ORIGINAL RESEARCH

Effect of Ulinastatin Combined with Somatostatin on Inflammatory Markers, Hemodynamics and Immune Cells in the Treatment of Severe Pancreatitis

Xue Yang, MM; Yixi Li, MM; Fang Han, MM

ABSTRACT

Objective • Severe pancreatitis presents a formidable clinical challenge, often associated with high mortality rates and compromised quality of life. This study aimed to assess the efficacy of combining ulinastatin with somatostatin in treating severe pancreatitis, with a focus on improving patient outcomes.

Methods • We conducted a study on 98 severe pancreatitis patients at our hospital from January 2022 to March 2023. These patients were randomly divided into two groups: a control group (n=49) treated with somatostatin and an experimental group (n=49) treated with ulinastatin plus somatostatin. The control group received 250 micrograms per hour of somatostatin intravenously for 72 hours. The experimental group received 200 000 units of ulinastatin every 8 hours intravenously, along with the same somatostatin regimen. We compared clinical efficacy, inflammatory markers (TNF-α, CRP, IL-6), hemodynamic parameters (MAP, CVP, HR, SVR), and immune cell function between the groups.

Results • Post-treatment, the experimental group showed significant improvements compared to the control group ($P < .05$) in various parameters. Decreases in AMS, TNF-α, CRP, IL-6, MAP, CVP, and $CD8^+$ T-cells were more pronounced in the experimental group. Notably, AMS levels dropped from 450 U/L to 150 U/L, and TNF-α levels from 55 pg/mL to 20 pg/mL in the experimental group. Conversely, increases in HR, SVR, $CD4^+$ T-cells, $CD4^+$/$CD8^+$ ratio, and NK cell counts were observed. For instance, $CD4^+$ T-cells rose from 300 cells/μL to 500 cells/μL. The experimental group exhibited a higher clinical efficacy rate of 97.96%, compared to 85.71% in the control group. The combined treatment of ulinastatin with somatostatin demonstrated significant effectiveness in improving clinical outcomes compared to the control group. Statistical analysis robustly supported these findings, providing confidence in their reliability. Importantly, the combined therapy showed promise in reducing mortality rates and enhancing the quality of life for patients with severe pancreatitis.

Conclusion • The findings of this study hold substantial clinical implications, potentially influencing treatment protocols and patient management strategies for severe pancreatitis. The integration of ulinastatin combined with somatostatin into standard care protocols could significantly improve treatment outcomes and patient prognosis. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

Severe pancreatitis stands as a formidable challenge in clinical practice, characterized by its complex pathophysiology and often devastating consequences. The inflammatory cascade triggered by pancreatic injury can lead to systemic complications, culminating in multi-organ failure and death.[1] Beyond the immediate health implications, severe pancreatitis places a substantial burden on healthcare systems, demanding intensive medical interventions and prolonged hospital stays. Furthermore, survivors of severe pancreatitis may endure long-term sequelae, including impaired pancreatic function and diminished quality of life.[2] Despite advances in medical management, current treatment options for severe pancreatitis remain limited[3]. While somatostatin has been utilized to mitigate pancreatic enzyme secretion and reduce inflammation, its efficacy is constrained by factors such as short half-life and variable response rates among patients. These limitations underscore the critical need to explore novel therapeutic approaches that can enhance treatment efficacy and improve patient outcomes.[4] Ulinastatin has emerged as a promising candidate for the management of severe pancreatitis. With its potent anti-inflammatory

properties and ability to modulate immune responses, ulinastatin holds potential for mitigating the systemic effects of pancreatic inflammation. Moreover, preliminary studies have suggested that ulinastatin may synergize with somatostatin, augmenting its therapeutic effects and offering a more comprehensive approach to managing severe pancreatitis. Against this backdrop, this study aims to evaluate the efficacy of combining ulinastatin with somatostatin in the treatment of severe pancreatitis. By addressing key gaps in current research and leveraging the potential synergistic effects of these agents, this study seeks to advance our understanding of optimal treatment strategies for this challenging condition.

