Research Paper

The Impact of Early Goal-Directed Therapy in Conjunction with Glucocorticoids in the Prognosis of Septic Shock

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To assess the efficacy of early goal-directed therapy in conjunction with glucocorticoids on the prognosis of septic shock is the objective of the study. 60 septic shock patients admitted to the hospital from June 2019 to August 2022 were split into control cohort and observation cohort according to the method of random number table, with 40 patients in every cohort. Both cohorts underwent standard therapy, with the observation cohort additionally receiving intravenous hydrocortisone drip and early goal-directed therapy, all of which were continuously treated for 7 d. The baseline data of all patients, such as sex, age, infection site, sequential organ failure assessment score and immune cell level, were recorded in detail, and the C-reactive protein, intensive care unit hospitalization time, and the duration of mechanical ventilation was observed for patients. The therapeutic impact of early goal-directed therapy combined with glucocorticoids on septic shock in the analysis period aims to inform the optimal therapy strategy selection. Following therapy, the cluster of differentiation 4^+, cluster of differentiation 8^+ and cluster of differentiation 4^+/cluster of differentiation 8^+ ratios in both the therapy and control cohorts increased significantly, exhibiting statistical significance. The therapy cohort demonstrated a notable decrease in C-reactive protein, intensive care unit hospitalization duration and mechanical ventilation time when compared to the control cohort, with the difference being statistically significant. Early goal-directed therapy combined with glucocorticoid can enhance the cellular immune function of patients with septic shock, reduce the systemic inflammatory reaction and improve the prognosis.

Key words: Early goal-directed therapy, septic shock, glucocorticoids, C-reactive protein

The prevalence of purulent toxic shock is always high, but most clinicians are currently based on conventional indicators when diagnosing purulent toxic asphyxia. Therefore, the final diagnosis time is often delayed and the patient's prognosis is not good. Patients with purulent toxic shock are usually accompanied by increased blood lactic acid, but higher lactic acid levels have occurred in early shock or without hypotension. This experiment carried out Early Target-Oriented Therapy (EGDT) and the use of hydrogenated pine vein injection methods. At different stages of patients with purulent shock, patients with orderly heart failure, Sequential Organ Failure Assessment (SOFA) scores were given. To explore, monitor and control the medical effect of early prevention and treatment of patients in the early stage of purulent shock is the objective of the study.

MATERIALS AND METHODS

General data:

60 patients with septic shock who received treatment in the Intensive Care Unit (ICU) of our hospital were included in the study. Among which 35 patients were male and 25 patients were female, aged 38-65 y old, average (57.3±7.82) y old. Another 31 patients (observation cohort) had blood lactic acid≥4 mmol/l, systolic blood pressure>90 mmHg and blood lactic acid<2 mmol/l for 3 d after treatment for 6 h, 19 of them were male and 15 were female, aged 38-62 y, mean (52.8±6.81) y old. Control cohort include 29 patients among which systolic blood pressure<90 mmHg or lower than the baseline value>40 mmHg, defecation time<0.5 ml/kg/h, accompanied by traditional septic shock symptoms with clammy skin, of which 15 were

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males and 11 were females, aged 42-63 y, average (50.1±6.3) y old. All cases of pregnancy, liver and kidney failure, pulmonary embolism, patients who required continuous blood purification treatment, patients who were contraindicated for cardiac vein catheterization, patients who needed emergency rescue treatment and those who had undergone shock or fluid resuscitation therapy were excluded from the study. There were no differences in gender and age between the two cohorts of patients ($p>0.05$).

