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Original Article

Efficacy and safety analysis of double plasma molecular adsorption system plus plasma exchange for treating acute-on-chronic liver failure

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Abstract: Objective: This retrospective study aimed to evaluate the efficacy and safety of the double plasma molecular adsorption system (DPMAS) plus plasma exchange (PE) in treating acute-on-chronic liver failure (ACLF). Methods: A total of 200 ACLF patients were enrolled and divided into two groups: the control group received PE therapy alone, while the observation group received DPMAS in addition to PE. Clinical data were collected from both groups, including treatment efficacy, safety, clinical indicators, symptom improvement, liver function, coagulation function, electrolytes, nutritional status, inflammatory markers, and short-term prognosis (assessed by the Model for End-Stage Liver Disease (MELD) score), and 12-week survival rate. Results: Compared to the control group, the observation group showed notably higher total effective rates and greater symptom improvement at 4 weeks post-treatment. The fluctuation range of all coagulation indices after treatment was smaller in the observation group relative to the control group. Moreover, after treatment, the observation group showed a smaller number of PE treatments, less plasma volume used, and shorter length of hospital stay compared to the control group, as well as lower liver function indicator levels and MELD scores. Conclusion: DPMAS combined with PE therapy demonstrates definite efficacy in ACLF treatment without increasing side effects.

Keywords: Liver failure, plasma exchange, dual plasma molecular adsorption system, therapeutic effect

Introduction

As a severe form of acute compensated cirrhosis, characterized by acute hepatic dysfunction and multi-organ failure, acute-on-chronic liver failure (ACLF) significantly increases the risk of short-term mortality in affected patients [1]. Its etiology involves various intrahepatic and extrahepatic injuries; bacterial infections, alcoholism, and reactivated viral hepatitis are common causes [2]. Specifically, hepatitis B virus (HBV)-related ACLF accounts for the vast majority of cases (up to 80%), characterized by rapid onset, rapid progression, and poor prognosis, with a mortality risk of 50%-90% [3]. The pathophysiology of ACLF is closely associated with extensive hepatocyte necrosis, severe coagulation dysfunction, systemic inflammatory response, and cytokine storms, resulting in immune paralysis, which leads to secondary infections and multi-organ failure [4]. Evidence has highlighted that dysregulation of programmed cell death pathways, particularly those mediated by key molecules such as caspase-8, plays a critical role in extensive hepatocyte loss and amplification of inflammatory responses observed in ACLF [5]. Furthermore, dysfunction of the ubiquitin-proteasome system, which is essential for maintaining protein homeostasis and regulating inflammatory signaling (e.g., the NF-κB pathway), may exacerbate cellular damage and systemic inflammation in liver failure [6]. Liver transplantation remains the only curative treatment for ACLF. However, due to a high financial burden, severe donor shortage, and potentially life-threatening complications for living donors, many patients die during the waiting period [7].

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Plasma exchange (PE), a classic non-biological artificial liver support technique, is formally recognized as an effective therapy for liver failure in both China and the United States. PE removes small- and medium-molecular-weight metabolic toxins, immune complexes, and other macromolecules from circulation, corrects electrolyte imbalances, balances pH levels, and improves internal homeostasis [8]. However, PE may also result in the loss of beneficial substances (e.g., coagulation factors, proteins), with limited efficacy in removing blood ammonia, creatinine, and inflammatory mediators. Moreover, hypocalcemia and cerebral edema may be triggered in case of excessive plasma infusion [9, 10]. Meta-analyses have shown that ACLF patients receiving PE therapy have significantly improved one-year survival compared to those receiving standard drug therapy, proving a survival benefit [11].

The double plasma molecular adsorption system (DPMAS) is a novel non-biological artificial liver technique that rapidly removes bilirubin, inflammatory mediators, and various toxic substances from plasma. However, it cannot effectively correct coagulation abnormalities in the absence of plasma supplementation during treatment [12]. When DPMAS is combined with PE, the two therapies complement each other to maximize clinical efficacy; nevertheless, there are certain disadvantages, including high cost, procedural complexity, time-consuming procedures, and increased risk of infection [13]. Geng et al. [14] suggested that in pediatric patients with acute liver failure, DPMAS plus PE effectively improved liver function and survival outcomes, suggesting that this combined approach may also benefit ACLF patients.

