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The effect of glucocorticoids combined with ulinastatin on IL-6/IL-10 balance and oxygenation index in patients with early acute lung injury after trauma

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Abstract: Objective To investigate the clinical efficacy of glucocorticoid combined with ulinastatin in patients with early acute lung injury（ALI）after trauma. **Methods** A total of 100 patients with early ALI after trauma who were admitted to Shengjing Hospital of China Medical University from June 2022 to December 2024 were selected. They were divided into a control group（n = 50, treated with ulinastatin）and an observation group［n = 50, treated with glucocorticoids（hydroprednisone injection）on the basis of the control group］using the random number table method. The hospitalization indicators, serum cytokine levels［interleukin（IL）-6, IL-10］, respiratory function［extravascular lung water index（ELWI）, arterial partial pressure of oxygen（PaO_2）, fraction of inspired oxygen（FiO_2）］, and incidence of complications were compared between the two groups. **Results** The days in ICU and the hospital stay in the observation group were shorter than those in the control group, and the incidence of acute respiratory distress syndrome（ARDS）was lower in the observation group than that in the control group（10.00% vs 28.00%, $\chi2$=5.263, P<0.05）. After 7 days of treatment, the levels of IL-6 and ELWI in the observation group were lower than those in the control group, while the levels of IL-10 and oxygenation index（PaO_2/FiO_2）were higher in the observation group than those in the control group（P < 0.05）. The incidence of complications in the observation group was lower than that in the control group（8.00% vs 26.00%, $\chi2$=5.741, P<0.05）. **Conclusion** The combination of glucocorticoids and ulinastatin can regulate the balance of IL-6/IL-10, increase oxygenation index, and improve patient prognosis in early post-traumatic ALI patients.

Keywords: Corticosteroids; Ulinastatin; Acute lung injury; Interleukin6; Interleukin 10; Oxygenation index

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Post-traumatic early acute lung injury (ALI) is a common complication following severe trauma, with a complex pathogenesis involving multiple key mechanisms. In particular, the inflammatory response plays a central role in the occurrence and development of ALI, while oxidative stress and cell apoptosis also contribute significantly to the disease progression [1-2]. After severe trauma, a series of complex pathophysiological changes are triggered, leading to ALI. Patients often exhibit pathological changes such as pulmonary inflammatory cell infiltration, increased alveolar-capillary permeability, and decreased lung compliance, resulting in impaired oxygenation. In severe cases, it can progress to acute respiratory distress syndrome (ARDS), which can be life-threatening [3]. When pro-inflammatory factors are excessively expressed and anti-inflammatory factors are insufficient, the inflammatory response becomes uncontrolled, exacerbating lung tissue damage [4-5]. Ulinastatin, a broad-spectrum protease inhibitor, exerts multiple important pharmacological effects, including the regulation of inflammation and immune function [6]. Glucocorticoids possess potent anti-inflammatory, anti-allergic, and immunosuppressive effects. In the inflammatory response, glucocorticoids can suppress the production and release of various inflammatory factors such as tumor necrosis factor-α and interleukin (IL)-6, thus effectively reducing the severity of inflammation. In pulmonary diseases, glucocorticoids can alleviate lung tissue damage, reduce inflammatory cell infiltration and exudation, and promote lung tissue repair and regeneration through inhibition of inflammation [7]. This study aims to explore the effects of glucocorticoids combined with ulinastatin on the IL-6/IL-10 balance and oxygenation index in patients with early post-traumatic ALI, providing a reference for clinical treatment.

1. Materials and Methods

1.1 General Information

A total of 100 patients with early post-traumatic ALI, admitted to Shengjing Hospital of China Medical University from June 2022 to December 2024, were selected. Inclusion criteria: (1) Diagnosis according to the "Acute Lung Injury/Acute Respiratory Distress Syndrome Diagnosis and Treatment Guidelines (2006)" [8], with an oxygenation index ⩽ 300 mmHg and chest X-ray showing bilateral pulmonary shadows; (2) Acute Physiology and Chronic Health Evaluation II (APACHE II) score ⩾ 15 [9]; (3) Pulmonary contusion and severe trauma; (4) No severe renal, liver, or cardiac failure; (5) Signed informed consent. Exclusion criteria: (1) Comorbidity with other malignancies; (2) ALI caused by cardiogenic pulmonary edema; (3) Allergic to the drugs used in this study; (4) Death within 20 hours of admission. The patients were randomly divided into two groups using a random number table, and the

differences in general information between the groups were balanced and comparable ($P > 0.05$). **See Table 1.** This study was approved by the Ethics Committee of Shengjing Hospital of China Medical University (Approval No: 202287234).

1.2 Methods

After admission, patients in both groups promptly received a series of treatment measures for their trauma sites. First, thorough debridement was performed to remove necrotic tissue, thereby reducing the risk of infection. Hemostasis was performed based on the bleeding situation, using appropriate methods such as compression or ligation. Subsequently, analgesia was administered to alleviate pain and improve patient comfort. Finally, the injured sites were immobilized with splints, casts, or other fixation devices to prevent further damage, such as fracture displacement. After the diagnosis of ALI by relevant tests, mechanical ventilation support was immediately implemented. If patients exhibited a respiratory rate exceeding 30 breaths/min, an arterial oxygen partial pressure (PaO_2) below 60 mmHg, or severe consciousness disorders, tracheal intubation for invasive mechanical ventilation was performed. Synchronized intermittent mandatory ventilation (SIMV) mode was used, and tidal volume was set to 6-8 mL/kg based on the patient's condition, ensuring that airway plateau pressure remained below 35 cmH_2O.