Therapy approaches:

Upon admission of patients from both cohorts to the ICU, they were cultured with blood, sputum or aspiration fluid, placed in the subclavian or internal jugular vein, underwent hemodynamic examination and received broad-spectrum antibiotics, mechanical ventilation, glucocorticoids, analgesic sedation and symptomatic technical support. Hydrocortisone intravenous infusion is widely used in drug therapy for 7 d. The time of admission in the ICU was recorded and the SOFA scores were monitored. When EGDT is performed on this basis, 500-1000 ml of crystallization solution or 300-500 ml of colloid solution is administered intravenously within 30 min, so that the central venous pressure reaches 8-12 cm H_2O and the mean arterial pressure reaches 65-90 mmHg. Inject high-concentration hemoglobin solution to make hemoglobin specific volume>0.30 and use dobutamine hydrochloride solution (Shandong Fang Ming Pharmaceutical Group Co., Ltd., H20053297) to increase myocardial output by 2.5-20.0 μg/kg/min.

Observation indicators:

Before treatment and after treatment for 1, 2 and 3 d, we conducted observation on respiratory, circulatory, coagulation and bilirubin levels within the two cohorts, with a comparison of scores according to the SOFA scoring table. Flow cytometry was employed to monitor C-Reactive Protein (CRP), T lymphocyte subsets (Cluster of Differentiation (CD) 4^+, $CD8^+$) and $CD4^+/CD8^+$ ratios before and after therapy, and the date of hospitalization in ICU and date of mechanical ventilation were marked.

Statistical analysis:

Statistical Package for the Social Sciences (SPSS) 18.0 application software was used for data processing to complete the data analysis, which was displayed as mean±standard deviation. The comparison within and between cohorts was performed using independent sample t-test and $p<0.05$ was considered statistically different.

RESULTS AND DISCUSSION

Comparison of CRP outcomes before and after therapy in the two cohorts is displayed in Table 1. As depicted in Table 1, there was no statistically significant difference in CRP levels between the two patient cohorts prior to diagnosis ($t=0.823$, $p>0.05$). After 1 d, 2 d, as well as 3 d of diagnosis and therapy, the CRP levels in the diagnostic cohort were lower than those in the control cohort, with the observation cohort exhibiting a further decrease in CRP levels ($p<0.05$).

Comparison of cellular immunological indicators before and after therapy in both cohorts were shown in Table 2-Table 4. This reveals no statistically significant disparities in T lymphocyte subsets ($CD4^+$, $CD8^+$, $CD4^+/CD8^+$ ratio) between the therapy cohort and control cohort prior to therapy (all $p>0.05$). Following 3 d of therapy, T lymphocyte subsets ($CD4^+$, $CD8^+$, $CD4^+/CD8^+$ ratio) in both the observation and control cohorts increased, with the observation cohort demonstrating significantly higher $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ ratios compared to the control cohort. All differences were statistically significant ($p<0.05$).

Comparison of mechanical ventilation duration and ICU hospitalization time between the two cohorts is displayed in Table 5. Table 5 indicates that the observation cohort experienced considerably shorter durations of mechanical ventilation as well as ICU stays compared to the control cohort, with the differences being statistically significant (all $p<0.05$).

Comparison of SOFA scores between the two cohorts is presented in Table 6. This table reveals that no significant differences were observed in SOFA values between the observation cohort and the control cohort before therapy and 1 d after therapy ($p>0.05$). However, after 2 and 3 d of therapy, the observation cohort's SOFA values were significantly lower than those of the control cohort, with the difference being statistically significant ($p<0.05$).

In recent years, in the process of exploring the pathogenesis of sepsis, we have gradually learned that the human body is not always in the pro-inflammatory stage and the emergence of sepsis is