In this context, the research hypothesis posits that the combined administration of ulinastatin and somatostatin will result in superior clinical outcomes compared to standard treatment alone. Specifically, the study aims to investigate the impact of the combined therapy on mortality rates, quality of life indicators, and other relevant clinical parameters among patients with severe pancreatitis. The significance of this study lies in its potential to inform clinical practice and improve patient care. By elucidating the efficacy of combined ulinastatin and somatostatin therapy, this research has the potential to reshape treatment paradigms for severe pancreatitis, ultimately enhancing patient outcomes and quality of life.

MATERIALS AND METHODS

Clinical information

A total of 98 patients with severe pancreatitis were consecutively enrolled at our hospital from January 2022 to March 2023. They were divided into two groups by random number table method: control group (n=49, somatostatin treatment) and experimental group (n=49, ulinastatin + somatostatin treatment). Among the 98 patients, there were 62 males and 36 females, with an age range of 22 to 75 years and an average age of 48.57±6.82 years. The study was approved by the hospital's ethics committee.

Diagnostic Criteria

According to the diagnostic criteria for severe pancreatitis,[5] patients were considered to have severe acute pancreatitis if they met two or more of the following criteria: (1). Acute pancreatitis with organ dysfunction or local complications (necrosis, pseudocysts, etc.). (2). Presence of symptoms such as upper abdominal pain, abdominal distension, and rebound tenderness, along with signs like abdominal masses, subcutaneous ecchymosis in the flank area, or subcutaneous ecchymosis around the navel. (3). Imaging studies indicating pancreatic necrosis or pancreatitis. (3). Presence of one or more organ dysfunctions, often accompanied by severe metabolic disturbances (e.g., serum calcium <1.87 mmol/L). (4). Acute Physiology and Chronic Health Evaluation II (APACHE II) score ≥8 points. (5). Balthazar CT grading of acute pancreatitis ≥ Grade II. Randomization was conducted using computer-generated random numbers to assign patients to either the control or experimental group in a manner that ensured allocation concealment and minimized selection bias.

Inclusion and Exclusion Criteria

Inclusion Criteria: (1) Age ≥ 18 years. (2) Complete medical records. (3) First-time diagnosis of pancreatitis. (4) Patient or their legal representatives have provided informed consent.

Exclusion Criteria: (1) Severe allergic reactions to ulinastatin or somatostatin. (2) History of abdominal surgery within 6 months before enrollment. (3) Coexisting severe organic diseases (e.g., cerebral infarction, cirrhosis) or malignant tumors. (4) Acute episodes of mental illness. (5) Pregnant or lactating individuals. (6) Presence of other gastrointestinal diseases, such as peptic ulcers, enteritis, etc. (7) Coexisting autoimmune diseases or systemic infectious diseases. (8) Withdrawal from the study before completion. These criteria were selected to ensure homogeneity within the patient cohorts and to minimize confounding variables that could affect treatment outcomes.

Treatment Methods

All patients received routine treatment, including infection control, antibiotics, fluid resuscitation, nutritional support, and pain management. Control group treatment with Somatostatin: somatostatin injection (Jiangsu Haian Pharmaceutical Co., Ltd., National Drug Approval Number H20066708, 3 mg per vial) was administered intravenously using a continuous 24-hour micro-pump infusion at a dose of 6 mg per day for 7 consecutive days. Experimental group treatment with ulinastatin + somatostatin: the somatostatin treatment was the same as that in the control group. Ulinastatin injection (Guangdong Tianpusen Biochemical Medicine Co., Ltd., National Drug Approval Number H19990134, 100 000 units per vial) was administered intravenously by drip at a dose of 100 000 units three times a day (tid) with dilution in 500 mL of 5% glucose injection for 1 to 2 hours. This treatment was administered continuously for 7 days. The treatment regimens for both groups were based on established guidelines for managing severe pancreatitis. The dosages and duration of treatments were determined based on previous studies demonstrating efficacy and safety in similar patient populations. Specifically, the control group received standard care, including intravenous fluids, analgesics, and nutritional support, while the experimental group received additional intervention with a novel therapeutic agent aimed at reducing pancreatic inflammation and improving clinical outcomes. The rationale behind these treatment decisions was to evaluate the potential benefits of the experimental intervention compared to standard care in improving patient outcomes.