Currently, few studies have evaluated DPMAS in combination with PE in patients with ACLF. This study aims to provide a comprehensive, multidimensional evaluation to further validate the specific clinical advantages of this combined therapy in ACLF.

Patients and methods

General data

From December 2022 to December 2025, 200 ACLF patients admitted to Zhoukou Central Hospital were included in this retrospective study. The control group comprised 99 patients who received PE therapy alone, while the observation group included 101 patients who received DPMAS in addition to PE. There were no significant differences in baseline characteristics between the groups ($P > 0.05$), indicating clinical comparability. Given that this study utilized only anonymized retrospective data and did not involve any intervention or contact with patients, the Ethics Committee waived the requirement for written informed consent. All data were anonymized before analysis. The study protocol was reviewed and approved by the Ethics Committee of the Zhoukou Central Hospital.

The total effective rate was deemed as the primary efficacy endpoint for *post-hoc* power evaluation. With $\alpha = 0.05$ (two-tailed) and $\beta = 0.20$, and using the Pearson χ^2 test, the minimum sample size required for each group was calculated to be 84 cases. This study included 99 cases in the control group and 101 cases in the observation group, yielding an actual test power exceeding 0.85, which indicates that the sample size was sufficient to detect differences between groups.

Inclusion and exclusion criteria

Inclusion criteria: Diagnosis of ACLF based on computed tomography (CT), ultrasound, or other imaging techniques [15]; aged 18-80 years; no contraindications to the study treatment regimen; no history of liver transplantation; normal cognitive and communication abilities; complete clinical documentation.

Exclusion criteria: Presence of malignant tumors; severe complications involving the heart, brain, or kidneys; serious electrolyte or acid-base imbalance; circulatory failure; concurrent autoimmune diseases or infectious diseases; extravascular hemolysis, unstable hemodynamics, active bleeding, decompensated ascites, or disseminated intravascular coagulation; with liver diseases such as hepatitis A; pregnancy or lactation.

Treatment method

Patients in the control group received PE therapy using the WLXGX-8888 blood purification system (artificial liver support) and plasma sep-

arator. Tubing was connected following the plasma exchange mode and flushed with heparinized solution. Dexamethasone sodium phosphate was intravenously administered at a dose of 3 mg (1 mL: 2 mg; Shanghai Aladdin Bio-Chem Technology Co., Ltd., D107196). To prevent allergic reactions, 20 mL of 10% calcium gluconate (10 mL: 0.5 g; Shanghai Aladdin Biochemical Technology Co., Ltd., C422111) was mixed with 250 mL of 5% glucose and sodium chloride solution (100 mL: 5 g glucose + 0.9 g sodium chloride; Guangdong Kelun Pharmaceutical Co., Ltd., H20033622) for intravenous drip infusion. Fresh frozen plasma (FFP) was used for plasma replacement therapy, with a volume of 2000-3000 mL per session. The intraoperative blood flow rate was 100-150 mL/min, and the plasma separation rate was 20-30 mL/min. Each treatment session lasted 120-180 minutes. Patients received an average of 2-3 treatments, spaced 3-5 days apart, and the number of treatments adjusted based on clinical conditions. Following treatment, heparin neutralization was performed using protamine sulfate (5 mL: 50 mg, 85 vials in total; Shanghai Aladdin Biochemical Technology Co., Ltd., P123670), with a maximum dose not exceeding 50 mg.

Patients in the observation group received additional DPMAS. Prior to DPMAS sequential therapy, 1000 mL of 0.9% saline (Shanghai Aladdin Biochemical Technology Co., Ltd., M485988) was used for pre-rinsing to remove air from the column and tubing. The pre-rinsing solution contained 500 mL of saline and 20 mg of heparin sodium (2 mL: 500 units; Shanghai Zhongqiao Xinzhou Biological Technology Co., Ltd., CSP057). After heparinization for 10-30 minutes, the tubing was sealed. During DPMAS, anticoagulation was maintained with 10-20 mg of sodium heparin, adjusted according to coagulation status and clinical condition. The intraoperative blood flow rate was 100-120 mL/min, plasma separation rate was 20-30 mL/min, and adsorption time was controlled at 120-180 min or until plasma processing volume of 3600-5400 mL was reached. Following DPMAS, the blood pump flow was minimized, and the arterial and venous ends, along with the adsorption column end, were clamped. The mode was switched to standalone PE with a plasma separation pump to plasma return pump ratio of 1:1, a temperature at 38°C, plasma separation rate of 24%, fresh frozen plasma replacement volume of 600-1000 mL, blood flow rate of 100-120 mL/min, and replacement duration of 30-40 minutes. The interval of treatment was 3-5 days, with DPMAS performed prior to each PE session. The total number of DPMAS and PE treatments was determined based on the patient's clinical condition. Following each treatment, heparin was neutralized with protamine sulfate at the same dosing protocol as in the aforementioned PE regimen. Both groups received continuous treatment for 12 weeks.

