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Article

Effectiveness of Ulinastatin in Combination with Amino Acid Solutions in Patients with Sepsis

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Abstract: Sepsis remains one of the leading causes of mortality in intensive care units, particularly in obstetric pathology. Despite advances in modern treatment methods, mortality rates remain high due to the complex pathogenesis of sepsis. The systemic inflammatory response, characterized by excessive production of pro-inflammatory cytokines such as IL-6 and TNF-α, plays a central role in the development of multiple organ dysfunction. Ulinastatin, a protease inhibitor with pronounced anti-inflammatory and organ-protective properties, has shown promise in modulating the inflammatory cascade. At the same time, specialized amino acid solutions provide metabolic support, improve nitrogen balance, and restore immune function. The combined use of ulinastatin and amino acid solutions may represent a synergistic therapeutic strategy. This study evaluates the clinical efficacy of this combination in patients with sepsis based on cytokine dynamics, organ dysfunction (SOFA score), and mortality outcomes.

Keywords: Sepsis, Obstetric Sepsis, Ulinastatin, Amino Acid Solutions, Cytokines, IL-6, TNF-A, SOFA, Intensive Care

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1. Introduction

Sepsis continues to be one of the leading causes of mortality in intensive care units, especially in obstetric patients. Although modern treatment methods have been introduced, mortality rates remain high due to the complex pathogenesis of the disease [1], [2]. The systemic inflammatory response, accompanied by excessive production of pro-inflammatory cytokines such as IL-6 and TNF-α, leads to multiple organ dysfunction and poor outcomes. Pathogenetic therapy is of particular importance in this context [3]. Ulinastatin (Roan), a protease inhibitor, has significant anti-inflammatory and organ-protective effects. In parallel, specialized amino acid solutions play an important role by providing metabolic support, improving nitrogen balance, and restoring immune function. The combined administration of ulinastatin and amino acid solutions is considered a promising therapeutic approach, as it combines anti-inflammatory and metabolic effects, potentially improving treatment efficacy and clinical outcomes [4].

Objective

To evaluate the clinical efficacy of ulinastatin in combination with amino acid solutions in patients with sepsis, based on the dynamics of cytokines (IL-6, TNF-α), organ dysfunction scores (SOFA), and mortality.

2. Materials and Methods

Study design: A prospective comparative study was conducted in the intensive care unit. A total of 45 patients with sepsis were included between 2022 and 2024.

Inclusion criteria:

a. Confirmed diagnosis of sepsis according to Sepsis-3 criteria.
b. Age 18–55 years.
c. Presence of systemic inflammatory response and multiple organ dysfunction.

Group distribution: Patients were randomly assigned into 3 groups of 15 each:

a. Group 1 (control): Standard sepsis therapy.
b. Group 2 (ulinastatin): Standard therapy + ulinastatin (Roan) 300,000 U/day IV.
c. Group 3 (combination): Standard therapy + ulinastatin (Roan) 300,000 U/day IV + amino acid solutions (Alvezin® or analogs) 1.0–1.5 g/kg/day.

Assessment methods:

a. Clinical indicators: ICU length of stay, duration of mechanical ventilation, mortality.
b. Laboratory parameters: IL-6 and TNF-α levels measured by ELISA before and on day 7 of treatment.
c. Organ dysfunction: SOFA score before treatment and on day 7.

3. Results

Dynamics of pro-inflammatory cytokines: IL-6 and TNF-α levels were comparable across all groups at baseline [5], [6]. Therapy resulted in a significant reduction in these markers, most pronounced in the combination group ($p < 0.05$). "Therapy resulted in a significant reduction in IL-6 and TNF-α levels, with the most pronounced effect in the combination group ($p < 0.05$), see Table 1."

Table 1. Dynamics of IL-6 and TNF-α levels before and after treatment in different groups.

Parameter	Group 1 (Control)	Group 2 (Ulinastatin)	Group 3 (Combination)
IL-6 before	220 ± 25	225 ± 30	230 ± 28
IL-6 after	180 ± 20	120 ± 15	85 ± 10
TNF-α before	95 ± 10	98 ± 11	96 ± 12
TNF-α after	80 ± 9	55 ± 7	38 ± 6

SOFA score dynamics: The control group showed only slight improvement, whereas the ulinastatin group showed better outcomes. The combination group achieved the greatest reduction in SOFA score ($p < 0.05$). "The greatest improvement in SOFA scores was also observed in the combination group ($p < 0.05$), see Table 2."

Table 2. Changes in SOFA scores before and after treatment across study groups.

Group	Before treatment	After treatment
Control	9.2 ± 1.1	7.5 ± 1.0
Ulinastatin	9.5 ± 1.2	6.0 ± 0.9
Combination	9.4 ± 1.0	4.8 ± 0.7

Mortality: The highest mortality was observed in the control group (26.7%), lower in the ulinastatin group (13.3%), and minimal in the combination group (6.7%). "Mortality analysis revealed the highest rate in the control group and the lowest in the combination group, see Table 3."

Table 3. Mortality rates in patients with sepsis by treatment group.

Group	Mortality
Control	26.7% (4/15)
Ulinastatin	13.3% (2/15)
Combination	6.7% (1/15)

4. Discussion

The results confirm that ulinastatin exerts a strong anti-inflammatory effect in sepsis patients, demonstrated by significant reductions in IL-6 and TNF-α levels [7], [8]. This aligns with previous studies reporting its ability to inhibit protease activity and suppress excessive cytokine release. Notably, the combination of ulinastatin and amino acid solutions provided the greatest clinical benefits, including the largest reduction in cytokines, improved SOFA scores, and the lowest mortality rate (6.7%) [9], [10], [11]. The likely mechanism involves synergistic effects: ulinastatin mitigates inflammation and tissue damage, while amino acids support metabolism, restore nitrogen balance, enhance protein synthesis, and boost immune response [12], [13]. Therefore, combination therapy not only attenuates systemic inflammation but also optimizes metabolic processes, which is critical in the hypercatabolic state of sepsis [14], [15]. From a clinical standpoint, these findings suggest broader application of this therapeutic approach. However, larger multicenter studies are required to validate these results.

5. Conclusion

Ulinastatin demonstrated pronounced anti-inflammatory effects in sepsis treatment, contributing to reduced IL-6 and TNF-α levels, improved SOFA scores, and lower mortality. The combined administration of ulinastatin with amino acid solutions was the most effective, achieving:

a. Greater reductions in pro-inflammatory cytokines.
b. Significant improvements in organ function.
c. Minimal mortality (6.7%). Thus, incorporating ulinastatin with amino acid solutions into sepsis therapy is pathogenetically justified and a promising strategy for improving patient outcomes.

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