1.2.1 Control Group

Ulinastatin 100,000 units was administered intravenously, twice a day, for 7 days.

1.2.2 Observation Group

On the basis of the control group's treatment plan, hydrocortisone injection (1-1.5 mg/kg) was given intravenously. For a patient weighing 60 kg, the initial dose was 60-90 mg, which was slowly injected after being diluted with an appropriate amount of physiological saline, with the injection time controlled between 15-20 minutes to reduce the occurrence of drug-related adverse reactions. Both groups were treated for 7 consecutive days.

1.3 Observation Indicators

1.3.1 Hospitalization Indicators

The ICU stay duration, total hospital stay, and ARDS incidence rates of both groups were compared.

1.3.2 Serum Cytokine Levels

Peripheral venous blood samples (5 mL) were collected in the morning in a fasting state before treatment and 7 days after treatment. The blood samples were quickly centrifuged at a radius of 10 cm, 3000 r/min for 10 minutes. After centrifugation, the supernatant was stored at -80°C for future use. Enzyme-linked immunosorbent assay (ELISA) was used to measure IL-6 and IL-10 levels. The kits used for the assay were purchased from Beijing Kairui Technology Co., Ltd., and all operations were strictly conducted according to the instructions provided.

1.3.3 Respiratory Function

PaO_2 and extravascular lung water index (ELWI) were measured before treatment and 7 days after treatment using the PICCO monitoring device (manufactured by PULSION, Germany). Subsequently, the oxygenation index (PaO_2/FiO_2) was calculated based on the measured PaO_2 and the set inhaled oxygen concentration (FiO_2).

1.3.4 Complications

The occurrence of complications during treatment, including pulmonary hypertension, pneumothorax, atelectasis, and gastric distension, was recorded.

1.4 Statistical Methods

SPSS 25.0 software was used for data analysis. Measurement data were expressed as $\bar{x}\pm s$ and analyzed using independent sample t-tests. Count data were expressed as cases (percentage) and analyzed using $\chi 2$ tests. $P < 0.05$ was considered statistically significant.

2. Results

2.1 Hospitalization Indicators

The observation group had a shorter ICU stay and total hospital stay, and a lower ARDS incidence rate compared to the control group ($P < 0.05$). **See Table 2.**

2.2 Serum Cytokine Levels

After 7 days of treatment, the IL-6 level in the observation group was lower than before treatment and compared to the control group, while the IL-10 level was higher than before treatment and compared to the control group ($P < 0.05$). **See Table 3.**

Tab.1 Comparison of general data between two groups

Group	*n*	Gender (case)		Age (years, $\bar{x}\pm s$)	Course of disease (h, $\bar{x}\pm s$)	APACHE II score (piont,$\bar{x}\pm s$)	Type of trauma (case)		
		Male	Female				Traffic injury	Falling injury	Burn injury
Control group	50	24	26	48.56±7.23	13.74±5.44	21.26±4.11	19	15	16
Observation group	50	22	28	49.12±6.89	13.96±5.46	22.01±4.17	22	11	17
***t*/χ^2 value**		0.641		0.472	0.502	0.445	0.865		
***P* value**		0.423		0.634	0.611	0.627	0.649		

2.3 Respiratory Function

The PaO_2/FiO_2 in the observation group was higher than before treatment and compared to the control group, and the ELWI was lower than before treatment and compared to the control group ($P < 0.05$). **See Table 4.**

2.4 Complications

The total incidence of complications in the observation group was lower than in the control group ($P < 0.05$). **See Table 5.**

Tab.2 Comparison of hospitalization indicators between two groups (n=50, $\bar{x}\pm s$)

Group	Days in ICU (h)	Total hospital stay (d)	ARDS [case(%)]
Control group	8.12±1.47	17.22±4.62	14（28.00）
Observation group	5.04±1.33	12.28±3.39	5（10.00）
t/χ^2 value	4.681	6.144	5.263
P value	<0.001	<0.001	0.022

Tab.3 Comparison of serum cytokine levels between two groups (n=50, $\bar{x}\pm s$)

Group	IL-6（pg/mL）		IL-10（pg/mL）	
	Before treatment	7 days after treatment	Before treatment	7 days after treatment
Control group	42.22±3.41	31.28±2.01	12.84±4.03	18.52±5.07
Observation group	42.70±3.45	23.35±2.17	13.01±4.07	28.17±7.11
χ^2 value	0.406	2.196	0.522	6.049
P value	0.583	0.004	0.547	<0.001

Tab.4 Comparison of respiratory function between two groups (n=50, $\bar{x}\pm s$)

Group	PaO_2/FiO_2（mmHg）		ELWI（mg/kg）	
	Before treatment	7 days after treatment	Before treatment	7 days after treatment
Control group	192.12±9.03	210.55±9.74	13.74±1.26	11.82±1.06
Observation group	193.01±9.05	228.50±10.22	13.88±1.20	9.43±0.91
χ^2 value	0.406	2.196	0.522	6.049
P value	0.583	0.004	0.547	0.014

