP.[18,19] Fenofibrate can also increase the activity of lipoprotein lipase and activate the peroxidase receptor, which has a good anti-inflammatory effect.[20] Acipimox is a new anti-lipidation drug with a positive lipid-lowering effect, which can reduce the release of free fatty acids from adipose tissue reduce TG level and low-density lipoprotein cholesterol (LDL-C) level. Increasing the level of high-density lipoprotein (HDL) has a significant effect on hypertriglyceridemia. The use of a single drug has great side effects and poor therapeutic outcomes. At present, more and more patients are treated with drug combinations, having achieved good results. The combination of the two drugs in the treatment of HTG-AP has better clinical effects, fewer side effects, and high clinical application value.

The mechanism of action of these drugs in the context of AP involves their lipid-lowering effects and their potential anti-inflammatory and antioxidant properties, which may help mitigate pancreatic inflammation and reduce the risk of complications.

While several studies have investigated the use of lipid-lowering agents in AP, more research is needed to establish

their optimal use and efficacy in HTG-AP specifically. This study aims to address this gap in the current literature and provide valuable insights into the comparative effectiveness of these specific drugs in the treatment of HTG-AP.

MATERIALS AND METHODS

Subjects

150 HTG-AP patients admitted to the first hospital of Putian from June 2020 to December 2022 were enrolled. The ages of the patients ranged from 30 to 70 years. The mean age was approximately 48 years. The cohort consisted of 90 males and 60 females. This results in a male-to-female ratio of 3:2. Disease severity was evaluated using the APACHE II scoring system. Scores ranged from 5 to 20, with a higher score indicating more severe disease. The average APACHE II score was around 12. Serum triglyceride levels at admission ranged from 500 to 1500 mg/dL.

According to the use of different therapeutic drugs, they were divided into atorvastatin calcium (12 cases), acipimox (2 cases), fenofibrate (29 cases), fenofibrate + atorvastatin calcium (5 cases), fenofibrate + acipimoxx (11 cases), and no drug groups (91 cases). The remission and clinical indicators of patients with different drugs in the six groups were compared. It obtained approval from the Medical Ethics Committee.

Inclusion criteria: (1) complete medical records; (2) all patients were diagnosed with HTG-AP. (3) no contraindication to use drugs; (4) no other malignant tumors; (5) patients voluntarily participated in this trial and signed informed consent. Exclusion criteria: (1) incomplete medical records; (2) patients with vital organ diseases; (3) patients with hereditary diseases; (4) patients with immune system diseases; (5) patients with mental disorders, unable to communicate normally; (6) patients unwilling to participate in the trial.

Methods

Patient data were collected from electronic medical records. This included demographic information (age, sex), clinical data (diagnosis, duration of symptoms), and treatment details (type of medication, dosage, duration). Laboratory values such as serum amylase, triglycerides, cholesterol levels, white blood cell count, neutrophil count, C-reactive protein (CRP), and APACHE II scores were recorded at admission and monitored throughout the hospital stay.

All patients received basic treatment; the patients in no drug group were given a placebo for comparison, and the other groups were given atorvastatin calcium (20 mg/qn, oral), acipimox (0.25 g/time, twice daily, oral), fenofibrate (0.2 g/qn, oral), fenofibrate + atorvastatin calcium, fenofibrate + acipimox. The relief of abdominal pain, gastrointestinal function, and clinical indicators were observed.

The study protocol, including all methods and procedures, was rigorously reviewed and approved by the Medical Ethics Committee of the First Hospital of Putian. Before commencing the study, submit a detailed research proposal outlining the study objectives, design, participant recruitment strategy, data collection methods, and analysis plan. The proposal also included provisions for managing potential risks and ensuring participants' well-being. The Ethics Committee reviewed the proposal to ensure compliance with national and international ethical standards, including the Declaration of Helsinki and local regulations governing clinical research. Particular attention was paid to the ethical justification of the study, potential benefits and risks to participants, and the processes for obtaining informed consent.

