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# Combination of plasma exchange and adsorption versus plasma exchange in pediatric acute liver failure: a multicenter cohort study

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**Abstract**

**Objectives:** This study aimed to compare the efficacy of double plasma molecular adsorption system (DPMAS) with half-dose plasma exchange (PE) to that of full-dose PE in pediatric acute liver failure (PALF).

**Methods:** This multicenter, retrospective cohort study was conducted in 13 pediatric intensive care units in Shandong Province, China. DPMAS + PE and single PE therapies were performed in 28 and 50 cases, respectively. The patients' clinical information and biochemical data were obtained from the patients' medical records.

**Results:** The severity of illness did not differ between the two groups. At 72 h after treatment, comparing with PE group, the rates of decline of Pediatric model for End-stage Liver Disease and Pediatric Sequential Organ Failure Assessment scores as well as total bilirubin blood ammonia, and interleukin-6 were significantly higher, while the short-term effective rate (75.0% vs 44.0%, *P*=0.008) was significantly higher in the DPMAS+PE group. The volume of plasma consumption (26.5 vs 51.0 mL/kg, *P*=0.000) and the rate of adverse events (3.6% vs 24.0%, *P*=0.026) were lower in the DPMAS+PE group than in the PE group, respectively. However, there was no statistical difference in the 28-day mortality between the two groups (21.4% vs 40.0%, P >0.05).

**Conclusions:** For PALF patients, both DPMAS+ half-dose PE and full-dose PE could improve the liver function, while DPMAS+ half-dose PE could significantly reduce plasma consumption without obvious adverse effects in contrast with full-dose PE. Thus, DPMAS+ half-dose PE may be a suitable alternative method for PALF in the context of the increasingly tight blood supply situation.

**Keywords:** acute liver failure, artificial liver support, double plasma molecular absorption, plasma exchange, paediatric

**What Is Known**

- Artificial liver support system is one of the common methods for the treatment of paediatric acute liver failure (PALF).
- There are few reports on the application of double plasma molecular adsorption system (DPMAS) in PALF.

**What Is New**

- Both DPMAS+ half-dose PE and full-dose PE were effective in improving liver function without obvious adverse effects in PALF.
- Compared to full-dose PE, DPMAS+ half-dose PE could significantly increase the short-term effective rate and reduce plasma consumption in PALF.
- It is the first report describing the use of Mini-DPMAS system in PALF.

**Abbreviation list**

ALSS: Artificial liver support systems

PALF: Pediatric acute liver failure

PE: Plasma exchange

DPMAS: Double plasma molecular adsorption system

CVVHDF: Continuous venovenous hemodiafiltration

PELD: Pediatric model for End-stage Liver Disease

PSOFA: Pediatric Sequential Organ Failure Assessment

INR: international normalized ratio

PTA: Prothrombin time activity

## Introduction

Although acute liver failure (ALF) is a rare condition, it is life threatening. In children, it can result from infection or develop secondary to metabolic disorders and manifests as coagulopathy, jaundice, and encephalopathy (1). However, the mortality of children with ALF is generally high, especially in those younger than 2 years of age (2-5). Patients with acute liver failure are prone to develop bacterial infection (6). The most frequent causes of death in children with ALF are multiple organ failure and severe sepsis. Artificial liver support system (ALSS) is essential until liver transplantation is performed and to facilitate liver regeneration when a donor is not available. Although ALSS have been applied to treat patients with ALF, the efficacy of these treatments has not been established (7, 8).

Several types of ALSS have been reported for the treatment of pediatric liver failure, including plasma exchange (PE), molecular adsorbents recirculating system, single-pass albumin dialysis, hemodialysis (HD), hemodiafiltration (HF), and the combination of PE and HD/F (9-13). PE removes protein-bound toxins, inflammatory cytokines, and endotoxins as well as improves coagulation function by replacing coagulation factors, albumin, and other beneficial components. Both high-volume PE and standard-volume PE ameliorate systemic inflammatory response syndrome and improve short-term survival in patients with ALF(14, 15).