Outcome measures

Efficacy [16]. *Markedly effective* is defined as the disappearance of clinical symptoms and signs such as fatigue, poor appetite, and abdominal distension, the reduction of jaundice, normalization of liver size, and near-normalization of liver function indicators. *Effective* is defined as a marked improvement in clinical symptoms, significant reduction of jaundice, partial restoration of liver size, and noticeable improvement in liver function indicators compared with baseline. *Ineffective* is defined as failure to meet the above criteria, with the condition worsening or death.

Safety. The incidence of adverse events after intervention was observed and recorded, including rash, chills, hypotension, hypocalcemia-related symptoms (e.g., perioral/limb numbness, muscle twitching), and thrombocytopenia. The overall incidence of adverse events was calculated for both groups.

Clinical indicators. The number of PE treatments, plasma volume used, and length of hospital stay were recorded for both groups.

Symptom improvement. Gastrointestinal and jaundice symptoms after treatment were recorded. Improvement in gastrointestinal symptoms was defined as significant relief or disappearance of abdominal distension. Jaundice improvement was defined as a reduction in total bilirubin (TBIL) to slightly above normal levels and a decrease in skin yellowing.

Liver function. 5 mL of fasting venous blood was collected in the morning before and after treatment. Serum was separated by centrifugation, and levels of alanine aminotransferase

(ALT), aspartate aminotransferase (AST), and total bilirubin (TBil) were measured using a fully automated biochemical analyzer (Shanghai Jumu Medical Equipment Co., Ltd., Atellica CH930). All procedures strictly followed the instructions of the corresponding kits (Shanghai JingKang Biotechnology Co., Ltd., JK-(a)-3185; Shanghai Youlike Biotechnology Co., Ltd., YLK-E1997D, YLK-EXS552).

Coagulation function. Serum prothrombin time (PT), prothrombin activity (PTA), and activated partial thromboplastin time (APTT) were determined before and after treatment using a fully automated coagulation analyzer (Shanghai Scientific Instrument Co., Ltd., CS-1300). PT and APTT were determined in strict accordance with the instructions provided with the corresponding kits (Shanghai Jingke Chemical Technology Co., Ltd., JK3930, JK39282). PTA was automatically calculated by the instrument using PT results and the standard curve.

Electrolytes. A fully automated biochemical analyzer was used to determine the serum levels of potassium and sodium before and after treatment, with all procedures performed in strict accordance with the instructions provided with the corresponding kits (Bailaiyuan (Tianjin) Biotechnology Co., Ltd., E2540, E2590).

Nutritional indicators. Serum levels of albumin (Alb) and prealbumin (PA) before and after treatment were measured using a fully automated biochemical analyzer, following kit instructions (Guangzhou Aoruida Biotechnology Co., Ltd., ARD11466, ARD11428).

Inflammatory markers. Serum levels of interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and high-sensitivity C-reactive protein (hs-CRP) were determined by enzyme-linked immunosorbent assay (ELISA) before and after treatment, following kit instructions (Shanghai Zhongqiao Xinzhou Biological Technology Co., Ltd., EKH021-P, EKH218-P, EKH012).

Short-term prognosis. Pre- and post-treatment Model for End-Stage Liver Disease (MELD) scores and 12-week survival rates were evaluated as primary outcomes. The MELD score was used to predict mortality in end-stage liver disease, with scores ranging from 0-40 corresponding to a 3-month survival rate of 90%-7% [17]; higher scores indicate greater mortality risk and lower survival rates.