Observation indicators

The general information of the patients was collected, including the average age and sex ratio. The length of hospital stay, the remission time of abdominal pain and gastrointestinal function, the highest value of amylase, triglyceride (TG), cholesterol, white blood cell (WBC) count, NEUT increase, CRP, and APACHEII and procalcitonin of the six groups were compared and analyzed.

Statistical processing

Excel 2016 was adopted to record and summarize the data. SPSS 20.0 software was adopted for data statistics and analysis. Mean ± standard deviation (**±s**) was presented as measurement data, and *t* test was adopted. Percentage (%) was the representation of count data, and χ^2 test was adopted. $P < .05$ was considered statistically meaningful.

RESULTS

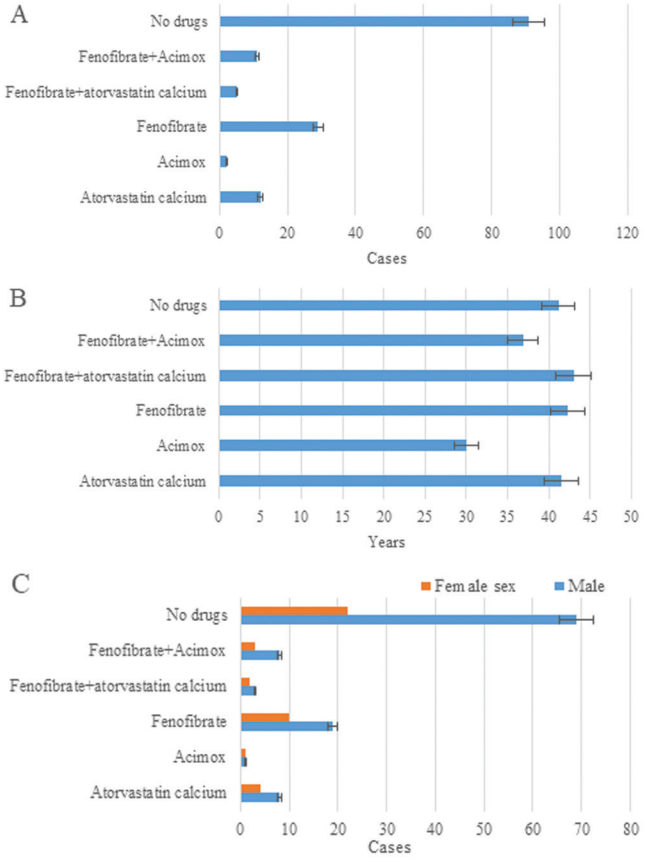
Comparative analysis of basic conditions of patients

Figure 1 shows the general data of the six groups of patients: A is the number of patients, B is the average age, and C is the number of men and women. The number of patients in the atorvastatin calcium group was 12, the acipimox group was 2, the fenofibrate group was 29, the fenofibrate + atorvastatin calcium group was 5, the fenofibrate + acipimox group was 11, and the number of patients in no drug group was 91. The average age of patients in the six groups was 41.58±5.67, 30.00±5.95, 42.28±5.21, 43.00±5.58, 36.91±5.62, and 41.15±5.82 years old, respectively. The male-to-female ratio was 8/4, 1/1, 19/10, 3/2, 8/3, and 69/22 in the six groups, respectively.

Comparative analysis of length of hospital stay and remission time of abdominal pain and gastrointestinal function of patients.