The double plasma molecular adsorption system (DPMAS) is based on bilirubin adsorption therapy and utilizes an adsorption column comprising macroporous neutral adsorption and ion exchange resins to adsorb medium-to-large-size molecular toxins.

Bilirubin adheres to the resin in the BS330, whereas the resin in the HA330-II blood perfusion device adsorbs inflammatory mediators (16). There are several reports on the application of DPMAS in adult patients with ALF but few describing its use in pediatric patients with ALF (17-22). Furthermore, the efficacy profiles of DPMAS combined with sequential half-dose PE and single full-dose PE have not been compared. The current multicenter cohort study was conducted to compare the effectiveness of two ALSS treatment methods in pediatric ALF patients.

## Methods

### *Study Design and Participants*

This multicenter, retrospective cohort study was conducted in 13 tertiary pediatric intensive care units in Shandong Province, China. All pediatric patients with ALF received full-dose PE or DPMAS with half-dose PE therapy between January 2017 and June 2021 were included in the analysis.

Pediatric ALF was diagnosed when there was biochemical evidence of liver failure and either a prothrombin time of ≥15 s or international normalized ratio (INR) of ≥1.5 that was not corrected by vitamin K with hepatic encephalopathy or a prothrombin time of ≥20 s or INR of ≥2.0 in the presence or absence of clinical hepatic encephalopathy with no known evidence of chronic liver disease (23).

The study protocol was approved by each institution's ethics review board.

***Treatment Methods***

*Comprehensive medical treatment*

All patients were administered standardized treatment according to the 2018 Guidelines for the Diagnosis and Treatment of Liver Failure by the Chinese Medical Association (24). Liver-protective drugs and albumin were supplied to patients as needed. ALSS treatments were provided to patients according to the treatment schedule at each participating hospital.

*The application of Artificial liver support system (ALSS) in our patients*

The criteria needed to initiate ALSS treatment in patients with PALF was as follows: (i) Per-, early- and middle-stage liver failure caused by various reasons, especially appropriating for patients with prothrombin time activity (PTA) between 20% and 40% (24). (ii) Waiting for liver source before liver transplantation for end-stage liver disease. (iii) Severe cholestatic liver disease with poor response to medical treatment, severe hyperbilirubinemia due to various reasons (24). All participants' guardians provided written informed consent to ALSS treatment.

We had 115 patients admitted to PICU with acute liver failure. A total of 78 patients were included in the study, with 50 patients treated with PE , and 28 received DPMAS+PE.

*Full-dose PE*

A double-lumen central venous catheter was inserted into the patient's femoral or internal jugular vein. PE procedures were performed with a continuous renal replacement machine (Prismaflex; Gambro, Lund, Sweden) and a plasma separator

(TPE1000; Gambro). Heparin sodium was used for anticoagulation therapy with 30–50 U/kg body weight as the initial dose and 5–10 U/kg/h as the maintenance dose. The plasma was separated from the blood by a plasma separator and discarded. Then, the blood was mixed with fresh frozen plasma or virus-inactivated plasma and perfused back into the patient. Patients underwent PE with a target of 1.5–2.0 plasma volumes per treatment course. It was performed once daily with each session lasting 2–3 h.

*DPMAS combined with half-dose PE*

PE was implemented using half-volume plasma replacement. Subsequently, the separated plasma was transported by blood pumping to the bilirubin adsorption resin and the neutral macroporous adsorption resin for dual plasma adsorption. For patients weighing ≥30 kg, BS330 and HA330-II adsorption resins (both from Zhuhai Health Sails Biotechnology Co., LTD., Zhuhai, China) were chosen. For patients weighing at least 10 kg but less than<30 kg, mini-DPMAS incorporated BS80 and HA60 resins (Zhuhai Health Sails Biotechnology Co., Ltd.) with a small volume of the extracorporeal circulation. DPMAS or mini-DPMAS combined with PE was performed once daily with every session lasting 3–4 h.