Statistical methods

SPSS 24.0 statistical software was applied for data analysis. Continuous variables with a non-normal distribution were expressed as median (interquartile range) [M (Q1, Q3)] and compared between groups using the Mann-Whitney U test. Continuous variables with a normal distribution were expressed as mean ± Standard Deviation (SD), with inter-group comparison conducted using independent-samples t-test and intra-group comparison before and after treatment using paired t-test. Categorical variables were presented as number/percentage (n/%), and compared between groups using the χ^2 test. A P value < 0.05 was considered significant.

Results

Comparison of baseline characteristics between the two groups

There were no significant differences between the two groups in terms of sex, age, disease duration, disease stage, hepatic encephalopathy, or etiology (all P > 0.05), indicating baseline comparability (**Table 1**).

Comparison of treatment efficacy between the two groups

As presented in **Table 2**, the total effective rate was 74.75% in the control group, significantly higher than 90.10% in the observation group (P = 0.004).

Comparison of safety profiles between the two groups

As demonstrated in **Table 3**, the control group reported 11 cases of rash, 6 cases of chills, 7 cases of hypotension, 12 cases of hypocalcemia-related symptoms, and 5 cases of thrombocytopenia. In the observation group, there were 6 cases of rash, 2 cases of chills, 6 cases of hypotension, 20 cases of hypocalcemia-related symptoms, and 15 cases of thrombocytopenia. The overall incidence of adverse reactions was 41.41% and 48.51% in the control and observation groups, respectively, demonstrating no significant differences (P > 0.05).

Table 1. Comparison of baseline characteristics between the two groups

Data	Control group (n = 99)	Observation group (n = 101)	χ^2/t	P
Sex			0.333	0.564
Male	55 (55.56)	52 (51.49)		
Female	44 (44.44)	49 (48.51)		
Age (years)	57.73 ± 6.79	59.27 ± 7.72	1.497	0.136
Disease duration (years)	5.47 ± 2.32	5.76 ± 2.30	0.888	0.376
Disease stage			0.124	0.940
Early stage	34 (34.34)	34 (33.66)		
Middle stage	57 (57.58)	60 (59.41)		
Advanced stage	8 (8.08)	7 (6.93)		
Hepatic encephalopathy			0.157	0.692
Absent	74 (74.75)	73 (72.28)		
Present	25 (25.25)	28 (27.27)		
Etiology			0.463	0.793
Hepatitis B	68 (68.69)	65 (64.36)		
Hepatitis E	18 (18.18)	20 (19.80)		
Hepatitis complicated with hepatitis E	13 (13.13)	16 (15.84)		

Note: ACLF, acute-on-chronic liver failure.

Table 2. Comparison of treatment efficacy between the two groups

Efficacy	Control group (n = 99)	Observation group (n = 101)	χ^2	P
Cured	20 (20.20)	35 (34.65)		
Improved	54 (54.55)	56 (55.45)		
No effect	25 (25.25)	10 (9.90)		
Total effective rate	74 (74.75)	91 (90.10)	8.161	0.004

Note: ACLF, acute-on-chronic liver failure.

Table 3. Comparison of safety profile between the two groups

Safety	Control group (n = 99)	Observation group (n = 101)	χ^2	P
Rash	11 (11.11)	6 (5.94)		
Chills	6 (6.06)	2 (1.98)		
Hypotension	7 (7.07)	6 (5.94)		
Hypocalcemia-related symptoms	12 (12.12)	20 (19.80)		
Thrombocytopenia	5 (5.05)	15 (14.85)		
Overall incidence	41 (41.41)	49 (48.51)	1.018	0.313

Note: ACLF, acute-on-chronic liver failure.

Comparison of clinical indicators between the two groups

As depicted in **Figure 1**, the observation group required significantly fewer PE sessions, had notably lower plasma volumes, and shorter length of hospital stays compared to the control group (all $P < 0.01$).

Comparison of symptoms improvement between the two groups

As shown in **Table 4**, the rates of improvement in gastrointestinal symptoms and jaundice were much higher in the observation group than in the control group at 4 weeks post-treatment (57.43% vs. 39.39%, 65.35% vs. 42.42%).