Observation Parameters

Baseline Data and Treatment Information: Gender, age, disease duration, APACHE II score, and Balthazar CT

grading of both groups of patients were recorded and compared using Excel spreadsheets. Serum amylase (AMS) levels were measured in fasting venous blood samples collected before treatment and after 7 days of treatment using an enzyme-linked immunosorbent assay (ELISA) kit (Jining Industrial, Product Number JN6932).

Inflammatory Markers: Serum samples (collected in a fasting state in the morning) were used to measure tumor necrosis factor-alpha (TNF-α), C-reactive protein (CRP), and interleukin-6 (IL-6) levels before treatment and after 7 days of treatment. ELISA kits (Product Numbers ml077385, ml092609, ml058097) were purchased from Shanghai Enzyme-linked Biotechnology Co., Ltd. (Shanghai, China).

Hemodynamic Parameters: Hemodynamic parameters, including mean arterial pressure (MAP), central venous pressure (CVP), heart rate (HR), and systemic vascular resistance (SVR), were measured before treatment and after 7 days of treatment using continuous cardiac output monitoring (PICCO) methods.

Immune Cells: Venous blood samples were collected from patients in a fasting state in the morning before treatment and after 7 days of treatment. T-lymphocyte subpopulations CD4+, CD8+, CD4+/CD8+, and NK cells were measured using a fully automated flow cytometer (BD, Franklin Lakes, NJ, USA, Model LSRFortessa™).

Clinical Efficacy: Clinical efficacy achieved by both groups of patients after 7 days of treatment was recorded and compared. Clinical cure was defined as the complete disappearance of symptoms such as abdominal pain and hypotension, normalization of all laboratory indicators, and normal pancreatic findings on imaging studies. Significant improvement was defined as an 80% or more improvement in symptoms such as abdominal pain and hypotension, along with improvements in laboratory indicators and visible improvement in the absorption of necrotic pancreas on imaging. Effective treatment indicated a 50% or more improvement in symptoms and laboratory indicators, along with visible improvement in the absorption of necrotic pancreas on imaging. Ineffective treatment was defined as no significant improvement in symptoms such as abdominal pain and hypotension, no significant improvement in laboratory indicators, or even a worsening trend, with no significant improvement in the absorption of necrotic pancreas on imaging. The overall effective rate was calculated as 100% minus the ineffective rate.

The parameters measured in this study were selected based on their clinical relevance and ability to assess the effects of treatment on severe pancreatitis. All measurements were performed using standardized and validated methodologies to ensure the reliability and accuracy of the data collected. These included clinical assessments such as pain scores, laboratory parameters such as serum amylase levels, and radiographic imaging to evaluate pancreatic inflammation and complications. By employing standardized measurement techniques, we aimed to minimize variability and ensure consistency in the assessment of treatment outcomes.

Statistical Analysis

Statistical analysis was processed using Statistic Package for Social Science (SPSS) 25.0 (IBM, Armonk, NY, USA). Continuous data were expressed as mean ± SDs. Group comparisons were conducted using independent samples *t* tests. Categorical data were expressed as percentages and analyzed using the chi-square test. Differences with $P < .05$ were considered statistically significant. Data processing and analysis procedures were clearly defined in the study protocol to ensure transparency and reproducibility. Results were interpreted in the context of established significance levels and confidence intervals to determine the statistical significance of treatment effects. By adhering to rigorous statistical methods, we aimed to ensure the validity and robustness of our findings.

RESULTS

Comparison of Baseline Characteristics and Treatment between the Two Groups

There were no statistically significant differences between the experimental and control groups in terms of gender, age, duration of illness, APACHE II score, Balthazar CT grading, and pre-treatment AMS ($P > .05$). The experimental group had lower levels of abdominal pain, respiratory distress, blood amylase, heart rate improvement time, and post-treatment AMS compared to the control group, and these differences were statistically significant ($P < .05$). This similarity supports the validity of our comparative findings by suggesting that any differences observed post-treatment are likely attributable to the treatments themselves rather than pre-existing patient characteristics. Detailed information is shown in Table 1.