Figure 2 illustrates the comparison of the length of hospital stay and the remission time of abdominal pain and gastrointestinal function in the six groups. A is the length of hospital stay, B is the remission time of abdominal pain, and C is the remission time of gastrointestinal function. The length of hospital stay was 8.75 days in atorvastatin calcium group, 9.50 days in acipimox group, 7.62 days in the fenofibrate group, 8.40 days in fenofibrate + atorvastatin calcium group, 7.27 days in fenofibrate + acipimox group, and 7.77 days no drug group. The abdominal pain relief time of the six groups were 2.42, 2.50, 2.03, 2.40, 1.91, and 2.13 days, respectively. The remission time of gastrointestinal function in the six groups were 3.58, 3.50, 3.14, 3.60, 3.00,

Figure. 1 Contrast of basic conditions of patients. (A is the number of people, B is the average age, C is the number of men and women)



and 3.25 days, respectively. Patients in fenofibrate + acipimox and fenofibrate groups had shorter hospital stays, abdominal pain relief time, and relief time of gastrointestinal function as against other groups ($P < .05$).

Comparison of the highest value of amylase

Figure 3 illustrates that the highest value of amylase was 457.58 U/L in atorvastatin calcium group, 451.50 U/L in acipimox group, 333.83 U/L in fenofibrate group, 401.60 U/L in fenofibrate + atorvastatin calcium group, 371.73 U/L in fenofibrate + acipimox group, and 516.52 U/L in no drug group. The highest level of amylase in fenofibrate + acipimox and fenofibrate groups was markedly lower as against other groups ($P < .05$).

The highest TG value

Figure 4 shows that the highest TG value of patients was 26.91 U/L in atorvastatin calcium group, 17.54 U/L in acipimox group, 22.56 U/L in fenofibrate group, 20.57 U/L in fenofibrate + atorvastatin calcium group, 33.39 U/L in fenofibrate + acipimox group, and 22.80 U/L in no drug group. The highest TG value in the fenofibrate + acipimox group was clearly higher ($P < .05$).

Figure. 2 Contrast the length of hospital stay and remission time of abdominal pain and gastrointestinal function. (A is the length of hospital stay, B is the remission time of abdominal pain, C is the remission time of gastrointestinal function, * represents $P < .05$ compared with other groups).

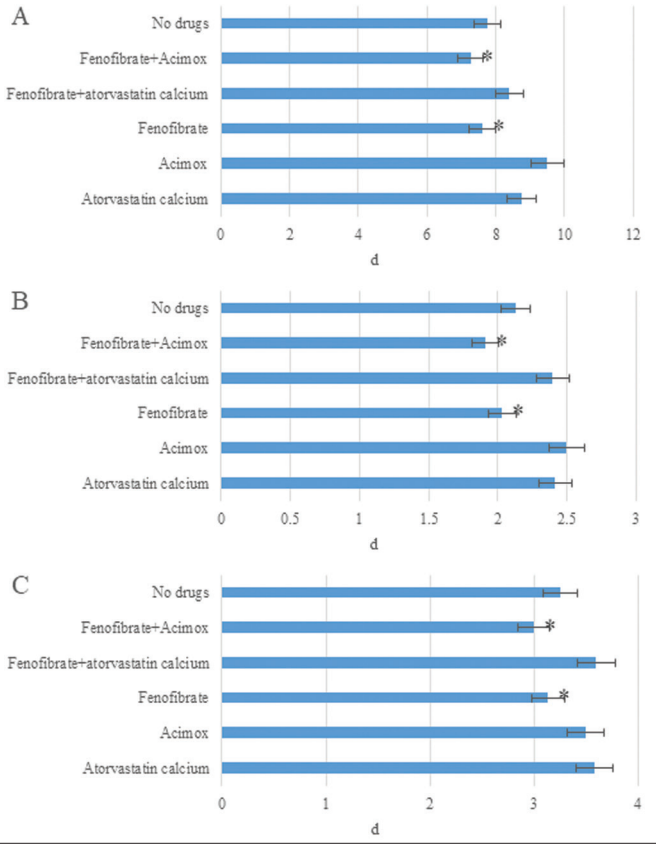


Figure. 3 Contrast of the highest value of amylase.