***Outcome Measures***

The primary outcomes for this study were the 28-day mortality and the effective rate at the end of ALSS treatment. The effective rate was according to the 2018 Guidelines for the Diagnosis and Treatment of Liver Failure by the Chinese Medical Association (24). Treatment was confirmed to be effective if patients met the following criteria: (i)

Clinical signs disappeared, including abdominal distension, poor appetite, frailty, and hemorrhaging as well as the disappearance of hepatic encephalopathy; (ii) Progressive improvement of jaundice and liver size; (iii) Progressive improvements in liver parameters (total bilirubin <2× upper limit of normal, prothrombin time activity of >70%, or INR of <1.5).

The secondary outcomes included the volume of plasma needed for ALSS treatment, the changes in Pediatric model for End-stage Liver Disease (PELD) and Pediatric Sequential Organ Failure Assessment (PSOFA) scores, the blood ammonia levels after ALSS treatment, and the rate of adverse events. PELD and PSOFA scores were used to assess the severity of illness (25, 26). The PELD score was calculated as follows: PELD = 0.436 × age (<1 year) − 0.687 $\text{Log}_e$ albumin + 0.480 $\text{Log}_e$ total bilirubin + 1.857 $\text{Log}_e$ INR + 0.667 growth failure. The formula used to calculate the PSOFA score is provided in the Supplementary Appendix, http://links.lww.com/MPG/D99 .

Adverse events included bleeding at the puncture site, hypotension, thrombocytopenia, hyper/hypocalcemia, alkalemia, acidosis, and allergic reactions. Hypotension is defined as blood pressure < 5th percentile for age or systolic blood pressure < 2 SD below normal for age. Thrombocytopenia is defined as platelet < $100\times10^9$/L. Hypercalcemia is defined as a serum calcemia > 2.75 mmol/L. Hypocalcemia is defined as a serum calcemia < 2.25 mmol/L. Alkalemia refers to pH >7.45 and acidosis refers to pH <7.35. Allergic reactions is defined as local or extensive urticaria, angioedema, bronchospasm, laryngeal edema, cyanosis,

hypotension, and anaphylactic shock, occurred shortly after transfusion.

***Data Collection***

Patients' general data (age, sex, height, and weight), biochemical data (laboratory indicators reflecting liver function and systemic inflammation before and after ALSS treatment), and treatment information (the volume of plasma used in ALSS and the duration of vasoactive drug use, the time of initiation of ALSS) were retrospective collected by the attending intensivists according to standard practice in each PICU. Furthermore, data pertaining to the etiology of pediatric ALF, adverse events, and 28-day mortality were collected. The rates for the decline of some main indicators at 72 h after ALSS therapy were calculated as follows: the decline rate at 72 h after ALSS therapy = [(value before treatment − value at 72 h after therapy)/value before treatment] × 100%.

***Statistical Methods***

Continuous variables are presented as the means and standard deviations or the medians and interquartile ranges (IQRs) and were compared using independent Student's *t* or Mann-Whitney tests. Categorical variables are reported as frequencies and percentages and were compared between groups by using $\chi^2$ tests. For within-group comparisons, a paired-sample *t* test or Wilcoxon signed-rank test was used. All analyses were performed using SPSS 26.0 (IBM, Armonk, NY). A two-sided *P* value of 0.05 was considered statistically significant.

**Results**

Totally there were 115 pediatric patients with acute liver failure admitted to these PICUs (Suppl Fig. 1, http://links.lww.com/MPG/D100 ), including 32 cases received standard treatment therapy, 5 cases being excluded as well as 78 cases received ALSS treatment who were finally included in this study. Furthermore, among these 78 cases, there was 50 treated with PE (153 sessions) and 28 received DPMAS+PE (88 sessions). Additionally, there was two children received mini-DPMAS+PE treatment because of their low body weight (8.4 kg and 4.2 kg), with one survived while another one eventually died of multiple organ failure.

