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Original Article

Plasma exchange-based artificial liver support system demonstrates short-term therapeutic efficacy in treating chronic severe hepatitis B

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Abstract: Objective: In this retrospective study, the short-term efficacy of the plasma exchange-based artificial liver support system (PE-ALSS) for chronic severe hepatitis B (CSHB) was explored. Methods: We selected 111 CSHB patients and divided them into control (53 cases with conventional treatment) and research (58 cases with conventional treatment+PE-ALSS) groups based on the treatment they received. We then conducted inter-group comparisons regarding therapeutic effectiveness, complications, hepatic function indicators (alanine aminotransferase [ALT], aspartate aminotransferase [AST], total bilirubin [TBIL]), hepatic fibrosis markers (hyaluronic acid [HA], laminin [LN], type IV collagen [IV-C]), serum biochemical indices (interleukin [IL]-18, intercellular adhesion molecule-1 [ICAM-1]), coagulation function indices (prothrombin time [PT], thrombin time [TT], activated partial thromboplastin time [APTT]), and inflammatory factors (procalcitonin [PCT], IL-6). Finally, efficacy-associated determinants were identified by univariate and multivariate analysis. Results: The research group had a superior total effective rate (94.83% vs. 69.81%, P < 0.001) and a lower complication rate (1.72% vs. 13.21%, P < 0.001) than the control group. Post-treatment, the research group exhibited statistically lower ALT (65.59±14.21 U/L vs. 89.47±17.44 U/L), AST (78.12±19.63 U/L vs. 94.91±22.27 U/L), TBIL (24.45±5.46 μmol/L vs. 45.77±7.43 μmol/L), HA (84.83±7.00 ng/mL vs. 100.47±10.41 ng/mL), LN (69.90±8.18 ng/mL vs. 80.81±8.71 ng/mL), IV-C (76.21±5.52 ng/mL vs. 85.21±7.97 ng/mL), IL-18 (343.34±108.3 pg/mL vs. 543.92±138.18 pg/mL), ICAM-1 (282.57±128.8 μg/L vs. 406.3±158.26 μg/L), PT (13.79±4.03 s vs. 15.68±3.15 s), TT (17.97±2.91 s vs. 20.11±2.23 s), APTT (35.79±11.08 s vs. 40.06±8.09 s), PCT (2.25±0.91 μg/L vs. 3.24±1.15 μg/L), and IL-6 (46.33±10.21 pg/mL vs. 50.75±11.11 pg/mL) than controls. Moreover, treatment modality (B = -1.865, odds ratio = 0.155, 95% confidence interval: 0.038-0.628) was an independent determinant of efficacy (P=0.009). Conclusion: PE-ALSS has significant short-term efficacy for CSHB patients.

Keywords: Chronic severe hepatitis B, plasma exchange-based artificial liver support system, short-term efficacy, hepatic fibrosis, therapeutic efficacy

Introduction

Chronic hepatitis B (CHB), a major factor contributing to cirrhosis, hepatocellular carcinoma (HCC), and death, is a global health concern [1-3]. As a lifelong disease, the pathologic process of CHB involves dynamic changes in hepatitis B surface antigen and hepatitis B e antigen, along with hepatic function impairment, hepatic fibrosis, intrahepatic inflammation, and abnormal coagulation function [4, 5]. The occurrence of this disease is closely related to hepatitis B virus (HBV) infection. In 2019, it was estimated that nearly 300 million people were affected by this virus, with approximately 800,000 associated deaths worldwide [6]. Although several therapeutic drugs have been approved for CHB, treatment outcomes still require further improvement and optimization [7, 8].

CHB patients typically present with severe illness, poor prognosis, and a high risk of death [9]. This often leads to extensive hepatocyte necrosis and may trigger liver failure [10]. At present, the antiviral treatment effect in