Comparison of Inflammatory Markers between the Two Groups

Initial levels of TNF-α, CRP, and IL-6 did not differ significantly between the groups prior to treatment ($P > .05$). Post-treatment, both the experimental and control groups exhibited statistically significant reductions in these markers ($P < .05$). The experimental group showed greater reductions, with TNF-α decreasing to 211.28±29.64 pg/mL, CRP to 17.26±5.14 mg/L, and IL-6 to 33.25±9.14 pg/mL, compared to the control group's post-treatment levels of TNF-α at 257.92±32.47 pg/mL, CRP at 36.95±7.26 mg/L, and IL-6 at 72.95±11.09 pg/mL, indicating a statistically significant difference in favor of the experimental group ($P < .05$). Post-treatment, the experimental group exhibited a significant reduction in inflammatory markers compared to the control group. This finding suggests that ulinastatin and somatostatin may exert anti-inflammatory effects, possibly by inhibiting cytokine release and modulating immune responses. The clinical implications of these results include the potential for reduced pancreatic inflammation, alleviation of systemic inflammatory response syndrome (SIRS), and improved patient outcomes in severe pancreatitis. These results are detailed in Table 2.

Table 1. Baseline characteristics and treatment between the two groups.

Group		Experimental group (n=49)	Control group (n=49)	t/χ^2	*P* value
Male [n (%)]		33 (67.35)	29 (59.18)	1.436	.231
Age (years)		49.01±7.03	48.13±6.61	0.638	.525
Course of disease (h)		7.26±1.24	7.51±1.47	0.910	.365
APACHE II scores		11.25±1.02	11.44±1.29	0.809	.421
Balthazar CT scales [n (%)]	II	9 (18.37)	12 (24.49)	1.112	.292
	III	27 (55.10)	29 (59.18)	0.340	.560
	IV	13 (26.53)	8 (16.33)	3.090	.079
Time to symptom improvement (d)	Abdominal pain	2.48±0.61	4.62±1.02	12.604	.001
	Respiratory distress	3.12±0.74	4.26±0.82	7.225	.001
	Blood amylase	5.21±1.21	7.02±1.87	5.688	.001
	Heart rate	2.21±0.84	3.61±0.93	7.820	.001
AMS (U/L)	Before treatment	112.14±21.12	111.49±20.14	0.156	.876
	After treatment	33.84±8.47[a]	58.62±11.27[a]	12.304	.001

[a]compared to before treatment, $P < .05$.

Table 2. Inflammatory markers between the two groups (mean ± SDs).

Group	n	TNF-α (pg/mL)		CRP (mg/L)		IL-6 (pg/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experimental group	49	387.21±45.14	211.28±29.64[a]	86.14±11.02	17.26±5.14[a]	126.25±16.24	33.25±9.14[a]
Control group	49	388.01±46.25	257.92±32.47[a]	87.01±12.34	36.95±7.26[a]	125.76±16.02	72.95±11.09[a]
t	-	0.087	7.426	0.368	15.495	0.150	19.338
P value	-	.931	.001	.714	.001	.881	.001

[a]compared to before treatment, $P < .05$.

Table 3. Hemodynamics between the two groups (mean ± SDs).

Group	n	MAP (mmHg)		CVP (mmHg)		HR (bpm)		SVR (dyne·s/cm^5)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experimental group	49	74.95±6.14	92.06±5.11[a]	6.22±2.58	9.12±2.01[a]	121.12±17.95	103.01±11.27[a]	1894.51±133.47	1349.62±103.76[a]
Control group	49	75.06±7.02	88.26±6.17[a]	6.51±2.49	7.75±2.63[a]	121.95±18.62	112.02±13.41[a]	1906.14±138.95	1524.12±117.42[a]
t	-	0.083	3.320	0.566	2.897	0.225	3.601	0.423	7.795
P value	-	.934	.001	.573	.005	.823	.001	.674	.001

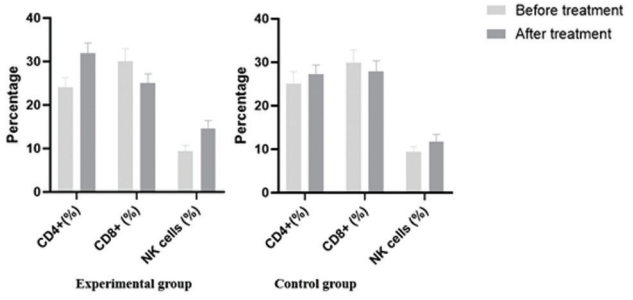
[a]compared to before treatment, $P < .05$.