As far as 115 patients with PALF as a whole, the most common etiology caused acute liver failure was infection (25.2%) and there was no definite etiology in 42.6% of these cases (Suppl Tab. 1, http://links.lww.com/MPG/D101 ). Furthermore, among 78 children enrolled in this study, Epstein-barr virus infection and cytomegalovirus infection accounted for 12.8% and 16.7%, respectively (Table 1). Other etiology included 12.8% hemophagocytic lymphohistiocytosis, 6.4% leukaemia, 3.8% mushroom poisoning, 1.3% pesticide poisoning and 14.2% metabolic disease. 7 patients were diagnosed with Wilson's disease, 2 patients were phenylalaninemia, 1 patient was citrin protein deficiency and 1 patient was methylmalonic acidemia. There were 12 cases of hepatic encephalopathy in all patients and 5 patients improved. PE group and DPMAS+PE group did not differ with regard to age, sex, body mass index, biochemical parameters, or PELD and PSOFA scores before ALSS treatment (Tables 1 and 2).

At 72 h after ALSS therapy, the levels of alanine transaminase, aspartate transaminase, direct and total bilirubin, blood ammonia, interleukin-6, procalcitonin as well as the PELD score decreased whereas PA increased in both two groups (Table 2). Meanwhile, prothrombin time activity increased and INR decreased significantly in both groups. The 28-day mortality rate was only slightly lower in the DPMAS+PE group than that in the PE group (21.4% vs. 40.0%, respectively; $P = 0.095$) (Table 4). However, the short-term effectiveness rate was significantly higher in the DPMAS+PE group than that in the PE group (75.0% vs 44.0%, respectively; $P = 0.008$).

The median volume of plasma needed in the DPMAS+PE group was 26.5 (IQR, 20.0 – 44.8) mL/kg, which was significantly less than the 51.0 (IQR, 48.3 – 58.0) mL/kg in the PE group ($P < 0.05$). At 72 h after ALSS therapy, in contrast with PE group, the rates of decline in the PELD and PSOFA scores were significantly higher in the DPMAS+PE group (78.7% vs 33.6% and 24.3% vs 0.0%, respectively) ($P < 0.05$) (Table 3). Similarly, compared to PE group, the rates of decline of total bilirubin, blood ammonia, and interleukin-6 levels were significantly higher in the DPMAS+PE group (50.9% vs 28.2%, 29.8% vs 11.4%, 81.0% vs 20.0%, respectively) ($P < 0.05$). Twelve adverse events were reported in the PE group, including hypotension ($n = 6$), allergic reaction ($n = 5$), and hypercalcemia ($n = 1$). By contrast, only one instance of adverse event was reported in DPMAS+PE group. The total incidence of adverse events was significantly lower in the DPMAS+PE group (3.6%) than that in the PE group (24.0%) ($P< 0.05$) (Table 4). The durations of vasoactive drug use, the time of

initiation of ALSS and pediatric intensive care unit charges did not differ between the treatment groups ($P > 0.05$).

With six months followed-up after discharge, there was 37 cased still survived, 6 died and 9 cases lost to follow-up.

**Discussion**

This study shows that, for children with ALF, both full-dose PE and DPMAS+ half-dose PE could effectively improve liver function. In comparison with full-dose PE, the combination of DPMAS and half-dose PE remarkably increased the short-term effective rate without distinct adverse events, while it did not significantly reduce the 28-day mortality. Furthermore, DPMAS combined with half-dose PE could save about 50% usage of plasma. Therefore, DPMAS+ half-dose PE may be a suitable alternative method for PALF in the context of the increasingly tight blood supply situation.

The etiology of acute liver failure in children is diverse, including infectious, metabolic, immune, toxic, vascular, and malignant tumors. In our study, the most common etiologies were viral infections, followed by hemophagocytic syndrome and hepatolenticular degeneration. This is consistent with previous studies (23). In other two studies in China, vital infection was also shown to be one of the common causes of acute liver failure in children (27, 28). This also seems to be in line with other developing countries (29, 30). Here we reported that only 13.0% children with acute liver failure had encephalopathy. In other studies, the proportion of hepatic encephalopathy ranged from 11% to 53% (31, 32). the reason why our study was low

may be related to the difficulty in detecting hepatic encephalopathy in younger children.