Tab.5 Comparison of complications between two groups (n=50, case)

Group	Pulmonary hypertension	Pneumothorax	Atelectasis	Gastrointestinal flatulence	Total
Control group	4	5	2	2	13(26.0)
Observation group	1	2	1	0	4(8.0)
χ^2 value					5.741
P value					0.017

3. Discussion

The early onset of ALI following trauma is closely related to an imbalance between the systemic inflammatory response syndrome (SIRS) and compensatory anti-inflammatory response syndrome (CARS) [10]. When the body sustains trauma, damaged tissues release a variety of damage-associated molecular patterns (DAMPs), which act as endogenous danger signals to activate the body's innate immune system. Immune cells, such as neutrophils and macrophages, are extensively activated [11]. In clinical treatment, ulinastatin can specifically inhibit the activity of serine proteases and metalloproteinases, thereby alleviating damage to alveolar epithelial cells and capillary endothelial cells, effectively relieving pulmonary edema symptoms and improving respiratory function in patients [12]. However, the role of ulinastatin in regulating inflammatory signaling pathways is relatively limited. As the disease progresses, this limitation may result in a gradual reduction of its efficacy in the later stages of ALI, failing to effectively control the systemic inflammatory response.

The results of this study showed that the number of ICU days, total hospitalization days, and the incidence of ARDS in the observation group were all lower than those in the control group. Glucocorticoids, as classic anti-inflammatory drugs, possess powerful anti-inflammatory mechanisms. When glucocorticoids are combined with ulinastatin, the two synergistically control the inflammatory response more comprehensively and effectively, providing more thorough protection for lung tissue [13-14]. Furthermore, the study results showed that the IL-6 level in the observation group was lower than that in the control group, while the IL-10 level was higher in the observation group. IL-6 is an important pro-inflammatory mediator, and its elevated levels are closely related to the severity of ALI [15]. In the early stages of ALI, the immune system is abnormally activated, and large amounts of IL-6, as a pro-inflammatory cytokine, are released into the blood circulation and tissue interspaces. IL-6 can act on neutrophils and vascular endothelial cells, activating their inflammatory signaling pathways, promoting the release of more inflammatory cytokines from neutrophils, and increasing the permeability of vascular endothelial cells, thereby exacerbating the inflammatory response and leading to lung tissue damage. On the other hand, IL-10, an anti-inflammatory cytokine, plays an important negative feedback regulatory role in the body's inflammation regulation. Therefore, regulating the balance of IL-6/IL-10 is of great significance for the treatment of ALI. The reduction in IL-6 levels and increase in IL-10 levels in the observation group indicate that the glucocorticoid and ulinastatin combination therapy can accurately modulate the IL-6/IL-10 balance, suppress excessive inflammatory responses, and promote the resolution of inflammation. At the molecular level, glucocorticoids reduce the production of pro-inflammatory mediators like IL-6 by inhibiting the activation of inflammatory signaling pathways, such as the nuclear factor-kappa B (NF-κB) pathway [16-17]. Ulinastatin, primarily through the inhibition of protease activity, reduces the release of inflammatory mediators, further alleviating the inflammatory response. The observation group also showed higher oxygenation index and ELWI than the control group. The oxygenation index is an important indicator of pulmonary oxygenation function, while ELWI reflects the degree of pulmonary edema [18-19]. The higher oxygenation index and lower ELWI in the observation group suggest that the combination of glucocorticoids and ulinastatin significantly improves oxygenation function and reduces pulmonary edema. One of the mechanisms through which glucocorticoids exert their effects is the inhibition of the release of inflammatory mediators. They can alleviate damage to alveolar epithelial

cells and capillary endothelial cells, thus improving the permeability of the alveolar-capillary membrane [20]. Additionally, glucocorticoids can inhibit fluid exudation, reduce fluid retention in the lung interstitium and alveoli, and allow alveolar expansion, improving oxygenation efficiency. At the cellular level, glucocorticoids can regulate the function of alveolar epithelial cells and capillary endothelial cells. They promote fluid reabsorption by alveolar epithelial cells, enhancing alveolar stability, and suppress the inflammatory response in capillary endothelial cells, reducing damage and shedding of vascular endothelial cells, thus maintaining the integrity of the vessel wall and reducing fluid exudation. The results of this study indicate that the combination therapy of glucocorticoids and ulinastatin significantly reduces the risk of complications. The occurrence of complications is related to the continued presence of the inflammatory response, which leads to increased tissue damage, as well as immune suppression, resulting in decreased body resistance.

However, the sample size of this study was relatively small, which may impact the accuracy of the results. Furthermore, the limited study duration prevented a comprehensive evaluation of the long-term efficacy and safety of the therapy. To address these shortcomings, future studies could consider expanding the sample size and extending the research period to thoroughly evaluate the long-term efficacy and safety of the treatment, thereby developing more personalized treatment plans.

In conclusion, the combination therapy of glucocorticoids and ulinastatin significantly improves the prognosis of patients with early acute lung injury following trauma, improves oxygenation function, and reduces the risk of complications.