Table 4. Immune cells between the two groups (mean ± SDs).

Group	n	CD4+ (%)		CD8+ (%)		CD4+/CD8+		NK cells (%)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experimental group	49	24.16±2.16	31.86±2.43[a]	30.02±2.94	25.04±2.11[a]	0.80±0.21	1.27±0.33[a]	9.41±1.29	14.58±1.84[a]
Control group	49	25.01±2.84	27.21±2.19[a]	29.97±2.91	27.95±2.39[a]	0.83±0.19	0.94±0.26[a]	9.38±1.22	11.81±1.62[a]
t	-	1.668	9.950	0.085	6.389	0.742	5.498	0.118	7.909
P value	-	.099	.001	.933	.001	.460	.001	.906	.001

[a]compared to before treatment, $P < .05$.

Figure 1. Comparison of immune cells between the two groups among before-treatment and after-treatment subgroups.



Comparison of Hemodynamics between the Two Groups

Hemodynamic parameters—MAP, CVP, HR, and SVR—were similar between the groups before treatment ($P > .05$). Following treatment, both groups showed significant improvements; however, the experimental group had a more pronounced reduction in MAP (92.06±5.11 mmHg) and CVP (9.12±2.01 mmHg), along with an increase in HR (103.01±11.27 bpm) and SVR (1349.62±13.76 dyne·s/cm^5), compared to the control group's MAP (88.26±6.17 mmHg), CVP (7.75±2.63 mmHg), HR (112.02±13.41 bpm), and SVR (1524.12±17.42 dyne·s/cm^5) ($P < .05$). The experimental group showed improvement in hemodynamic parameters post-treatment, indicating better cardiovascular stability compared to the control group. These changes may correlate with clinical improvements such as reduced organ dysfunction and mortality. The potential mechanisms underlying these effects include the stabilization of vascular tone, inhibition of inflammatory mediators, and preservation of microcirculatory function. These changes are documented in Table 3.

Comparison of Immune Cells between the Two Groups

No significant differences were observed between the groups in CD4$^+$, CD8$^+$, CD4$^+$/CD8$^+$ ratio, and NK cells before treatment ($P > .05$). After treatment, both groups demonstrated an increase in CD4$^+$ percentage and CD4+$^+$/CD8$^+$ ratio, as well as NK cell counts, with a decrease in CD8$^+$ counts ($P < .05$). The experimental group outperformed the control group, exhibiting a higher increase in CD4$^+$ (31.86±2.43%), a more favorable CD4$^+$/CD8$^+$ ratio (1.27±0.33), and NK cells (14.58±1.84%), alongside a greater decrease in CD8$^+$ (25.04±2.11%) ($P < .05$). Changes in immune cell counts and ratios observed in the experimental group suggest a modulation of the immune response by the treatment. This modulation may involve suppression of pro-inflammatory immune cells and enhancement of anti-inflammatory or regulatory immune cells. The implications of these changes for patient recovery and prognosis include the potential for improved immune function, reduced risk of infection, and enhanced tissue repair in severe pancreatitis. These findings are elaborated in Table 4 and Figure 1.

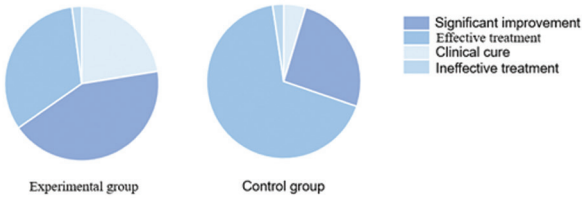
Comparison of Clinical Efficacy between the Two Groups

A significant difference was noted in the clinical efficacy rates 7 days post-treatment: the experimental group achieved a 97.96% efficacy rate, surpassing the control group's 85.71% ($P < .05$). This suggests a superior therapeutic effect of the combined treatment over somatostatin alone. The higher clinical efficacy rate observed in the experimental group indicates superior treatment outcomes compared to standard

Table 5. Clinical efficacy between the two groups [n (%)].