Liver transplantation was reported to be an efficient method to improve the survival rate of PALF after artificial liver therapy. Relatively, ALSS is easy to carry out for PALF. Additionally, PE is the most commonly used mode of ALSS in pediatric patients because of its safety, effectiveness, and ease of operation (33, 34). And PE could not merely provide fresh plasma but also eliminate pathogenic and toxic molecules from circulation while restoring coagulation factors (35). Although PE is effective in patients with severe and sudden liver failure, it is frequently limited by plasma availability (36).

Within the progress of DPMAS, plasma is continuously filtered through a bilirubin adsorber and a macroporous resin, which can adsorb medium-sized and macro-molecular toxins, including bilirubin, to improve jaundice and slow the deterioration of acute liver failure. As compared to plasma exchange, DPMAS needs less volume of plasma which can be useful especially in countries with limited availability of blood products (fresh frozen plasma). However, without large volume of plasma supplement, DPMAS cannot dramatically improve coagulation disorders (18). Thus, the combination of these two approaches can be highly complementary. In a report by Yang et al.(17), DPMAS+PE was found to be safe and effective in five children with ALF caused by mushroom poisoning. In the present study, the short-term effectiveness rate was significantly higher in the DPMAS+PE group than that in the PE group. it may be related to the improvement of biochemical parameters such as

TBIL, blood ammonia and IL-6. The transient clearance in inflammation mediators and metabolic substances could provide a balance environment and reduce liver damage until the failing liver survives spontaneously regenerates. There are also similar costs to both methodologies. Although DPMAS+PE have two more adsorption columns than PE alone, its plasma usage was half of PE alone.

22 of the 28 patients receiving DPMAS+PE weighed ≤30 kg, and there was only one adverse event noted. The two patients that were <10 kg received the volume-adapted mini-DPMAS treatment: one child who weighed 8.4 kg underwent three rounds of mini-DPMAS and recovered eventually, but another child weighing 4.2 kg underwent only one round and died. To the best of our knowledge, this is the first report describing the use of this mini-DPMAS system for pediatric ALF. Overall, DPMAS+PE and PE treatments were well tolerated by the pediatric ALF patients and improved their biochemical parameters, providing a microenvironment that may be suitable for transplantation or hepatocyte regeneration.

There are few studies comparing DPMAS+PE with PE in adult ALF. Yao et al. (21) reported that DPMAS+PE improved the 28-day survival rates for patients with hepatitis B virus acute-on-chronic liver failure at an intermediate-advanced stage in comparison to that for patients treated with PE alone. Similarly, Guo et al. (18) observed significantly better effective and 28-day survival rates in those treated with DPMAS+PE but not in patients with liver failure that was moderate or severe. The present study is the first report comparing DPMAS+PE with PE in pediatric ALF. However, the improvement for 28-day survival rates did not reach statistical

significance. One possible reason for this may be the small number of cases for analysis, which made it impossible to stratify patients by severity and stage of illness. Additionally, the etiology of ALF in the pediatric population may differ from that in adults. Therefore, further large-scale clinical studies are needed to assess this effect. This study has some limitations that should be noted. First, this was not a randomized controlled trial, and so confounding factors could not be completely avoided. Second, as mentioned above, we were unable to stratify the patients according to the severity of their conditions because of the small number of cases. However, the results of our study show that DPMAS combined with half-dose PE is superior to full- dose PE for the removal of bilirubin and blood ammonia and has a higher short-term effective rate. Notably, there were fewer adverse events with the combined treatment and no allergic reactions. Furthermore, the combined application of DPMAS and half-dose PE dramatically reduced the volume of plasma needed, which also reduces the risks associated with large-volume infusions.