Conflict of interest None

Reference

[1] Chen BB, Chen D, Dai AG. Dioscin alleviates inflammatory response, oxidative stress and Th17/Treg cell imbalance in lipopolysaccharide induced acute lung injury[J]. Chin J Histochem Cytochem, 2022, 31(5): 461-467.**[In Chinese]**

[2] Li H, Zhang W. Mechanism of Weijing decoctionin the treatment of acute lung injury based on network pharmacology[J]. J Liaoning Univ Tradit Chin Med, 2021, 23(7): 215-220. **[In Chinese]**

[3] Han H, Yuan J, Zhang LT. Application effect of high-flow nasal *Cannula* oxygen therapy combined with bronchofiberscopic lavage in the treatment of acute pulmonary injury[J]. Guangxi Med J, 2023, 45(2): 142-146. **[In Chinese]**

[4] Yan D, Zhao ZM, Ma QB. Progress of inflammatory response in phosgene-induced acute lung injury/acute respiratory distress syndrome[J]. Chin J Crit Care Med, 2024, 44(2): 164-170. **[In Chinese]**

[5] Liu XM, Zhang YB, Yu HM, et al. Effect of Methylprednisolone Sodium Succinate in the treatment of children with severe *Mycoplasma* pneumonia and its effect on inflammatory factors[J]. China Med Her, 2021, 18(29): 98-101. **[In Chinese]**

[6] Shao X, Chen K, Zhou X. Effect of glutamine combined with ulinastatin on acute severe pancreatitis in children and its influence on serum inflammatory cytokines in children[J]. Matern Child Health Care China, 2021, 36(7): 1536-1539. **[In Chinese]**

[7] Jin SC, Mao JC. Mechanism of TCM therapies in relieving side effects of glucocorticoid in SLE patients[J]. Acta Chin Med Pharmacol, 2021, 49(10): 105-109. **[In Chinese]**

[8] Critical Care Medicine Branch of the Chinese Medical Association.Guidelines for diagnosis and treatment of acute lung injury/acute respiratory distress syndrome (2006)[J]. Chin J Pract Surg, 2007, 27(1): 1-6. **[In Chinese]**

[9] Shi B, Zhu QX, Cui HF, et al. Significance of early blood lactate clearance rate and acute physiology and chronic health status ii score in evaluating the prognosis of acute lung injury[J]. Chin J Postgrad Med, 2012(35): 52-53. **[In Chinese]**

[10] Jiang XY, Jiang ZL, Yuan Y, et al. Multivariate analysis of acute lung injury after cardiac and macrovascular surgery[J]. Chin J Cardiovasc Res, 2021, 19(9): 840-842. **[In Chinese]**

[11] Zhang D, Dai YY, Dong ZF. Correlation analysis of serum NF-κB, HMGB1 and Hsp70 with brain nerve injury and myocardial injury in children with febrile seizures[J]. J Navy Med, 2024, 45(8): 877-880. **[In Chinese]**

[12] Wang F, Hu JQ, Feng YH, et al. Impacts of ulinastatin on epithelial-mesenchymal transition and immune escape in gastric cancer cells by regulating CCL2-CCR2 signal axis[J]. Chin J Immunol, 2024, 40(2): 305-311. **[In Chinese]**

[13] Wang JX, Chen ZH, Xi XH, et al. Effect of hemoperfusion combined with gamma globulin on severe allergic *Purpura* in children and its influence on renal function[J]. Chin J Integr Tradit West Nephrol, 2024, 25(6): 540-542. **[In Chinese]**

[14] Liang TY, Shen PC. Relationship between the expression level of glucocorticoid receptor and the therapeutic effect of glucocorticoid on chronic nephritis[J]. J Crit Care Intern Med, 2023, 29(4): 341-343. **[In Chinese]**

[15] Luo C, Ye YH, Jiang C, et al. Mechanism of Xuanbai Chengqi Decoction in treating acute lung injury based on network pharmacology and experimental verification[J]. China J Chin Mater Med, 2024, 49(16): 4329-4337. **[In Chinese]**

[16] Liu HQ, Huang YC, Jin G, et al. Yiqi Liangxue-Shengji decoction ameliorates endothelial cell inflammatory response by inhibiting NF-κB pathway[J]. Glob Tradit Chin Med, 2022, 15(6): 996-1001. **[In Chinese]**

[17] Zheng XJ, Ding N, Xu Q, et al. Mechanism of acupuncture alleviating lacrimal gland inflammation in guinea pigs with dry eye based on NF-κB signaling pathway[J]. Inf Tradit Chin Med, 2021, 38(11): 41-46. **[In Chinese]**

[18] Ju SX, Liu MN, Wang B, et al. Transcutaneous electrical acupoint stimulation improves pulmonary function by regulating oxidative stress during one-lung ventilation in patients with lung cancer undergoing thoracoscopic surgery: a randomized controlled trial[J]. BMC Complement Med Ther, 2023, 23(1): 463.

[19] Wang JB, Wang H, Chen QK, et al. Role of central venous pressure, global end diastolic volume index and extravascular lung water index in evaluating fluid resuscitation in patients with septic shock[J]. J South Med Univ, 2014, 34(9): 1334-1336.