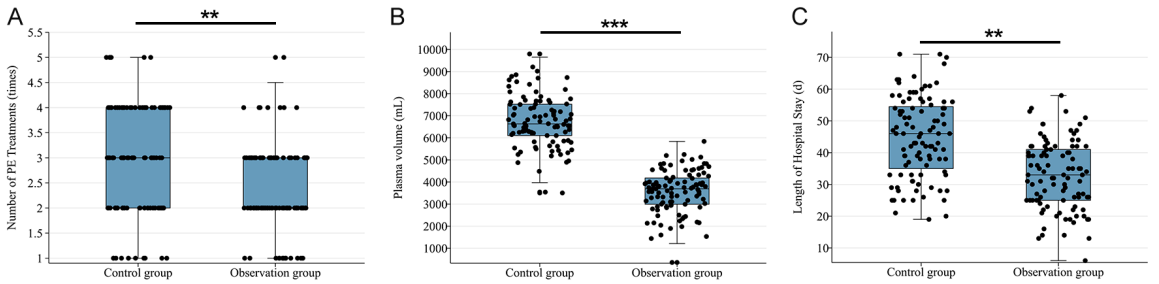

Figure 1. Comparison of treatment-related indicators between the two groups. A: Number of PE sessions. B: Plasma volume usage. C: Length of hospital stays. Note: **P < 0.01, ***P < 0.001. ACLF, acute-on-chronic liver failure; PE, plasma exchange.

Table 4. Comparison of symptom improvement between the two groups

Symptom improvement rate	Control group (n = 99)	Observation group (n = 101)	χ^2	P
Gastrointestinal symptoms				
At 4 weeks post-treatment	39 (39.39)	58 (57.43)	6.508	0.011
At 12 weeks post-treatment	83 (83.84)**	88 (87.13)**	0.437	0.509
Jaundice				
At 4 weeks post-treatment	42 (42.42)	66 (65.35)	10.575	0.001
At 12 weeks post-treatment	85 (85.86)**	90 (89.11)**	0.483	0.487

Note: **P < 0.01, compared with results at 4 weeks post-treatment. ACLF, acute-on-chronic liver failure.

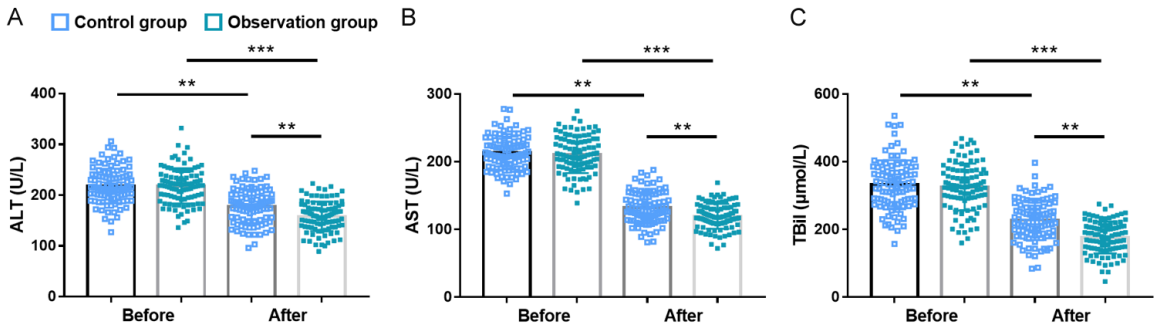

Figure 2. Comparison of liver function between the two groups before and after treatment. A: ALT level before and after treatment; B: AST level before and after treatment; C: TBil level before and after treatment. Note: **P < 0.01, ***P < 0.001. ACLF, acute-on-chronic liver failure; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBil, total bilirubin.

At 12 weeks post-treatment, both groups exhibited further improvement compared with post-treatment 4 weeks (P < 0.01), with no significant differences between groups (P > 0.05).

Comparison of liver function between the two groups

As shown in **Figure 2**, the two groups showed comparable baseline liver function indicators (ALT, AST, and TBil) (P > 0.05). Following intervention, all indicators decreased significantly in both groups (P < 0.05), with lower values observed in the observation group (P < 0.05).