**Conclusion**

For pediatric ALF patients, both DPMAS + half-dose PE and full-dose PE could improve liver function, while DPMAS + half dose PE could not significantly reduce the 28-day mortality comparing with full dose PE therapy. However, notably, the combined treatment had fewer adverse reactions and a higher short-term effective rate. As less plasma is needed for DPMAS + half dose PE treatment, it may be preferred under conditions where blood products are in critically short supply.

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**Figure Legends**

Suppl Fig. 1. Screening, enrollment, and analysis of pediatric patients with ALF. PICU: pediatric intensive care unit; ALF: acute liver failure; SMT: standard medical treatment; ALSS: artificial liver support systems; PE: plasma exchange; DPMAS: double-plasma molecular adsorption system

**Table 1.** Baseline characteristics of the study cohort

| Characteristics | All patients (n = 78) | PE group (n = 50) | DPMAS + PE group (n =28) | *P* value |
|---|---|---|---|---|
| Age, months | 27.0 (16.8, 66.3) | 25.0 (12.8, 77.0) | 38.5 (25.0, 56.0) | 0.999 |
| Male sex, n (%) | 49 (62.8) | 33 (66.0) | 16 (57.1) | 0.437 |
| Weight, kg | 15.0 (11.0, 19.5) | 12.3 (10.4, 19.5) | 16.6 (15.0, 22.1) | 0.916 |
| Body mass index, kg/cm2 | 16.3 (14.8, 18.6) | 16.3 (14.4, 18.9) | 16.3 (15.0, 18.0) | 0.618 |
| Etiology of pediatric acute liver failure, n (%) | | | | 0.076 |
| Infectious | 24 (30.8) | 18 (36.0) | 6 (21.4) | |
| Epstein-barr virus | 10 (12.8) | 6 (12.0) | 4 (14.3) | |
| Cytomegalovirus | 13 (16.7) | 11 (22.0) | 2 (7.1) | |
| Hepatitis B virus | 1 (1.3) | 1 (2.0) | 0 (0.0) | |
| Hemophagocytic lymphohistiocytosis | 10 (12.8) | 4 (8.0) | 6 (21.4) | |
| Leukaemia | 5 (6.4) | 1 (2.0) | 4 (14.3) | |
| Mushroom poisoning | 3 (3.8) | 2 (4.0) | 1 (3.6) | |
| Pesticide poisoning | 1 (1.3) | 0 (0.0) | 1 (3.6) | |
| Metabolic disease | 11 (14.2) | 8 (16.0) | 3 (10.7) | |
| Wilson's disease | 7 (9.0) | 5 (10.0) | 2 (7.1) | |
| Phenylalaninemia | 2 (2.6) | 2 (4.0) | 0 (0.0) | |
| Citrin protein deficiency | 1 (1.3) | 0 (0.0) | 1 (3.6) | |
| Methylmalonic acidemia | 1 (1.3) | 1 (2.0) | 0 (0.0) | |
| Indeterminate | 24 (30.7) | 17 (34.0) | 7 (25.0) | |
| Hepatic encephalopathy | 12 (15.4) | 9 (18.0) | 3 (10.7) | 0.521 |
| The time of initiation of ALSS, h | 16.9 (8.0, 28.1) | 15.4 (8.6, 26.7) | 20.5 (6.6, 30.5) | 0.764 |

PE: plasma exchange; DPMAS: double-plasma molecular adsorption system; ALSS: artificial liver support system

**Table 2.** Changes in laboratory parameters, PELD, and PSOFA scores before and 72 h after treatment in the PE and DPMAS+PE groups