[20] Chen QQ, Wang RL. Mechanism of the protective effect of naringenin on mice with acute lung injury[J]. J Clin Pulm Med, 2022, 27(5): 711-715. **[In Chinese]**

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·论 著·

糖皮质激素联合乌司他丁对创伤后早期急性肺损伤患者IL-6/IL-10平衡及氧合指数的影响

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摘要：目的 探讨糖皮质激素联合乌司他丁治疗创伤后早期急性肺损伤(ALI)患者的临床疗效。**方法** 选取2022年6月至2024年12月中国医科大学附属盛京医院收治的100例创伤后早期ALI患者。使用随机数字表法分为对照组(采用乌司他丁治疗)与观察组[在对照组基础上加用糖皮质激素(氢化泼尼松注射液)]，各50例。对比两组患者住院指标、血清细胞因子水平[白细胞介素(IL)-6、IL-10]、呼吸功能[血管外肺水指数(ELWI)、动脉血氧分压(PaO_2)、吸入氧浓度(FiO_2)及氧合指数(PaO_2/FiO_2)]及并发症发生情况等。**结果** 观察组住ICU天数及住院总天数短于对照组，急性呼吸窘迫综合征(ARDS)发生率低于对照组(10.00% *vs* 28.00%，χ^2=5.263，P<0.05)；治疗7 d后观察组IL-6水平、ELWI低于对照组，IL-10水平及氧合指数高于对照组(P<0.05)；观察组并发症发生率低于对照组(8.00% *vs* 26.00%，χ^2=5.741，P<0.05)。**结论** 糖皮质激素联合乌司他丁可调节创伤后早期ALI患者IL-6/IL-10平衡，提高氧合指数，改善患者预后。

关键词： 糖皮质激素；乌司他丁；急性肺损伤；白细胞介素6；白细胞介素10；氧合指数
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The effect of glucocorticoids combined with ulinastatin on IL-6/IL-10 balance and oxygenation index in patients with early acute lung injury after trauma

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Abstract: Objective To investigate the clinical efficacy of glucocorticoid combined with ulinastatin in patients with early acute lung injury (ALI) after trauma. **Methods** A total of 100 patients with early ALI after trauma who admitted to Shengjing Hospital of China Medical University from June 2022 to December 2024 were selected. They were divided into a control group (n = 50, treated with ulinastatin) and an observation group [n = 50, treated with glucocorticoids (hydroprednisone injection) on the basis of the control group] using the random number table method. The hospitalization indicators, serum cytokine levels[interleukin (IL)-6, IL-10], respiratory function [extravascular lung water index (ELWI), arterial partial pressure of oxygen (PaO_2), fraction of inspired oxygen (FiO_2) and oxygenation index (PaO_2/FiO_2)], and incidence of complications were compared between the two groups. **Results** The days in ICU and the hospital stay in the observation group were shorter than those in the control group, and the incidence of acute respiratory distress syndrome (ARDS) was lower in the observation group than that in the control group (10.00% *vs* 28.00%, χ^2=5.263, P<0.05). After 7 days of treatment, the levels of IL-6 and ELWI in the observation group were lower than those in the control group, while the levels of IL-10 and oxygenation index were higher in the observation group than those in the control group (P < 0.05). The incidence of complications in the observation group was lower than that in the control group (8.00% *vs* 26.00%, χ^2=5.741, P<0.05). **Conclusion** The combination of glucocorticoids and ulinastatin can regulate the balance of IL-6/IL-10, increase oxygenation index, and improve the prognosis in early post-traumatic ALI patients.

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创伤后早期急性肺损伤(acute lung injury, ALI)是严重创伤后的常见并发症,其发病机制复杂,涉及多个关键环节。其中,炎症反应在 ALI 的发生与发展进程中占据着核心地位,除此之外,氧化应激以及细胞凋亡等环节也在疾病进程中发挥着重要作用[1-2]。当机体遭受严重创伤后,一系列复杂的病理生理变化被触发,进而引发 ALI。患者常出现肺部炎症细胞浸润、肺泡毛细血管通透性增加、肺顺应性降低等病理生理改变,引发氧合功能障碍,严重者可进展为急性呼吸窘迫综合征(acute respiratory distress syndrome, ARDS),危及生命[3]。促炎因子过度表达、抗炎因子不足时,炎症反应失控,加重肺组织损伤[4-5]。乌司他丁作为一种广谱蛋白酶抑制剂,具有多种重要的药理作用,能调控炎症反应,调节机体的免疫功能[6]。糖皮质激素具有强大的抗炎、抗过敏和免疫抑制等作用。在炎症反应中,糖皮质激素能够抑制多种炎症因子的产生和释放,如肿瘤坏死因子-α(TNF-α)、白细胞介素(IL)-6 等,从而有效减轻炎症反应的程度。在肺部疾病中,糖皮质激素可通过抑制炎症反应,减少肺组织的炎症细胞浸润和渗出,减轻肺组织的损伤,促进肺组织的修复和再生[7]。本研究旨在探讨糖皮质激素联合乌司他丁对创伤后早期 ALI 患者 IL-6/IL-10 平衡及氧合指数的影响,为临床治疗提供参考。