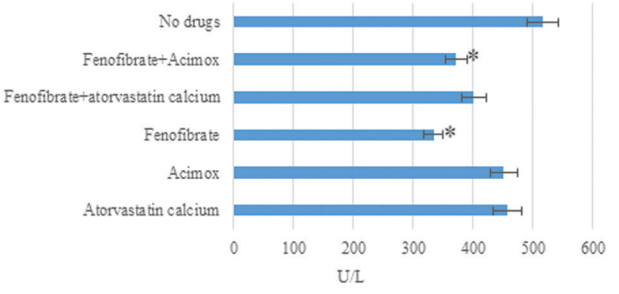


Figure. 4 Contrast of the highest TG value.

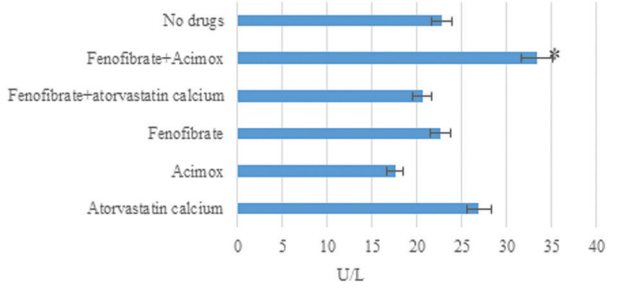


Figure 5. Contrast the highest value of cholesterol.

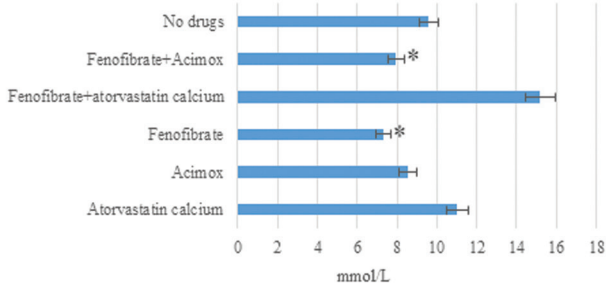
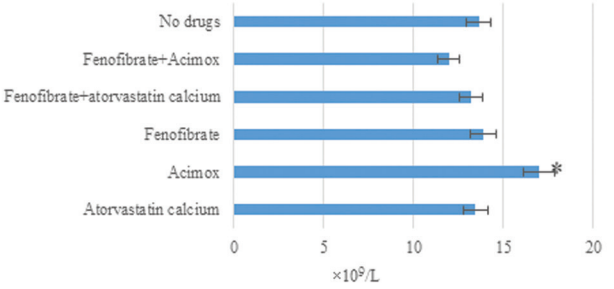


Figure 6. Contrast the highest value of WBC counts.



Comparison of highest cholesterol value

Figure 5 suggests that the highest cholesterol level was 11.02 mmol/L in atorvastatin calcium group, 8.55 mmol/L in acipimox group, 7.30 mmol/L in fenofibrate group, 15.17 mmol/L in fenofibrate + atorvastatin calcium group, 7.94 mmol/L in fenofibrate + acipimox group, and 9.57 mmol/L in no drug group. The highest level of cholesterol was lower in fenofibrate + acipimox and fenofibrate groups ($P < .05$).

Comparison of the highest value of WBC count

Figure 6 suggests that the highest WBC count was 13.46×10^9 in atorvastatin calcium group, 17.01×10^9 in acipimox group, 13.89×10^9 in fenofibrate group, 13.19×10^9 in fenofibrate + atorvastatin calcium group, 11.98×10^9 in fenofibrate +acipimox group, and 13.64×10^9 in no drug group. The highest value of WBC count in the acipimox group was higher ($P < .05$).

Comparison of the highest value of NEUT increase

Figure 7 reveals that the highest value of NEUT increase was 82.40% in the atorvastatin calcium group, 87.81% in the acipimox group, 80.68% in the fenofibrate group, 84.89% in fenofibrate + atorvastatin calcium group, 76.79% in fenofibrate +acipimox group, and 80.63% in no drug group. The highest value of NEUT increase in fenofibrate +acipimox, atorvastatin calcium, and fenofibrate groups was lower ($P < .05$).