Comparison of coagulation function between the two groups

As shown in **Table 5**, no differences were observed in baseline coagulation parameters (PT, PTA, and APTT) between the two groups (P > 0.05). Following intervention, both groups showed greatly reduced PT and APTT but elevated PTA (P < 0.05); in addition, the observation group exhibited significantly higher PT and

Table 5. Comparison of coagulation function between the two groups

Coagulation index	Control group (n = 99)	Observation group (n = 101)	t	P
PT (s)				
Before treatment	25.75 ± 7.21	24.45 ± 7.89	1.216	0.226
After treatment	17.80 ± 4.85**	19.86 ± 6.29**	2.590	0.010
PTA (%)				
Before treatment	36.58 ± 8.48	38.59 ± 11.65	1.393	0.165
After treatment	50.51 ± 7.68**	47.55 ± 9.21**	2.466	0.015
APTT (s)				
Before treatment	50.70 ± 9.30	50.01 ± 12.75	0.437	0.663
After treatment	39.96 ± 6.57**	43.89 ± 7.35**	3.984	<0.001

Note: **P < 0.01, intra-group comparison with pre-treatment results. ACLF, acute-on-chronic liver failure; PT, prothrombin time; PTA, prothrombin activity; APTT, activated partial thromboplastin time.

Table 6. Comparison of electrolyte levels between the two groups

Electrolyte	Control group (n = 99)	Observation group (n = 101)	t	P
Blood potassium (mmol/L)				
Before treatment	3.73 ± 0.81	3.74 ± 1.02	0.077	0.939
After treatment	3.83 ± 0.95	3.87 ± 0.91	0.304	0.761
Blood sodium (mmol/L)				
Before treatment	137.33 ± 9.87	138.52 ± 10.71	0.817	0.415
After treatment	137.59 ± 9.63	139.32 ± 9.02	1.312	0.191

Note: ACLF, acute-on-chronic liver failure.

APTT and lower PTA than the control group (all P < 0.05).

Comparison of electrolyte levels between the two groups

No significant differences in electrolyte levels (serum potassium and sodium) were observed between the two group before and after treatment (P > 0.05), and intragroup comparisons were also not significant (all P > 0.05) (**Table 6**).

Comparison of nutritional indicators between the two groups

As shown in **Table 7**, no considerable differences were observed in Alb or PA levels between the two groups before treatment (P > 0.05). After treatment, Alb and PA increased significantly in both groups (P < 0.01), with notably higher levels in the observation group (P < 0.001).

Comparison of inflammatory markers between the two groups

As presented in **Table 8**, no significant differences were observed in the levels of inflammatory markers (IL-6, TNF-α, and hs-CRP) between the two groups (P > 0.05). After treatment, all these markers decreased (P < 0.01), with lower levels in the observation group (P < 0.001).

Comparison of short-term prognosis between the two groups

As presented in **Figure 3**, no significant intergroup difference was observed in baseline MELD scores (P > 0.05). After intervention, MELD scores decreased significantly in both groups (P < 0.05), with lower scores in the observation group (P < 0.05). The 12-week survival rates were 70.71% and 80.20% in the control and observation groups, respectively, with no intergroup difference (P > 0.05).

Discussion

Acute-on-chronic liver failure (ACLF) is a clinical syndrome and a major cause of mortality in patients with cirrhosis and chronic liver disease, characterized by acute deterioration of liver function accompanied by extrahepatic organ failure [18]. Given the limitations associated with liver transplantation, there is an

Table 7. Comparison of nutritional indicators between the two groups

Nutritional indicator	Control group (n = 99)	Observation group (n = 101)	t	P
Alb (g/L)				
Before treatment	26.15 ± 4.89	27.32 ± 5.54	1.582	0.115
After treatment	31.44 ± 5.95**	36.36 ± 5.95**	5.847	<0.001
PA (mg/L)				
Before treatment	193.92 ± 11.32	194.03 ± 14.68	0.059	0.953
After treatment	202.26 ± 15.71**	213.34 ± 19.39**	4.435	<0.001

Note: **P < 0.01, intra-group comparison with pre-treatment results. ACLF, acute-on-chronic liver failure; Alb, albumin; PA, prealbumin.

Table 8. Comparison of inflammatory markers between the two groups

Inflammatory marker	Control group (n = 99)	Observation group (n = 101)	t	P
IL-6 (pg/mL)				
Before treatment	18.80 ± 3.37	18.79 ± 4.31	0.018	0.986
After treatment	8.75 ± 2.36**	6.92 ± 1.96**	5.970	<0.001
TNF-α (pg/mL)				
Before treatment	14.12 ± 3.31	14.42 ± 4.25	0.556	0.579
After treatment	7.13 ± 1.97**	6.24 ± 2.05**	3.130	0.002
hs-CRP (mg/L)				
Before treatment	18.17 ± 3.62	17.48 ± 4.06	1.268	0.206
After treatment	10.10 ± 3.29**	7.74 ± 2.36**	5.838	<0.001

Note: **P < 0.01, intra-group comparison with pre-treatment results. ACLF, acute-on-chronic liver failure; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; hs-CRP, high-sensitivity C-reactive protein.