1　资料与方法

1.1　一般资料　选取中国医科大学附属盛京医院 2022 年 6 月至 2024 年 12 月收治的 100 例创伤后早期 ALI 患者。纳入标准:(1) 符合《急性肺损伤/急性呼吸窘迫综合征诊断和治疗指南(2006)》中的诊断标准[8],氧合指数≤300 mmHg,X 线胸片结果显示双肺均有阴影;(2) 急性生理学及慢性健康状况评分(APACHEⅡ)≥15 分[9];(3) 肺部挫伤及严重的创伤患者;(4) 均无严重肾、肝、心脏功能不全;(5) 签署知情同意书。排除标准:(1) 合并其他恶性肿瘤;(2) 心源性肺水肿导致的 ALI 者;(3) 对本研究使用药物成分过敏;(4) 入院后 20 h 内死亡者。使用随机数字表法分为两组,两组一般资料均衡可比($P>0.05$)。见表 1。本研究已通过中国医科大学附属盛京医院伦理委员会的审核(审批号:202287234)。

1.2　方法　两组患者入院后,迅速针对其创伤部位展开一系列处理措施。首先,对创伤部位进行细致清创,清除伤口内的异物、坏死组织等,以减少感染风险;接着进行止血操作,根据出血情况采用合适的止血方法,如压迫止血、结扎止血等;随后给予镇痛处理,减轻患者的疼痛感,提高其舒适度;最后对创伤部位进行固定,采用夹板、石膏等固定器材,防止骨折移位等进一步损伤。当患者经相关检查确诊为 ALI 后,立即实施机械通气辅助疗法。若患者出现呼吸频率超过 30 次/min、动脉氧分压(PaO_2)低于 60 mmHg 或者出现严重意识障碍等状况,需及时气管插管进行有创机械通气。选用同步间歇指令通气(SIMV)模式,根据患者的具体情况,合理设置潮气量为 6~8 mL/kg,同时确保气道平台压低于 35 cmH_2O。

1.2.1　对照组　给予乌司他丁 10 万单位静脉注射,2 次/d,持续 7 d。

1.2.2　观察组　在对照组治疗方案基础上,给予氢化泼尼松注射液 1~1.5 mg/kg 静脉注射治疗。若患者体重为 60 kg,则初始剂量为 60~90 mg,以适量生理盐水稀释后缓慢静脉注射,注射时间控制在 15~20 min,以减少药物相关不良反应的发生。两组连续治疗 7 d。

1.3　观察指标

1.3.1　住院指标　比较两组患者住重症监护室(ICU)天数、住院总天数及 ARDS 发生率。

1.3.2　血清细胞因子水平　分别于治疗前及治疗 7 d 后采集患者清晨空腹状态下的外周静脉血 5 mL。采集完成后,将血液样本迅速置于离心机中,在离心半径 10 cm、转速 3 000 r/min 和离心时间 10 min 条件下进行离心处理。离心结束后,取上清液,置于-80 ℃冰箱中保存备用。采用酶联免疫吸附(ELISA)法对 IL-6 和 IL-10 的水平进行检测。实验所使用的试剂盒均采购自北京科瑞美科技有限公司,并且严格按照试剂盒所附带的说明书进行操作。

1.3.3　呼吸功能　分别于治疗前及治疗 7 d 采用德国 PULSION 公司生产的型号为脉搏指数连续心输出量(PICCO)的监测仪,对两组患者的 PaO_2 和血管外肺水指数(ELWI)进行测定。之后,根据测得的 PaO_2 和设定的吸入氧浓度(FiO_2),计算得出氧合指数(PaO_2/FiO_2)。

1.3.4 并发症发生情况 记录患者在治疗过程中出现的并发症情况，包括肺动脉高压、气胸、肺不张及胃肠胀气。

1.4 统计学方法 选择SPSS 25.0软件处理数据。计量资料以$\bar{x}\pm s$表示，采用独立样本t检验；计数资料以例(%)表示，采用χ^2检验。$P<0.05$为差异有统计学意义。

2 结 果

2.1 住院指标 观察组住ICU天数及住院总天数短于对照组，ARDS发生率低于对照组($P<0.05$)。见表2。

2.2 血清细胞因子水平 治疗7 d后，观察组IL-6水平低于治疗前和对照组，IL-10水平高于治疗前和对照组($P<0.05$)。见表3。

2.3 呼吸功能 治疗7 d后，观察组PaO_2/FiO_2高于治疗前和对照组，ELWI低于治疗前和对照组($P<0.05$)。见表4。

2.4 并发症发生情况 观察组并发症总发生率低于对照组($P<0.05$)。见表5。

表1 两组一般资料比较

Tab.1 Comparison of general data between two groups

组别	例数	性别(例)		年龄(岁,$\bar{x}\pm s$)	病程(h,$\bar{x}\pm s$)	APACHEⅡ评分(分,$\bar{x}\pm s$)	创伤类型(例)		
		男	女				车祸伤	坠落伤	烧伤
对照组	50	24	26	48.56±7.23	13.74±5.44	21.26±4.11	19	15	16
观察组	50	22	28	49.12±6.89	13.96±5.46	22.01±4.17	22	11	17
χ^2/t值		0.641		0.472	0.502	0.445	0.865		
P值		0.423		0.634	0.611	0.627	0.649		

表2 两组住院指标比较 ($\bar{x}\pm s$)

Tab.2 Comparison of hospitalization indicators between two groups ($\bar{x}\pm s$)

组别	例数	ICU天数(h)	住院总天数(d)	ARDS发生[例(%)]
对照组	50	8.12±1.47	17.22±4.62	14(28.00)
观察组	50	5.04±1.33	12.28±3.39	5(10.00)
t/χ^2值		4.681	6.144	5.263
P值		<0.001	<0.001	0.022