mainly related to immunological dysfunction[1], while the disorder is associated with extensive lymphocyte apoptosis and a phase of immunological suppression[2]. Immune cells are undergoing apoptosis at any time, which plays an important role in maintaining immune balance and self-immune tolerance. The control of immunological function is related to the apoptosis of lymphocytes. Controlling the apoptosis process of lymphoid bacteria can promote or improve the immune ability of the human body, thereby improving human survivability[3]. Septic shock is the most severe stage of sepsis, a clinical critical illness and has a very high mortality rate. Multiple Organ Dysfunction Syndrome (MODS) disease and refractory hypotension are the two most important causes of death. Recent scientific studies have proved that in the progress of septic shock, the human immune system is in a biphasic abnormality or disorder stage between the overactive immune bacteria and the control of lymphatic bacteria[4]. In patients with septic shock, there are often delayed apoptosis of white blood cells, accelerated apoptosis of lymphocytes and protein repair problems, resulting in two symptoms of specific immune system control and non-specific hyperinflammatory response[5]. The T cell cohort is generally composed of $CD4^+$ helper T bacteria (Th), $CD8^+$ direct inhibitory T bacteria (Ts), killer T bacteria (Tc), etc., which jointly participated in the corresponding process of immunology, but $CD4^+/CD8^+$ showed papillae. The degree of functional coordination between dots and film plates were significantly reduced, which indicated that the immune function of cells had been suppressed and also indicated that the disease was serious and the prognosis was poor.

CRP is an important parameter commonly used in medicine to reflect the inflammatory response of the human body. The results of this experiment showed that after EGDT combined with glucocorticoid therapy, the CRP of the cured cohort was significantly reduced and the difference was statistically significant compared to the control cohort ($p<0.05$), which indicates that it had the effect of reducing inflammation. T cell subsets (generally $CD4^+$, $CD8^+$ and $CD4^{+/}CD8^+$) play a very important role in the modern human immunological system. In this investigation, $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ in the cured cohort all increased in different ways after being cured. The differences between the control cohort and the experimental cohort were statistically significant ($p<0.05$), indicating that EGDT combined with glucocorticoid therapy has the effect of significantly adjusting the immune function of the human body. This study's outcomes also demonstrated that the duration of ICU stays and mechanical ventilation during therapy were significantly shorter than those of the control cohort (both $p<0.05$), which indicates that both EGDT and glucocorticoid therapy can promote the progression of septic shock develop and improve symptoms.

TABLE 1: CRP OUTCOMES BEFORE AND AFTER THERAPY IN BOTH COHORTS

Cohort name	n	Before treatment	1 d after treatment	2 d after treatment	3 d after treatment
Control cohort	29	152.13±23.12	122.13±18.83	100.38±17.24	92.10±20.41
Observation cohort	31	147.39±25.13	90.03±20.25	60.25±15.28	44.32±10.21
t value		0.823	0.628	1.533	1.486
p value		0.601	0.049*	0.025*	0.012*

Note: *Compared with the control cohort, $p<0.05$

TABLE 2: COMPARISON OF $CD4^+$ CELL LEVELS BEFORE AND AFTER THERAPY IN BOTH COHORTS

Cohort name	n	Before treatment	1 d after treatment	2 d after treatment	3 d after treatment
Control cohort	29	312.53±140.04	322.02±120.03	347.52±154.32	365.89±162.42
Observation cohort	31	298.09±150.30	315.37±112.78	368.29±148.21	400.31±159.52
t value		0.574	0.907	0.866	1.752
p value		0.398	0.431	0.298	0.033*

Note: *Compared with the control cohort, $p<0.05$

TABLE 3: COMPARISON OF $CD8^+$ CELL LEVELS BEFORE AND AFTER THERAPY IN BOTH COHORTS

Cohort name	n	Before treatment	1 d after treatment	2 d after treatment	3 d after treatment
Control cohort	29	187.02±103.60	185.28±118.16	190.68±125.37	195.35±134.49
Observation cohort	31	182.34±108.07	199.21±106.63	227.97±104.49	272.56±102.28
t value		0.071	1.356	1.686	1.292
p value		0.768	0.521	0.049*	0.020*