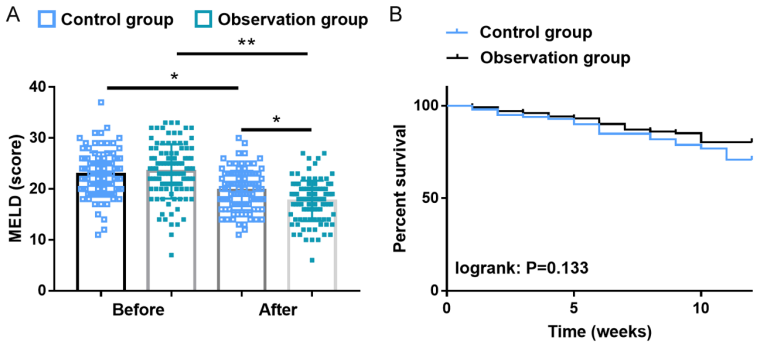

Figure 3. Comparison of short-term prognosis between the two groups. A: MELD scores before and after intervention; B: 12-week survival curves of ACLF patients. Note: *P < 0.05, **P < 0.01. ACLF, acute-on-chronic liver failure; MELD, Model for End-Stage Liver Disease.

urgent need to explore non-transplant therapeutic strategies to improve clinical outcomes in ACLF patients [19].

This study first demonstrated that the total effective rate in ACLF patients receiving DPMAS plus PE reached 90.10%, significantly higher than that achieved with PE monotherapy. The therapeutic advantages of the combined strategy is largely attributable to their complementary clearance mechanisms: PE effectively removes water-soluble toxins and replenishes beneficial substances (e.g., clotting factors, albumin), but its ability to clear protein-bound toxins such as bilirubin is limited, along with a risk of plasma-related adverse reactions [20]; in contrast, DPMAS efficiently eliminates bilirubin, bile acids, and medium-to-large-molecule inflammatory factors, but cannot replenish coagulation factors and may exacerbate albumin depletion [21]. The combination of the two allows for more comprehensive regulation of the internal environment in patients with liver failure, while the required plasma volume is reduced, thereby improving short-term treatment efficacy, especially in patients with mild ACLF [22].

In terms of safety, no significant difference was observed in the incidence of adverse reactions between patients receiving DPMAS plus

PE (48.51%) and PE alone (41.41%), indicating that the combined treatment did not substantially increase the overall incidence of adverse reactions. The synergistic action of the combination - DPMAS clears bilirubin and bile acids while PE effectively replenishes coagulation factors and albumin-further facilitates the removal of excess bilirubin and inflammatory mediators, thereby stabilizing the patient's condition, and potentially minimizing adverse reactions. Moreover, DPMAS plus PE led to significantly fewer PE sessions, lower plasma volume usage, and shorter hospital stays. These benefits can be attributed to DPMAS serving as a non-plasma intervention that reduces the reliance on large plasma volumes and mitigates treatment delays caused by plasma shortages, ultimately enhancing treatment efficiency and preventing disease progression. Similar results were reported in the study by Li et al. [8], showing that combining small-volume PE with DPMAS notably reduces intraoperative plasma volume requirements in patients with ACLF.

Significantly higher rates of improvement in gastrointestinal symptoms and jaundice at 4 weeks post-treatment were observed in ACLF patients treated with DPMAS plus PE. Despite further improvements were observed at 12 weeks post-treatment, no remarkable differences were noted compared to PE monotherapy, suggesting the need for future studies with larger sample sizes for further verification. In ACLF patients, liver function damage was effectively mitigated by DPMAS plus PE, with smaller impact on coagulation function. This may be attributed to the bilirubin-specific adsorption technology of DPMAS. Moreover, the combined therapy effectively removes endotoxins and harmful substances from plasma while preventing proenzyme loss, which contributes to hepatoprotection and improvement in coagulation dysfunction. Cheng et al. [13] reported that DPMAS was more effective than PE in improving liver function and coagulation profiles, supporting the findings of this study. Electrolyte disturbances, generally manifesting as hyponatremia, are common in ACLF and can impair brain function and trigger hepatic encephalopathy [23]. Neither therapy alone produced significant changes in electrolyte levels in ACLF patients. In a report by Xiang et al. [24], DPMAS plus PE had less effecton electrolyte levels in ACLF patients relative to PE alone, differing from the results obtained in this study. This discrepancy may be attributed to variations in baseline patient characteristics and treatment indices.