The highest value of CRP

Figure 8 suggests that the highest value of CRP was 159.23 mg/L in atorvastatin calcium group, 117.92 mg/L in acipimox group, 106.29 mg/L in fenofibrate group, 131.92 mg/L in fenofibrate + atorvastatin calcium group, 147.28 mg/L in fenofibrate +acipimox group, and 136.15 mg/L in no drug group. The highest levels of CRP in fenofibrate and acipimox groups were lower ($P < .05$).

Comparison of procalcitonin

Figure 9 reveals that the procalcitonin level was 2.60 ng/ml in atorvastatin calcium group, 0.29 ng/ml in acipimox group, 0.31 ng/ml in fenofibrate group, 0.48 ng/ml in fenofibrate + atorvastatin calcium group, 0.67 ng/ml in fenofibrate +acipimox group, and 0.67 ng/ml in no drug group. The procalcitonin level in the atorvastatin calcium group was higher ($P < .05$).

Figure 7. Contrast of the highest value of NEUT increase.

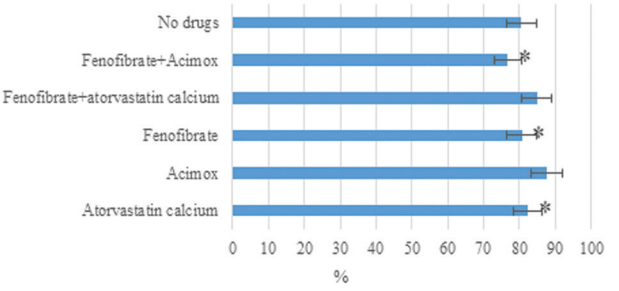


Figure 8. Contrast of the highest value of CRP.

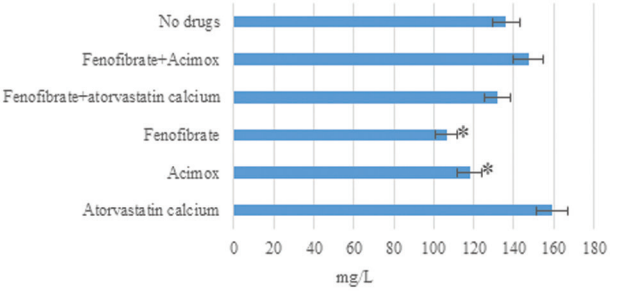


Figure. 9 Contrast of procalcitonin.

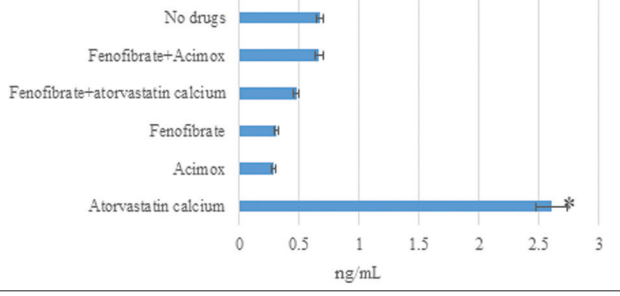
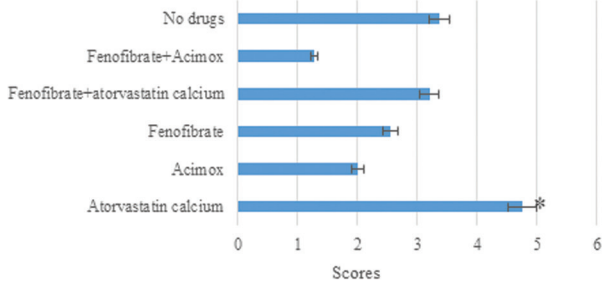


Figure. 10 Contrast of the highest APACHEII score.