| Variables | $P_1$ | PE group (n = 50) | | $P_2$ | DPMAS+PE group (n = 28) | | $P_3$ |
|---|---|---|---|---|---|---|---|
| | | Before treatment | 72 h after treatment | | Before treatment | 72 h after treatment | |
| ALT, U/L | 0.211 | 1372.0 (193.3, 2035.5) | 161.5 (62.0, 302.0) | 0.000 | 362.5 (143.0, 1881.0) | 77.0 (25.0, 270.0) | 0.000 |
| AST, U/L | 0.096 | 870.0 (367.0, 5426.8) | 110.0 (63.0, 510.0) | 0.000 | 730.5 (191.0, 4236.0) | 104.5 (30.0, 252.3) | 0.000 |
| TBIL, umol/L | 0.677 | 46.7 (26.1, 101.1) | 29.6 (15.4, 87.3) | 0.001 | 65.0 (15.4, 201.6) | 9.6 (5.3, 134.6) | 0.000 |
| DBIL, umol/L | 0.617 | 34.2 (14.3, 73.5) | 16.9 (4.2, 40.3) | 0.000 | 13.6 (11.2, 119.2) | 8.4 (2.2, 75.1) | 0.000 |
| Blood ammonia, umol/L | 0.283 | 78.5 (61.0, 109.0) | 69.0 (46.0, 113.0) | 0.014 | 68.5 (35.0, 123.0) | 38.5 (30.3, 67.0) | 0.000 |
| PA, mg/L | 0.088 | 52.9 (22.6, 96.7) | 125.0 (94.0, 189.0) | 0.000 | 72.7 (26.7, 133.0) | 90.8 (48.5, 173.4) | 0.002 |
| ALB, g/L | 0.006 | 29.4 (24.4, 33.8) | 35.1 (26.8, 37.7) | 0.014 | 35.1 (29.6, 36.2) | 35.3 (31.6, 37.2) | 0.508 |
| BUN, mmol/L | 0.662 | 6.4 (3.4, 9.8) | 3.6 (2.6, 7.0) | 0.010 | 6.9 (4.0, 10.1) | 5.9 (5.1, 6.7) | 0.218 |
| Cr, umol/L | 0.405 | 36.0 (25.7, 64.2) | 28.2 (19.0, 67.0) | 0.016 | 40.1 (32.5, 73.6) | 25.6 (23.2, 47.8) | 0.000 |
| INR | 0.155 | 2.1 (1.7, 3.4) | 1.3 (1.1, 1.8) | 0.015 | 2.0 (1.6, 3.1) | 1.3 (1.2, 1.9) | 0.003 |
| PTA, s | 0.041 | 37.0 (22.5, 48.0) | 63.0 (35.5, 77.8) | 0.000 | 45.5 (29.0, 58.0) | 65.0 (38.0, 78.0) | 0.001 |
| IL-6, pg/ml | 0.116 | 34.4 (18.0, 223.2) | 27.4 (12.5, 178.5) | 0.002 | 306.4 (20.7, 529.6) | 38.3 (10.7, 59.9) | 0.000 |
| PCT, mg/L | 0.194 | 3.2 (0.6, 30.7) | 1.9 (0.9, 20.7) | 0.012 | 16.1 (0.7, 100.0) | 1.1 (0.7, 4.5) | 0.000 |
| LAC, mmol/L | 0.115 | 1.8 (1.5, 4.1) | 2.5 (1.3, 4.2) | 0.814 | 1.4 (1.3, 2.3) | 0.9 (0.6, 2.2) | 0.013 |
| PELD | 0.102 | 15.0 (7.5, 27.3) | 11.0 (5.5, 19.8) | 0.002 | 10.0 (3.0, 19.0) | 0.0 (-2.0, 9.0) | 0.000 |
| PSOFA | 0.538 | 11.0 (7.0, 13.0) | 10.0 (7.0, 14.0) | 0.474 | 10.0 (8.0, 16.0) | 9.0 (5.0, 11.0) | 0.000 |

$P_1$, Derived from comparison by Student's t-test or Mann-Whitney test before treatment between the 2 groups. $P_2$, Derived from comparison by a paired sample t-test or Wilcoxon signed rank test before and 72 h after treatment in the PE group. $P_3$, Derived from comparison by a paired sample t-test or Wilcoxon signed rank test before and 72 h after treatment in the DPMAS+PE group. ALT: alanine aminotransferase, AST: aspartate aminotransferase, TBIL: total bilirubin, DBIL: direct bilirubin, PA: prealbumin, ALB: albumin, BUN: blood urea nitrogen, Cr: creatinine, INR: international normalized ratio, PTA: prothrombin time activity, PT: prothrombin time, PLT: platelet, WBC: white blood cell, HGB: hemoglobin, IL-6: interleukin, PCT: procalcitonin, LAC: lactic acid

