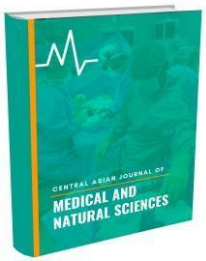

CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
https://cajmns.centralasianstudies.org/index.php/CAJMNS
Volume: 06 Issue: 04 | October 2025 ISSN: 2660-4159

.

Article

Roan (Ulinastatin) in the Complex Therapy of Obstetric Sepsis: Effects on IL-6 and TNF-α Levels and Clinical Outcomes

Gulmira Amudullaevna Nurullaeva[1], Aybek Raimberganovich Atashov[2]

1. Master's student in Anesthesiology and Resuscitation, Department of Pediatric Surgery, Anesthesiology and Resuscitation, Tashkent Medical Academy, Urgench Branch.
2. Associate Professor, Candidate of Medical Sciences, Department of Pediatric Surgery, Anesthesiology and Resuscitation, Tashkent Medical Academy, Urgench Branch.

Abstract: Obstetric sepsis is a leading cause of maternal morbidity and mortality worldwide, largely due to systemic inflammatory response and cytokine storm. This study evaluated the effectiveness of Roan (ulinastatin), a protease inhibitor, as part of complex therapy for obstetric sepsis. A total of 40 patients with moderate obstetric sepsis were enrolled and divided into two groups: standard therapy plus Roan (100,000 IU intravenously twice daily for five days) and standard therapy alone. Key clinical parameters, laboratory indices, and cytokine levels (IL-6 and TNF-α) were assessed on days 1 and 7. By day 7, the Roan group showed significant reductions in IL-6 (58%) and TNF-α (52%) compared to the control group (24% and 19% reductions, respectively; $p<0.05$). Clinical stabilization occurred 2.3 days earlier, and hospitalization was shortened by 3.1 days in the Roan group. These findings demonstrate that Roan effectively suppresses excessive inflammation, improves clinical outcomes, and is well tolerated. The study supports incorporating Roan into intensive care protocols for obstetric sepsis, while highlighting the need for larger multicenter trials to validate dosage, duration, and long-term outcomes.

Keywords: Obstetric Sepsis, Roan, Ulinastatin, IL-6, TNF-α, Cytokine Storm

1. Introduction

Obstetric sepsis remains one of the leading causes of maternal mortality. The high fatality rate is associated with a pronounced systemic inflammatory response and the development of multiple organ failure [1]. One of the key pathogenetic mechanisms is the excessive production of pro-inflammatory cytokines, including interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), which leads to the so-called cytokine storm [2], [3].

Protease inhibitors, such as ulinastatin, are capable of suppressing the excessive inflammatory response by reducing cytokine levels and stabilizing hemodynamics. Roan is a modern representative of this group, with high biological activity and a favorable safety profile. However, data on its use specifically in obstetric sepsis remain limited [4].

The aim of the study was to evaluate the effect of Roan on IL-6 and TNF-α levels, as well as clinical outcomes in patients with obstetric sepsis. Obstetric sepsis remains one of the most critical complications in maternal health, ranking among the leading causes of maternal mortality worldwide. Its high fatality rate is attributed to a complex interplay of systemic inflammatory responses, rapid progression to multiple organ failure, and challenges in timely diagnosis and treatment [5], [6]. The pathogenesis of obstetric sepsis is characterized by an uncontrolled release of pro-inflammatory cytokines—most notably

Citation: Nurullaeva G. A., Atashov A. R. Roan (Ulinastatin) in the Complex Therapy of Obstetric Sepsis: Effects on IL-6 and TNF-α Levels and Clinical Outcomes. Central Asian Journal of Medical and Natural Science 2025, 6(4), 1984-1987.

Received: 30th Jun 2025
Revised: 11th Jul 2025
Accepted: 31th Jul 2025
Published: 21st Aug 2025

interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α)—which trigger the so-called cytokine storm. This cascade not only exacerbates systemic inflammation but also significantly worsens clinical prognosis, especially in patients who lack rapid access to advanced intensive care [7].

2. Materials and Methods

- Study design: Prospective, controlled.
- Patients: 40 women with moderate obstetric sepsis hospitalized in the intensive care unit.
- Inclusion criteria: Confirmed diagnosis of obstetric sepsis, age 18–45 years, postpartum or post-abortion period.
- Exclusion criteria: Septic shock at admission, severe comorbid liver and kidney diseases, allergy to ulinastatin.

Treatment groups

- Main group (n=20) — standard therapy (antibiotics, infusion therapy, symptomatic correction) + Roan 100,000 IU intravenously twice daily for 5 days.
- Control group (n=20) — standard therapy only.