Comparison of the highest APCACHEII score

Figure 10 suggests that the highest APACHEII score was 4.75 in atorvastatin calcium group, 2.00 in the acipimox group, 2.55 in the fenofibrate group, 3.20 in the fenofibrate + atorvastatin calcium group, 1.27 in fenofibrate +acipimox group, and 3.37 in no drug group. The highest score of APACHEII in the atorvastatin calcium group was higher ($P < .05$).

DISCUSSION

The incidence of AP is increasing, and the patients are gradually becoming younger, and many young people have AP.[21] The etiology of AP is complex, and the treatment and prognosis are also different, which requires targeted clinical treatment.[22] Drug therapy is the most common treatment at present, which can better control the disease, improve the prognosis, and improve the quality of life of patients.[23,24] Acipimox can inhibit the decomposition of adipose tissue and reduce the synthesis of triglyceride. Acipimox has a good effect on lowering blood lipids with fewer adverse reactions and higher safety. Fenofibrate is also a lipid-lowering drug, which can obviously reduce serum TG and cholesterol levels and can be adopted in HTG-AP.[25-27] Atorvastatin calcium is a statin lipid modulator that acts on the liver, can reduce cholesterol levels, and has positive anti-inflammatory effects.[28,29] Combination therapy can enhance the therapeutic outcome and reduce adverse drug reactions, with high safety and good clinical application effects.[30] The therapeutic outcomes of atorvastatin calcium, fenofibrate, and acipimox used alone or in combination were analyzed. The clinical indexes of different drugs in the treatment of HTG-AP were compared, and the relief of abdominal pain and recovery of gastrointestinal function in different groups were analyzed.

AP caused by hypertriglyceridemia is a rare and serious disease, which requires fluid resuscitation, pain control, intestinal rest, and treatment with TG-lowering drugs. Fenofibrate plus Atorvastatin has a positive therapeutic outcome.[31] AP is prone to a variety of complications, such as local or systemic inflammatory responses as well as organ failure, which occurs in about 20% of AP patients and is defined as "severe AP". Organ failure usually occurs in the early stage of AP, but can also occur later due to sepsis caused by infected pancreatic necrosis. Although common bile duct stones and alcohol abuse are the two most common causes of AP, hypertriglyceridemia is also prone to AP, and the incidence is between 2% and 5%. The treatment of pancreatitis caused by hypertriglyceridemia focuses on lowering TG levels. The efficacy of treating pancreatitis caused by hypertriglyceridemia may vary according to the cause of hypertriglyceridemia. Heparin combined with Atorvastatin can effectively treat HTG-AP and clearly reduce TG levels.[32] The result suggested that patients in fenofibrate +acipimox and fenofibrate groups had shorter hospital stay, relief time of abdominal pain and gastrointestinal function than patients in other groups. In addition, it was found that the highest value of TG was higher, while the highest value of cholesterol was lower in fenofibrate +acipimox group.

Atorvastatin Calcium is a member of the statin class, which primarily functions by inhibiting HMG-CoA reductase, an enzyme in the liver responsible for cholesterol synthesis. By reducing the production of cholesterol, Atorvastatin can decrease the levels of low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL), both of which are associated with cardiovascular disease and, potentially, the exacerbation of acute pancreatitis. Additionally, Atorvastatin has anti-inflammatory properties, which may be beneficial in reducing the inflammation associated with acute pancreatitis. Fenofibrate works by activating peroxisome proliferator-activated receptors (PPARs), particularly PPAR-alpha. This activation leads to an increase in the expression of genes involved in fatty acid oxidation, ultimately enhancing the breakdown of triglycerides. This reduction in triglyceride levels is particularly relevant in the context of HTG-AP, where high triglyceride levels can exacerbate the condition. Moreover, fenofibrate's anti-inflammatory effects may also help alleviate the inflammatory response in pancreatitis.Acipimox is a niacin derivative that works by inhibiting the release of free fatty acids from adipose tissue. By reducing the availability of free fatty acids, the liver produces less VLDL, subsequently leading to lower triglyceride levels. This mechanism is particularly useful in managing hypertriglyceridemia, a key factor in HTG-AP. Acipimox's role in reducing VLDL can be especially critical in preventing the exacerbation of pancreatitis due to high triglyceride levels.