Note: *Compared to the control cohort, $p<0.05$

TABLE 4: COMPARISON OF $CD4^+/CD8^+$ CELL RATIOS IN BOTH COHORTS BEFORE AND AFTER THERAPY

Cohort name	n	Before treatment	1 d after treatment	2 d after treatment	3 d after treatment
Control cohort	29	1.51±0.52	1.67±0.60	1.80±0.88	1.92±0.58
Observation cohort	31	1.63±0.47	1.72±0.78	1.96±0.69	2.33±0.35
t value		1.381	1.115	1.25	1.426
p value		0.752	0.683	0.482	0.045

TABLE 5: COMPARISON OF MECHANICAL VENTILATION DURATION AND ICU HOSPITALIZATION TIME BETWEEN THE TWO COHORTS COMPARISON OF $CD4^+/CD8^+$ CELL RATIOS IN BOTH COHORTS BEFORE AND AFTER THERAPY

Cohort name	n	Mechanical ventilation time (d)	ICU hospital stay (d)
Control cohort	29	7.28±3.51	14.12±3.05
Observation cohort	31	4.31±2.12*	10.15±3.01*
t value		0.723	0.628
p value		0.039	0.031

Note: *Compared to the control cohort, $p<0.05$

TABLE 6: A COMPARISON OF SOFA SCORES BETWEEN THE TWO COHORTS

Cohort name	n	Before treatment	1 d after treatment	2 d after treatment	3 d after treatment
Control cohort	29	7.52±1.38	8.35±3.15	9.34±3.28	9.32±4.12
Observation cohort	31	8.18±1.59	8.40±2.87	9.03±4.82	8.58±5.29
t value		0.703	0.525	2.201	2.457
p value		0.581	0.751	0.048	0.023

In recent years, although the clinical diagnosis and treatment of sepsis and septic shock have been greatly developed, many doctors still implement fluid recovery based on traditional shock symptoms such as hypotension, thus delaying the best time for diagnosis and treatment. At present, in modern medical clinics, the sequential appearance of low tissue perfusion pressure, secondary to multiple organ dysfunction and multiple organ failure is an important marker of shock, rather than hypotension[6,7]. It is commonly used in medicine to increase blood lactic acid among patient's suffering from septic shock. However, the 2012 international diagnostic criteria for severe sepsis and septic shock all use blood lactate levels≥-1 as a diagnostic index for septic shock and shock recovery should be the principal purpose to reduce the lactic acid content to normal value after 6 h[8]. Improving the treatment compliance of patients with EGDT can reduce subarachnoid hemorrhage in septic shock[9,10] and monitoring lactic acid level has great clinical significance for the timely treatment and rehabilitation of septic shock, so reducing lactic

acid level can improve the prognosis of patients, reduce mortality and simple, relatively safe and effective[11]. Asphyxia is essentially tissue ischemia. Under hypoxic conditions, the human body produces a large amount of lactic acid due to anaerobic metabolism. Therefore, lactic acid can reflect low tissue perfusion and extracellular ischemia, which can be manifested as septic shock early. In this analysis, fluid resuscitation was performed on septic shock patients with blood lactic acid≥4 mmol/l and systolic blood pressure>90 mmHg, and the prognosis level was compared with that of the study cohort. The research cohort significantly decreased, pointing out that the detection of blood lactic acid level can detect the shock state of sepsis patients as early as possible, which plays an important role in early diagnosis, timely intervention and clinical practice, and because reducing blood lactic acid level can effectively improve the prognosis of patients, significantly reduces the SOFA score[12].

In summary, EGDT and glucocorticoid therapy can prevent and treat septic shock through non-selective elimination and control of circulating bacterial hormone levels and can change the immunological disorders of patients with septic shock and restructure immunology remains stable. Thus, by reducing sepsis patients inflammatory reactions, CRP levels are lowered, which reduces the persistence of mechanical ventilation and ICU waiting times and improves prognosis. As a result, selecting EGDT in conjunction with glucocorticoids in the therapy of septic shock could promote early intervention and enhance prognosis.

Conflict of interests:

The authors declared no conflict of interest.

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