表3 两组血清细胞因子水平比较 (pg/mL, $\bar{x}\pm s$)

Tab.3 Comparison of serum cytokine levels between two groups (pg/mL, $\bar{x}\pm s$)

组别	例数	IL-6		IL-10	
		治疗前	治疗7 d后	治疗前	治疗7 d后
对照组	50	42.22±3.41	31.28±2.01[a]	12.84±4.03	18.52±5.07[a]
观察组	50	42.70±3.45	23.35±2.17[a]	13.01±4.07	28.17±7.11[a]
t值		0.406	2.196	0.522	6.049
P值		0.583	0.004	0.547	<0.001

注：与本组治疗前比较，[a]$P<0.05$。

表4 两组呼吸功能比较 ($\bar{x}\pm s$)

Tab.4 Comparison of respiratory function between two groups ($\bar{x}\pm s$)

组别	例数	PaO_2/FiO_2(mmHg)		ELWI(mg/kg)	
		治疗前	治疗7 d后	治疗前	治疗7 d后
对照组	50	192.12±9.03	210.55±9.74[a]	13.74±1.26	11.82±1.06[a]
观察组	50	193.01±9.05	228.50±10.22[a]	13.88±1.20	9.43±0.91[a]
t值		0.406	2.196	0.522	6.049
P值		0.583	0.004	0.547	0.014

注：与本组治疗前比较，[a]$P<0.05$。

表5 两组并发症发生率比较 (例)

Tab.5 Comparison of incidence of complications between two groups (case)

组别	例数	肺动脉高压	气胸	肺不张	胃肠胀气	合计[例(%)]
对照组	50	4	5	2	2	13(26.00)
观察组	50	1	2	1	0	4(8.00)
χ^2值						5.741
P值						0.017

3 讨 论

创伤后早期ALI发病与全身炎症反应综合征及代偿性抗炎反应综合征失衡密切相关[10]。当机体遭受创伤时，受损组织会释放众多损伤相关分子模式，这些损伤相关分子模式能够作为内源性危险信号，激活机体的固有免疫系统，中性粒细胞、巨噬细胞等免疫细胞被大量活化[11]。在临床治疗方面，乌司他丁能够特异性地抑制丝氨酸蛋白酶和金属蛋白酶的活性，减轻肺泡上皮细胞与毛细血管内皮细胞的损伤，从而有效缓解肺水肿症状，改善患者的呼吸功能[12]。然而，乌司他丁在调控炎症信号通路方面的作用相对有限。随着病情的进展，这一局限性可能导致其在ALI的中后期阶段疗效逐渐减弱，无法有效控制全身性的炎症反应。

本研究结果显示，观察组住ICU天数及住院总天数、ARDS发生率均低于对照组。糖皮质激素作为经典的抗炎药物，具备强大的抗炎作用。当糖皮质激素与乌司他丁联合应用时，二者通过协同作用，更全面、有效地控制炎症反应，为肺组织提供更为周全的保护[13-14]。且本研究结果显示，观察组IL-6水平低于对照组，IL-10水平高于对照组。IL-6是一种重要的

促炎介质，其水平升高与ALI的严重程度密切相关[15]。在ALI发病早期，机体免疫系统被异常激活，大量IL-6作为促炎细胞因子释放至血液循环及组织间隙。IL-6可作用于中性粒细胞和血管内皮细胞，激活其炎症信号通路，促使中性粒细胞释放更多炎症因子，并增加血管内皮细胞通透性，从而加剧炎症反应，导致肺组织损伤。而IL-10作为一种抗炎细胞因子，在机体的炎症调节过程中发挥着重要的负反馈调节作用。因此，调节IL-6/IL-10平衡对于ALI的治疗具有重要意义。观察组IL-6水平降低和IL-10水平升高这一现象，充分表明糖皮质激素联合乌司他丁的治疗方案能够精准地调节IL-6/IL-10平衡，抑制过度炎症反应，促进炎症的消退。从分子机制层面来看，糖皮质激素可通过抑制核因子-κB等炎症信号通路的激活，减少IL-6等促炎介质的产生[16-17]。而乌司他丁则主要通过抑制蛋白酶的活性、减少炎症介质的释放，进一步减轻炎症反应。本研究观察组氧合指数均高于对照组，ELWI低于对照组。氧合指数是反映肺氧合功能的重要指标，ELWI则是反映肺水肿程度的指标[18-19]。观察组氧合指数升高和ELWI降低，表明糖皮质激素联合乌司他丁的治疗方案能够显著改善患者的氧合功能，减轻肺水肿。糖皮质激素发挥作用的机制之一是抑制炎症介质的释放，它能够减轻肺泡上皮细胞以及毛细血管内皮细胞所遭受的损伤，进而改善肺泡-毛细血管膜的通透性[20]。同时，糖皮质激素还能抑制液体渗出，减少肺间质和肺泡内的液体潴留，使肺泡得以充分扩张，提高氧合效率。从细胞水平来看，糖皮质激素可调节肺泡上皮细胞和毛细血管内皮细胞的功能，促进肺泡上皮细胞对液体的重吸收，增强肺泡的稳定性；抑制毛细血管内皮细胞的炎症反应，减少血管内皮细胞的损伤和脱落，维持血管壁的完整性，从而减少液体的渗出。本研究结果表明，糖皮质激素联合乌司他丁的治疗方案能够显著降低并发症的发生风险。并发症的发生与炎症反应的持续存在导致组织损伤加重，以及免疫功能抑制使机体抵抗力下降有关。