The PPARa agonist fenofibrate may help to improve the condition of such patients. Bao et al. (2021)[33] found that fenofibrate plus octreotide acetate had better efficacy in the treatment of patients with HTG-AP and revealed the effect of the combination of the two drugs on NF-κB P65 from the perspective of signaling pathways. The synergistic inhibition proved that the combined treatment was beneficial to the control of inflammation, and protect the liver function, and improve the prognosis of patients. It is worthy of clinical promotion. Ozcelik et al. (2019)[34] evaluated the efficacy and safety of the combination of heparin, insulin, and fenofibrate in HTG-AP patients and found that the combination of insulin, heparin, and fenofibrate was safe and effective. It revealed that the highest values of amylase and NEUT increase were lower, and the highest values of WBC count, CRP, APACHEII score, and procalcitonin level were higher in fenofibrate +acipimox and fenofibrate groups as against other groups. It revealed that the combination therapy of fenofibrate and acipimox had great therapeutic advantages, good abdominal pain relief effects, short recovery time, and positive clinical application value.

Collectively, the above findings can be attributed to these mechanisms: Atorvastatin Calcium: Atorvastatin calcium belongs to the class of statin medications, primarily used for lipid-lowering purposes. In addition to their cholesterol-lowering effects, statins have been shown to have anti-inflammatory and antioxidant properties. These pleiotropic effects are attributed to the inhibition of the enzyme

3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, which plays a key role in cholesterol synthesis. By reducing cholesterol levels, atorvastatin calcium may help restore lipid homeostasis and alleviate pancreatic inflammation observed in HTG-AP. Furthermore, the anti-inflammatory and antioxidant properties of atorvastatin calcium may further contribute to the attenuation of systemic inflammation and the mitigation of pancreatic injury. Fenofibrate: Fenofibrate, a fibrate medication, primarily targets hypertriglyceridemia by activating peroxisome proliferator-activated receptor alpha (PPARα). PPARα activation leads to the upregulation of genes involved in lipid metabolism, resulting in decreased triglyceride levels and increased high-density lipoprotein (HDL) cholesterol levels. In the context of HTG-AP, fenofibrate's lipid-modulating effects may help normalize lipid metabolism, reducing the risk of recurrent episodes and providing long-term management of hypertriglyceridemia. By restoring lipid homeostasis, fenofibrate may contribute to the overall management of HTG-AP, potentially reducing pancreatic injury and improving patient outcomes. Acipimox: Acipimox, a niacin derivative, acts as a lipid-lowering agent by inhibiting lipolysis in adipose tissue, thereby reducing the release of free fatty acids into circulation. By reducing triglyceride and free fatty acid levels, acipimox may help alleviate the pancreatic injury associated with HTG-AP. Additionally, acipimox has been shown to improve insulin sensitivity and reduce insulin resistance, which may have additional benefits in the management of HTG-AP, given the association between insulin resistance and pancreatic inflammation.

Each of these medications has its own set of potential side effects, which should be carefully evaluated and monitored. For example, statins like atorvastatin calcium may be associated with muscle-related adverse events, liver function abnormalities, and, rarely, pancreatitis itself. Fenofibrate and acipimox may have side effects such as gastrointestinal disturbances, liver function abnormalities, and myopathy. Therefore, close monitoring of patients for any potential adverse effects is crucial during long-term treatment. Moreover, it is important to consider potential drug interactions with other medications that patients with HTG-AP may be prescribed. For instance, statins and fibrates can interact with certain medications, such as anticoagulants, leading to an increased risk of bleeding. Therefore, a comprehensive evaluation of a patient's medication profile and potential drug interactions is essential to ensure the safe and effective use of these drugs in the long-term management of HTG-AP.