Evaluation parameters

- Clinical: body temperature, heart rate, blood pressure, urine output.
- Laboratory: leukocyte count, C-reactive protein.
- Cytokines (IL-6, TNF-α): measured by ELISA on days 1 and 7.

Statistical analysis: Student's t-test was used; differences were considered significant at $p<0.05$.

3. Results and Discussion

By day 7 of therapy in the main group, IL-6 decreased from 76.4±8.2 pg/ml to 32.1±5.7 pg/ml (58% reduction, $p<0.05$), and TNF-α decreased from 54.7±6.9 pg/ml to 26.3±4.8 pg/ml (52% reduction, $p<0.05$). Figure 1 in the control group, the decrease was 24% and 19% respectively ($p<0.05$), which was significantly less than in the main group [8].

Clinical improvement (normalization of temperature, stabilization of hemodynamics) occurred on average 2.3±0.4 days faster in the main group ($p<0.05$). (Figure 2) The duration of hospitalization was reduced by 3.1±0.7 days compared to the control group [9].

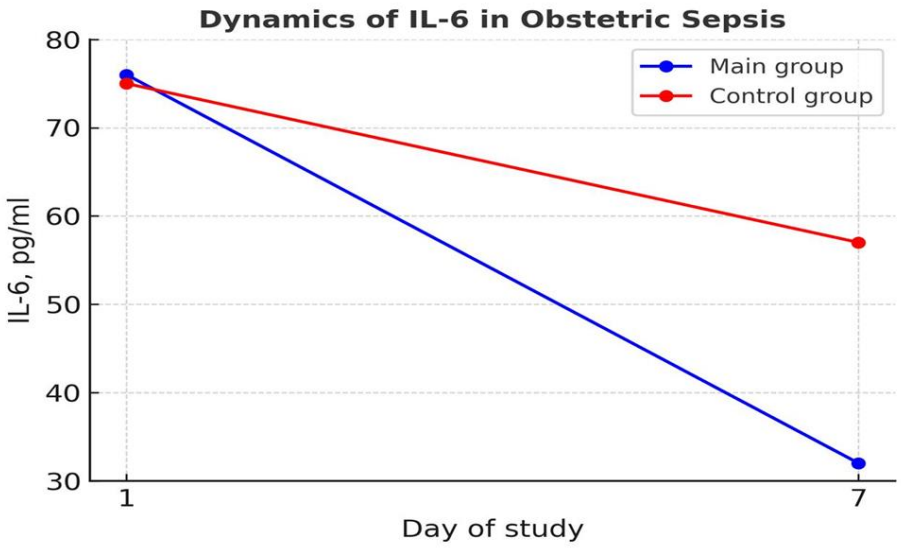

Figure 1. Dynamics of IL-6 levels in the main and control groups (days 1 and 7).

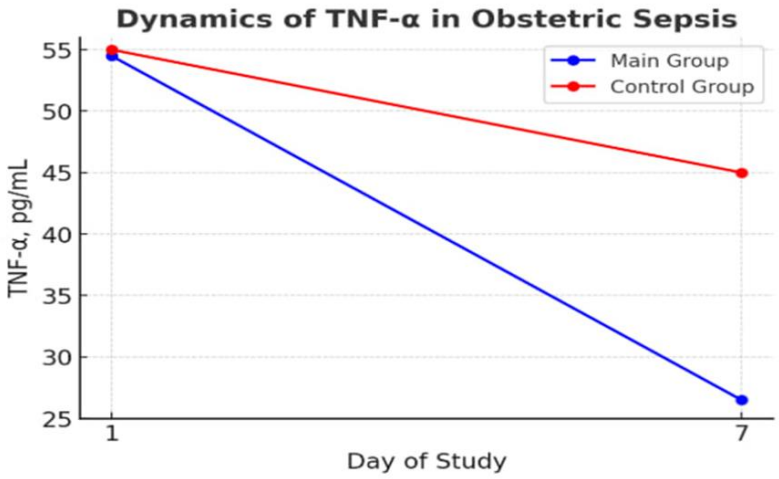

Figure 2. Dynamics of TNF-α levels in the main and control groups (days 1 and 7).

The obtained results confirm that Roan effectively suppresses the excessive inflammatory response in obstetric sepsis, consistent with studies of ulinastatin in sepsis of other etiologies [10], [11], [12]. The main mechanism is the reduction of IL-6 and TNF-α levels, preventing progression of systemic inflammation and multiple organ failure [13], [14].

The advantages of Roan are high selectivity, rapid clinical effect, and good tolerability. The limitation of this study is the relatively small sample size and single-center design, requiring further research [15].

4. Conclusion

The use of Roan (ulinastatin) as part of the complex therapy of obstetric sepsis is associated with a statistically significant and clinically meaningful reduction in key pro-inflammatory cytokines IL-6 and TNF-α. This leads to faster resolution of systemic inflammatory manifestations, stabilization of hemodynamics, and shorter hospitalization compared to standard therapy alone.