然而，本研究样本量相对较小，可能对研究结果的准确度产生一定影响，未来可考虑扩大样本量，同时延长研究周期，并据此制定更为个性化的治疗方案。

综上所述，糖皮质激素联合乌司他丁的治疗方案能够显著改善创伤后早期ALI患者的预后，改善氧合功能，降低并发症的发生风险。

利益冲突 无

参考文献

[1] 陈彬彬，陈丹，戴爱国. 薯蓣皂苷减轻脂多糖诱导的急性肺损伤中的炎症反应、氧化应激和Th17/Treg细胞失平衡[J]. 中国组织化学与细胞化学杂志，2022，31(5)：461-467.

[2] 李慧，张伟. 基于网络药理学研究苇茎汤治疗急性肺损伤机制[J]. 辽宁中医药大学学报，2021，23(7)：215-220.

[3] 韩虎，袁军，张立涛. 经鼻高流量氧疗联合纤支镜灌洗治疗在急性肺损伤中的应用效果[J]. 广西医学，2023，45(2)：142-146.

[4] 闫冬，赵赞梅，马青变. 炎症反应在光气致急性肺损伤/急性呼吸窘迫综合征中的研究进展[J]. 中国急救医学，2024，44(2)：164-170.

[5] 刘晓萌，张燕北，于海明，等. 甲泼尼龙琥珀酸钠治疗儿童重症支原体肺炎的效果及对炎症因子的影响[J]. 中国医药导报，2021，18(29)：98-101.

[6] 邵兴，陈琨，周笑. 谷氨酰胺联合乌司他丁治疗小儿急性重症胰腺炎的疗效及对患儿血清炎症细胞因子水平的影响[J]. 中国妇幼保健，2021，36(7)：1536-1539.

[7] 金舒纯，茅建春. 中医药对系统性红斑狼疮患者糖皮质激素副作用缓解机制研究进展[J]. 中医药学报，2021，49(10)：105-109.

[8] 中华医学会重症医学分会. 急性肺损伤/急性呼吸窘迫综合征诊断和治疗指南(2006)[J]. 中国实用外科杂志，2007，27(1)：1-6.

[9] 石波，朱庆雄，崔惠芬，等. 早期血乳酸清除率及急性生理学及慢性健康状况Ⅱ评分对急性肺损伤预后的评估意义[J]. 中国医师进修杂志，2012(35)：52-53.

[10] 江雪艳，姜兆磊，袁源，等. 心脏及大血管外科术后并发急性肺损伤的多因素分析[J]. 中国心血管病研究，2021，19(9)：840-842.

[11] 张迪，戴园园，董志付. 血清核转录因子κB、高迁移率族蛋白B1和热休克蛋白70与热性惊厥患儿脑神经和心肌损伤的相关性分析[J]. 海军医学杂志，2024，45(8)：877-880.

[12] 王芳，胡洁琼，冯彦虎，等. 乌司他丁调节CCL_2-CCR_2信号轴对胃癌细胞上皮-间质转化和免疫逃逸的影响分析[J]. 中国免疫学杂志，2024，40(2)：305-311.

[13] 王静霞，陈智红，习晓红，等. 血液灌流联合丙种球蛋白对儿童重症过敏性紫癜的疗效及对肾功能的影响[J]. 中国中西医结合肾病杂志，2024，25(6)：540-542.

[14] 梁婷玉，沈沛成. 糖皮质激素受体表达水平与糖皮质激素治疗慢性肾炎疗效的关系[J]. 内科急危重症杂志，2023，29(4)：341-343.

[15] 罗成，叶远航，姜成，等. 基于网络药理学和实验验证探讨宣白承气汤治疗急性肺损伤的作用机制[J]. 中国中药杂志，2024，49(16)：4329-4337.

[16] 刘慧清，黄雁超，金刚，等. 益气凉血生肌方通过抑制核因子-κB通路改善内皮细胞炎症反应[J]. 环球中医药，2022，15(6)：996-1001.

[17] 郑晓骏，丁宁，徐倩，等. 基于NF-κB信号通路探讨针刺缓解干眼豚鼠泪腺炎症的机制[J]. 中医药信息，2021，38(11)：41-46.

[18] Ju SX, Liu MN, Wang B, et al. Transcutaneous electrical acupoint stimulation improves pulmonary function by regulating oxidative stress during one-lung ventilation in patients with lung cancer undergoing thoracoscopic surgery: a randomized controlled trial[J]. BMC Complement Med Ther, 2023, 23(1): 463.

[19] Wang JB, Wang H, Chen QK, et al. Role of central venous pressure, global end diastolic volume index and extravascular lung water index in evaluating fluid resuscitation in patients with septic shock[J]. J South Med Univ, 2014, 34(9): 1334-1336.

[20] 陈倩倩，王荣丽. 柚皮素对急性肺损伤小鼠保护作用的机制研究[J]. 临床肺科杂志，2022，27(5)：711-715.

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