In addition, DPMAS plus PE significantly improved nutritional status and reduced inflammatory markers. These effects may result from the effective removal of large-molecule inflammatory mediators (e.g., TNF-α, IL-6) and toxins, alleviating the inhibition of systemic metabolism by inflammatory responses, thus enhancing hepatic synthesis overall nutritional status. Chen et al. [25] reported similar inhibitory effects of DPMAS on TNF-α and IL-6 levels in patients with chronic severe hepatitis.

Previous studies have reported that normal reference ranges for IL-6, TNF-α, and hs-CRP in healthy adults are <7 pg/mL, <8.1 pg/mL, and <3 mg/L, respectively [26]. In this study, post-treatment IL-6, TNF-α, and hs-CRP levels in the observation group were (6.92 ± 1.96) pg/mL, (6.24 ± 2.05) pg/mL, and (7.74 ± 2.36) mg/L, respectively. While IL-6 and TNF-α approached normal levels, hs-CRP remained significantly elevated. In the control group, none of the three markers returned to the normal range after treatment. These results suggest that patients with ACLF retain a persistent state of low-grade chronic inflammation even after effective artificial liver therapy. Nevertheless, the combination of DPMAS and PE maximally improved inflammatory profiles, likely through inhibition of lymphocyte and monocyte activation and proliferation [27].

Short-term prognosis assessment revealed that DPMAS combined with PE reduced MELD scores compared to PE alone. However, the 12-week survival rates were comparable between the two therapies (70.71% vs. 80.20%), suggesting that the advantage of the combined therapy may lie in faster disease control. The potential prognostic benefit of this approach warrants extended follow-up for further confirmation. Beran et al. [28] reported that PE therapy was associated with remarkably higher 30-day and 90-day survival rates in ACLF patients compared to standard medical management. In contrast, Xu et al. [29] reported higher 12-week overall survival rates in patients with middle-stage hepatitis B virus-associated ACLF treated with DPMAS plus sequential low-

volume PE therapy, different from the findings of this study. This may be attributable to differences in the study population, as the current study included ACLF patients across both early and advanced stages, with etiologies ranging from hepatitis B virus, hepatitis E, to co-infection with hepatitis B and E viruses.

The innovation of this study is primarily reflected in the following aspects. First, comprehensive evaluation: in addition to conventional indicators of liver function (ALT, AST, TBil), coagulation function (PT, PTA, APTT), and prognosis indicators (MELD score, 12-week survival rate), the study specifically incorporated nutritional indicators (Alb, PA) and inflammation markers (IL-6, TNF-α, hs-CRP), which are often neglected. This approach elucidates the potential advantages of the combined therapy in enhancing anabolic metabolism and suppressing inflammation. Second, refined safety analysis: beyond documenting common adverse reactions (e.g., rash, chills, and hypotension), hypocalcemia-related symptoms and thrombocytopenia associated with artificial liver therapy were included, providing safety data that better reflect clinical practice. Third, integrated assessment of efficacy and efficiency: by comparing therapeutic efficacy, the number of PE treatments, plasma volume used, length of hospital stays, and symptom improvement, this study evaluated both clinical efficacy and healthcare resource utilization for the first time. This research provides robust and comprehensive evidence-based support for the clinical application of DPMAS plus PE in treating ACLF through multidimensional data analysis under real-world conditions.

Conclusion

In ACLF patients, DPMAS plus PE demonstrated superior clinical efficacy compared to PE alone, offering enhanced therapeutic efficacy and efficiency without notably increasing the incidences of adverse reactions. The combined therapy facilitates more rapid improvement in gastrointestinal symptoms and jaundice, effectively improves liver function and nutritional status, and suppresses inflammatory responses, with minimal impact on coagulation function. It should be noted that, as a single-center study, the level of evidence is limited. The above conclusions require further validation through multicenter, large-scale prospective studies to clarify the clinical value and broader applicability of this combination therapy in patients with ACLF.

Disclosure of conflict of interest

None.

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