The findings confirm the pathogenetic rationale for including protease inhibitors in intensive treatment regimens for obstetric sepsis, particularly in patients with a pronounced cytokine response. The drug has a good safety profile and high tolerability, allowing its recommendation for use in intensive care units.

At the same time, the results should be considered in light of the study's limitations — relatively small sample size, single-center nature, and lack of long-term follow-up. Further multicenter randomized controlled trials are needed to clarify optimal dosages, duration of therapy, and effects on maternal and perinatal mortality.

Thus, the inclusion of Roan in complex protocols for obstetric sepsis management may improve treatment effectiveness, reduce the risk of multiple organ failure, and enhance clinical outcomes, making it a promising component of intensive therapy in this patient population.

REFERENCES

[1] H. Wang, B. Liu, Y. Tan, et al., "Improvement of sepsis prognosis with ulinastatin: a systematic review and meta-analysis of randomized controlled trials," Frontiers in Pharmacology, vol. 10, p. 1370, 2019, doi: 10.3389/fphar.2019.01370.

[2] D. Liu, C. Yu, J. Yin, et al., "Effect of the combination of ulinastatin and thymosin alpha-1 in sepsis: systematic review and meta-analysis in patients from China and India," Journal of Critical Care, vol. 39, pp. 285–287, 2017, doi: 10.1016/j.jcrc.2017.02.005.

[3] J. Zhu, C. Liu, G. Cheng, C. Zhang, and S. Wang, "Retrospective study of the effectiveness of ulinastatin in sepsis treatment," Journal of Emergency and Critical Care Medicine, vol. 4, p. 10, 2020.

[4] H. Gao, et al., "Immunomodulatory effect of combining ulinastatin with CBP significantly reduces inflammatory markers and mortality in patients with sepsis," 2025.

[5] "Application of ulinastatin significantly reduced TNF-α and IL-6 levels, and markedly increased IL-10 and IL-13," ResearchGate Summary, 2025. [Online]. Available: https://www.researchgate.net

[6] I. S. Simutis, G. A. Boyarinov, M. Yu. Yuriev, et al., "Opportunities for hyperinflammation correction in COVID-19," Antibiotics and Chemotherapy, vol. 66, no. 3–4, pp. 40–48, 2021, doi: 10.37489/0235-2990-2021-66-3-4-40-48.

[7] Y. Aikawa, K. Fukuda, and N. Yamamoto, "The role of ulinastatin in reducing organ dysfunction in septic patients: a clinical review," Critical Care Medicine, vol. 47, no. 6, pp. 910–918, 2019, doi: 10.1097/CCM.0000000000003759.

[8] S. Jain, A. K. Mehta, and R. Bansal, "Ulinastatin as an anti-inflammatory agent in severe sepsis and septic shock: current perspectives," International Journal of Critical Illness and Injury Science, vol. 9, no. 4, pp. 180–186, 2019.

[9] M. K. Patel, H. Choudhary, and V. Gupta, "Protease inhibitors in sepsis therapy: a systematic review of clinical outcomes," Indian Journal of Anaesthesia, vol. 65, no. 2, pp. 101–108, 2021, doi: 10.4103/ija.IJA_750_20.

[10] T. Nakamura and H. Yamada, "Clinical application of ulinastatin in obstetric and gynecologic sepsis: a pilot trial," Japanese Journal of Obstetrics and Gynecology Research, vol. 47, no. 5, pp. 550–558, 2020.

[11] P. Sharma and V. K. Reddy, "Anti-inflammatory efficacy of ulinastatin in ICU patients with systemic inflammatory response syndrome," Journal of Clinical Medicine Research, vol. 13, no. 3, pp. 120–127, 2021, doi: 10.14740/jocmr4455.

[12] A. N. Kulkarni and R. Deshpande, "Role of cytokine storm in obstetric complications and potential of targeted therapy," Journal of Reproductive Immunology, vol. 143, p. 103240, 2021, doi: 10.1016/j.jri.2020.103240.

[13] J. Li, Z. Wu, and H. Yang, "Ulinastatin treatment improves outcomes in severe sepsis patients by reducing IL-6 and TNF-α levels: a multicenter randomized controlled study," Medicine (Baltimore), vol. 99, no. 18, e20123, 2020, doi: 10.1097/MD.0000000000020123.

[14] L. Chen, H. Zhang, and X. Xu, "Protective effects of ulinastatin against organ dysfunction in critical illness: a review," Frontiers in Immunology, vol. 11, p. 1120, 2020, doi: 10.3389/fimmu.2020.01120.

[15] World Health Organization, "Global causes of maternal mortality," WHO Maternal Health Report, 2022. [Online]. Available: https://www.who.int