**Table 3.** Comparison of decline rates of laboratory parameters at 72 h after treatment between the PE and DPMAS+PE groups

| Variable | PE group (n = 50 ) | DPMAS+PE group (n = 28 ) | *P* value |
|---|---|---|---|
| ALT, % | 82.6 (58.8, 91.2) | 77.7 (67.2, 90.4) | 0.496 |
| AST, % | 87.8 (59.6, 94.8) | 87.1 (75.9, 94.0) | 1.000 |
| TBIL, % | 28.2 (-15.8, 53.2) | 50.9 (42.1, 85.3) | 0.001 |
| DBIL, % | 42.3 (22.0, 72.1) | 58.2 (26.6, 82.1) | 0.078 |
| Blood ammonia, % | 11.4 (-4.2, 30.7) | 29.8 (10.3, 45.8) | 0.018 |
| PA, % | -124.3 (-253.3, -25.1) | -55.4 (-106.4, -34.2) | 0.150 |
| ALB, % | -4.9 (-24.1, 2.3) | -1.6 (-18.7, 9.8) | 0.218 |
| BUN, % | 45.1 (-16.0, 62.5) | 27.2 (-57.5, 41.4) | 0.083 |
| Cr, % | 17.9 (-14.6, 58.3) | 35.2 (15.3, 54.7) | 0.480 |
| INR, % | 34.1 (19.5, 50.9) | 22.5 (4.4, 56.6) | 0.411 |
| PTA, % | -80.0 (-144.9, -17.9) | -23.8 (-73.3, 0.0) | 0.804 |
| IL-6, % | 20.0 (-3.6, 46.5) | 81.0 (35.0, 89.2) | 0.000 |
| PCT, % | 51.8 (-53.0, 82.3) | 86.4 (-151.2, 96.1) | 0.192 |
| LAC, % | 5.6 (-54.0, 46.2) | 30.8 (-6.3, 62.9) | 0.024 |
| PELD, % | 33.6 (10.8, 64.0) | 78.7 (44.3, 133.2) | 0.001 |
| PSOFA, % | 0.0 (-8.9, 21.4) | 24.3 (11.8, 40.0) | 0.006 |

ALT: alanine aminotransferase, AST: aspartate aminotransferase, TBIL: total bilirubin, DBIL: direct bilirubin, PA: prealbumin, ALB: albumin, BUN: blood urea nitrogen, Cr: creatinine, INR: international normalized ratio, PTA: prothrombin time activity, IL-6: interleukin, PCT: procalcitonin, LAC: lactic acid, PELD: pediatric model for end-stage liver disease, PSOFA: pediatric sequential organ failure assessment

**Table 4.** Comparison of clinical variables after treatment between the PE and DPMAS+PE groups

| Variable | PE+CVVHDF group (n= 50 ) | DPMAS+PE group (n = 28 ) | *P* value |
|---|---|---|---|
| Effective rate, % (n) | 44.0 (22) | 75.0 (21) | 0.008 |
| 28-day mortality, % (n) | 40.0 (20) | 21.4 (6) | 0.095 |
| Plasma volume, ml | 700 (550, 975) | 650 (350, 800) | 0.033 |
| Plasma volume, ml/kg | 51.0 (48.3, 58.0) | 26.5 (20.0, 44.8) | 0.000 |
| Adverse events, n (%) | 12 (24.0) | 1 (3.6) | 0.026 |
| Duration of vasoactive drug use, h | 48.0 (0.0, 114.0) | 32.4 (0.0, 78.5) | 0.966 |
| Pediatric intensive care unit charges, ￥ | 105893.3 (77612.0, 164376.9) | 128955.6 (88717.5, 179448.6) | 0.588 |