However, age, lifestyle, and the severity of hypertriglyceridemia, might influence treatment outcomes in HTG-AP. Considering these factors can provide more personalized treatment insights and optimize patient care. Age and Lifestyle: The increasing incidence of AP among young individuals necessitates a thorough understanding of the impact of age on treatment outcomes. Younger patients may have different underlying risk factors and disease presentations compared to older individuals. Lifestyle factors, such as dietary habits and physical activity levels, can also vary among different age groups and influence the effectiveness of treatment strategies. Therefore, tailoring treatment approaches to address specific age-related characteristics and incorporating lifestyle modifications may enhance treatment outcomes in HTG-AP. Severity of Hypertriglyceridemia: The severity of hypertriglyceridemia plays a crucial role in the management of HTG-AP. Patients with extremely high triglyceride levels may require more aggressive interventions, such as combination therapy or specialized lipid-lowering procedures, in addition to pharmacotherapy. Understanding the relationship between baseline triglyceride levels and treatment response can guide clinicians in selecting the most appropriate treatment approach for individual patients.

The findings of this study have important implications for clinical practice in the management of HTG-AP. Patient Selection: Based on the study results, identifying patients with hypertriglyceridemia who are at a higher risk of developing AP and promptly initiating lipid-lowering therapy could be an effective approach. Consideration of patient characteristics, such as the severity of hypertriglyceridemia and potential underlying risk factors, can aid in patient selection for specific treatment options. Monitoring and Follow-up: Regular monitoring of lipid levels and other relevant parameters during treatment is crucial to assess treatment response and adjust therapy if needed. Developing guidelines or protocols for monitoring and follow-up of patients undergoing pharmacotherapy can help ensure optimal treatment outcomes and early detection of any potential complications.

The limitations of the study should be acknowledged. Small sample size: The study had a small sample size, which may limit the generalizability and statistical power of the results. Conducting larger studies with a more substantial number of participants would provide more robust findings. Geographic confinement: The study was limited to a specific geographic region, which may introduce geographical bias and restrict the applicability of the conclusions. Expanding the research scope to include multiple regions and diverse patient populations would enhance the external validity of the findings. Lack of long-term follow-up data: The study did not provide information on the long-term efficacy and safety of the treatment options. Future research should incorporate long-term follow-up to assess the sustained benefits and potential risks associated with the interventions. Lack of cost-effectiveness assessment: The study did not consider the cost-effectiveness of the treatment options. Future research should include economic evaluations to determine the cost-effectiveness of different treatment strategies and their impact on healthcare resource allocation.

Therefore, future research directions should focus on larger multicenter studies: Conducting larger multicenter studies involving diverse patient populations would strengthen the generalizability of the findings. Collaboration

among multiple institutions and regions can provide more comprehensive insights into the effectiveness of different treatment modalities for HTG-AP. Long-term efficacy and safety assessment: Future research should focus on evaluating the long-term efficacy and safety of the treatment options investigated in this study. Assessing treatment outcomes and potential complications over an extended period will provide a better understanding of the sustained benefits and risks associated with the interventions. Cost-effectiveness analysis: Incorporating cost-effectiveness analysis into future research would provide valuable information for healthcare decision-makers. Evaluating the economic implications of different treatment options can guide resource allocation and ensure efficient use of healthcare resources.

CONCLUSION

In conclusion, this study identified the increasing incidence of AP among young individuals and the variability in etiology. It highlighted the importance of considering patient characteristics such as age, lifestyle, and the severity of hypertriglyceridemia for personalized treatment approaches in HTG-AP. The findings suggest a promising approach to managing HTG-AP, but the study has limitations, including a small sample size and geographic confinement. Future research should address these limitations, incorporate long-term follow-up data, assess cost-effectiveness, and conduct larger multicenter studies to confirm and expand upon the current findings.

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