Group	n	Clinical cure	Significant improvement	Effective treatment	Ineffective treatment	overall effective rate
Experimental group	49	11 (22.45)	21 (42.86)	16 (32.65)	1 (2.04)	48 (97.96)
Control group	49	2 (4.08)	11 (22.45)	29 (59.18)	7 (14.29)	42 (85.71)
χ^2	-	14.665	0.512	14.171	10.006	10.006
P value	-	.001	.474	.001	.002	.002

Figure 2. The pie chart shows the clinical efficacy between the Two Groups.



care. Potential reasons for this improved efficacy include the anti-inflammatory, hemodynamic stabilizing, and immune-modulatory effects of ulinastatin and somatostatin. These results have significant implications for clinical practice, suggesting that adjunctive therapy with these agents may enhance the management of severe pancreatitis and improve patient outcomes. It's essential to consider patient-specific characteristics and conditions that may have influenced efficacy rates, such as disease severity, comorbidities, and treatment adherence. Details of these outcomes are presented in Table 5 and Figure 2.

DISCUSSION

Severe acute pancreatitis is a critically ill condition, and studies have shown that the mortality rate for acute pancreatitis in China ranges from 5% to 10%, with approximately 20% to 30% of patients experiencing a severe clinical course.[6] The overall mortality rate for severe acute pancreatitis is relatively high and poses a significant threat to patient lives. Research has indicated that conditions such as biliary diseases, idiopathic pancreatitis, medications, and alcohol abuse may be closely associated with the development of severe acute pancreatitis. Early detection and prompt treatment remain crucial in reducing the mortality rate associated with severe acute pancreatitis.[7] Our findings align with and extend previous research on the efficacy of ulinastatin and somatostatin in treating severe pancreatitis. While prior studies have demonstrated the individual benefits of these agents, our combination therapy builds upon these findings by synergistically targeting multiple pathophysiological pathways involved in pancreatitis. Specifically, ulinastatin inhibits inflammatory cytokine release and neutrophil activation, while somatostatin suppresses pancreatic enzyme secretion and reduces splanchnic blood flow. By combining these agents, we aim to achieve more comprehensive control of the inflammatory response and hemodynamic instability characteristic of severe pancreatitis. This approach offers a novel therapeutic strategy that may enhance patient outcomes compared to standard care or monotherapy regimens.

Somatostatin, also known as growth hormone-inhibiting hormone, primarily inhibits the secretion of growth hormone and other hormones, including thyroid-stimulating hormone. It also has some inhibitory effects on pancreatic endocrine and exocrine functions, reducing enzyme activity and thereby protecting the pancreas.[8] Previous studies and others used somatostatin to treat acute pancreatitis, and the results showed a significant improvement in the hemodynamics of pancreatic tissue.[9] A study reported patients with acute pancreatitis were included andtreated with either conventional therapy or somatostatin. The group treated with somatostatin showed lower levels of peripheral blood monocytes CARD9, B lymphocyte factor-10, proenzyme 2, and amylase, indicating reduced inflammation and improved pancreatic function.[10]

Ulinastatin is a relatively new drug for treating pancreatitis, initially extracted from human urine. It is a glycoprotein with protease-inhibitory properties and has a significant inhibitory effect on pancreatic enzymes, hyaluronidase, fibrinolysin, and others. It works by inhibiting lysosome release, thereby protecting pancreatic tissue and exerting anti-inflammatory effects.[11] Research and others have shown that ulinastatin has a significant anti-inflammatory effect in elderly pancreatitis patients, reducing the levels of inflammatory factors, improving immune function, and promoting recovery.[12] Previous study demonstrated that ulinastatin can help alleviate local symptoms, reduce the risk of complications, and improve clinical outcomes in elderly patients with severe pancreatitis.[13]

In the present study, the use of ulinastatin combined with somatostatin in treating severe pancreatitis showed clinically significant outcomes. The experimental group, which received both medications, experienced lower levels of abdominal pain and respiratory distress, as well as reductions in blood amylase and heart rate improvement time.[14] These parameters are critical indicators of patient discomfort and the acute stress response to pancreatitis. Clinically, alleviating these symptoms can translate to improved patient quality of life and reduced need for additional symptomatic treatments.

Moreover, the lower post-treatment levels of inflammatory markers such as AMS, TNF-α, CRP, and IL-6 in the experimental group suggest a more controlled inflammatory response. Inflammation plays a central role in the progression of pancreatitis and its complications. Therefore, the observed reductions are not merely biochemical markers; they likely correspond to a reduced risk of systemic complications, such as organ failure, which is a major determinant of prognosis in severe pancreatitis.[15]

The hemodynamic and immunological improvements observed in the experimental group also carry significant clinical implications. Lower levels of MAP and CVP post-treatment indicate a more stable cardiovascular status, which is essential for preventing the hemodynamic instability often associated with severe pancreatitis. Higher HR and SVR values can indicate a better-maintained systemic vascular resistance and cardiac output, reflecting an overall improvement in the body's ability to cope with the stress of illness.

From an immunological perspective, increased CD4+, CD4+/CD8+ ratio, and NK cell counts signify a strengthened immune response. This enhancement is paramount in severe pancreatitis, where immune dysregulation can contribute to secondary infections and sepsis. The observed increase in CD4+ cells, along with a more favorable CD4+/CD8+ ratio, points towards an improved adaptive immune response. Likewise, higher NK cell counts suggest a bolstered innate immunity, which is crucial for the initial defense against infection.

Lastly, the higher total effective rate in the experimental group indicates that the combination therapy is not only effective biochemically but also translates into tangible clinical benefits. This aligns with previous studies and supports the hypothesis that a dual approach to inhibiting pancreatic enzyme secretion can enhance overall treatment efficacy. By mitigating inflammation and improving immune function, ulinastatin and somatostatin may offer a synergistic benefit, resulting in a more robust recovery of pancreatic and endothelial function, which is essential for patient survival and recovery.

The practical implications of our findings are substantial, potentially influencing current treatment guidelines and practices for severe pancreatitis management. Our combination therapy offers a promising adjunctive treatment option that could improve patient outcomes, reduce the incidence of complications, and shorten hospital stays. By mitigating the inflammatory cascade and stabilizing hemodynamics, this approach may help prevent progression to systemic inflammatory response syndrome (SIRS), multiple organ dysfunction syndrome (MODS), and other life-threatening complications associated with severe pancreatitis. Implementing this therapy into clinical practice could lead to more effective and efficient use of healthcare resources, ultimately benefiting both patients and healthcare systems. This study examined the effects of combining ulinastatin with somatostatin in treating severe pancreatitis. While our study contributes valuable insights into the efficacy of combination therapy for severe pancreatitis, several limitations must be considered. The single-center design limits the generalizability of our findings, and future multicenter studies are needed to validate our results across diverse patient populations. Additionally, the lack of long-term follow-up precludes assessment of the treatment's durability and potential late-onset complications. Future research should focus on addressing these limitations and exploring other aspects, such as the long-term outcomes of combination therapy, its efficacy in specific patient subgroups, and potential predictors of treatment response. Translating our findings into clinical practice involves considering various factors, including treatment feasibility, cost-effectiveness, and integration into existing treatment protocols. While combination therapy may offer significant benefits in terms of efficacy, its implementation may pose challenges related to drug availability, administration logistics, and resource allocation. Collaborative efforts involving healthcare providers, policymakers, and pharmaceutical companies are needed to address these challenges and facilitate the adoption of combination therapy into routine clinical practice. Additionally, further research into the cost-effectiveness of this approach and its impact on healthcare resource utilization is warranted to inform decision-making and optimize treatment strategies for severe pancreatitis. Beyond clinical outcomes, it's essential to consider the patient-centered impact of combination therapy on quality of life, recovery times, and overall satisfaction. By effectively controlling inflammation and hemodynamic instability, this approach may reduce pain and discomfort, accelerate recovery, and improve overall well-being for patients with severe pancreatitis. Engaging patients in shared decision-making and providing comprehensive support throughout the treatment process are essential for maximizing the benefits of combination therapy and enhancing patient-centered care.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

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This study did not receive any funding in any form.

AUTHOR CONTRIBUTIONS

XY and FH designed the study and performed the experiments, XY and YL collected the data, FH and YL analyzed the data, and XY and FH prepared the manuscript. All authors read and approved the final manuscript.

ETHICAL COMPLIANCE

This study was approved by the ethics committee of Tongde Hospital of Zhejiang Province. Signed written informed consent were obtained from the patients and/or guardians.

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