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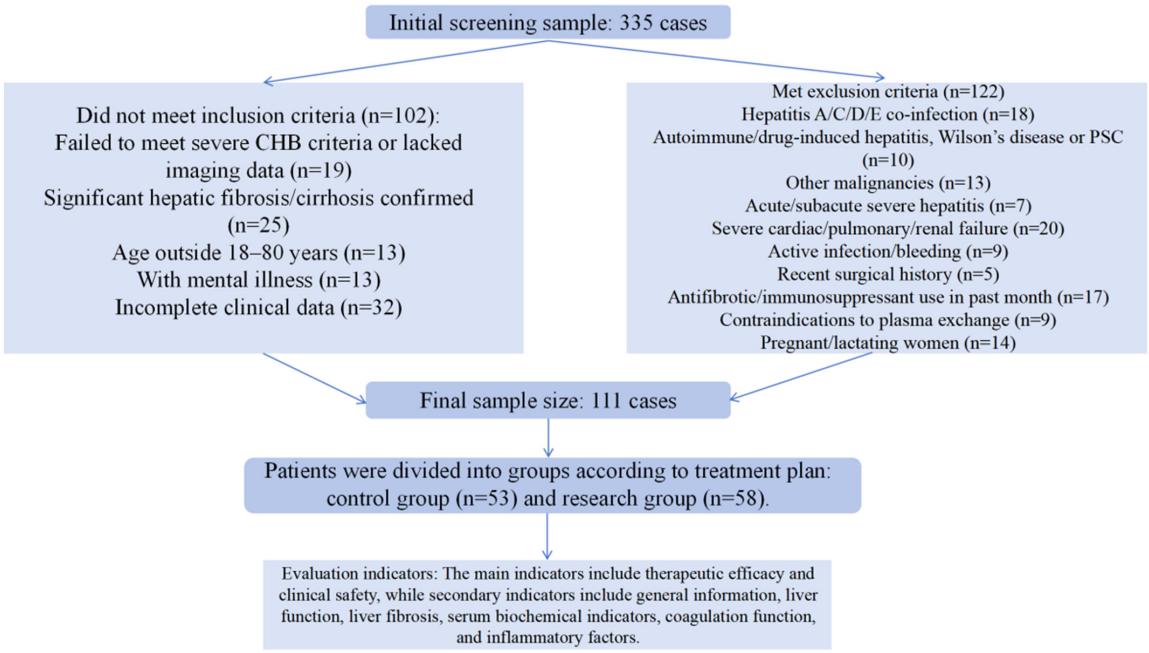

Figure 1. Flow chart of patient selection. Note: CHB, chronic hepatitis B; PSC, primary sclerosing cholangitis.

patients with chronic severe hepatitis B (CSHB) remains unsatisfactory. Although liver transplantation offers good therapeutic outcomes, it is costly and limited by the scarcity of suitable donor livers [11]. The plasma exchange-based artificial liver support system (PE-ALSS) can remove viral antigens and immune complexes from the blood, clear toxins, reduce hepatic burden, improve the internal environment, and promote hepatocyte regeneration [12, 13]. In a report by Maiwall et al. [14], PE-ALSS application in patients with acute liver failure helped attenuate systemic inflammatory responses and inhibit the progression of multiple organ failure. However, research on the use of PE-ALSS in CSHB patients - particularly regarding short-term efficacy and hepatic fibrosis markers - remains relatively limited. This study attempts to conduct relevant analyses into the feasibility of this therapy to explore its potential clinical advantages.

Good clinical value of PE-ALSS was shown in CSHB patients. In addition to validating its short-term efficacy and safety, we reveal its effects on improving liver and coagulation functions, inhibiting liver fibrosis, and modulating serum biochemical indexes and inflammatory factors. These findings offer a new direction and a reliable reference for optimizing treatment strategies in this patient population.

Patients and methods

Patient selection

This retrospective study enrolled 111 CSHB patients admitted to Zhoukou Central Hospital between April 2022 and April 2024. Patients were divided into two groups according to the treatment they received: a control group (n = 53) treated with conventional medical therapy, and a research group (n = 58) treated with conventional therapy plus PE-ALSS. The study protocol was approved by the Ethics Committee of Zhoukou Central Hospital Affiliated with Henan Medical University. All data were collected by the hospital's medical record inquiry system. The patient selection process is shown in **Figure 1**.

Inclusion criteria: All patients (aged 18-80 years) who met the diagnostic criteria for SCHB [15], with the diagnosis confirmed by imaging modalities including abdominal ultrasound, computed tomography, and magnetic resonance imaging. Significant liver fibrosis or cirrhosis was diagnosed based on abdominal imaging, liver stiffness measurement (FibroScan), or serum biomarkers (aspartate aminotransferase [AST] to platelet ratio index/Fibrosis-4 index). Patients had no mental illness and had complete clinical records.

Exclusion criteria: Hepatitis A, C, D, or E; coexistence with autoimmune hepatitis, drug-induced hepatitis, Wilson's disease, or primary sclerosing cholangitis; other malignant tumors; acute or subacute severe hepatitis; severe cardiac, pulmonary, or renal insufficiency (New York Heart Association cardiac function class ≥III, requiring mechanical ventilation, or estimated glomerular filtration rate < 30 mL/min/1.73 m^2); active infection or bleeding; recent surgery; use of anti-fibrosis agents or immunosuppressants within the last month; contraindications to plasma exchange (e.g., severe allergy, hemodynamic instability, active intracranial hemorrhage); pregnancy or lactation.

Treatment protocol

In the control group, conventional treatment was administered. Patients received an intravenous drip of hepatocyte growth-promoting factor once daily, with each infusion ranging from 40 to 120 mg. They received oral Simeitai (1000-2000 mg once daily), compound glycyrrhizin (80-120 mg calculated as glycyrrhizin once daily), and reduced glutathione (400 mg three times daily). In addition, alprostadil was given by intravenous drip once daily, at a dose of 5-10 μg per administration.

In addition to the treatment received by the control group, the research group was additionally treated with PE-ALSS. Plasma exchange was performed using a PE-ALSS device. Depending on the patient's condition, 1 to 3 exchanges were conducted. A catheter was inserted into the patient's subclavian vein and connected to the blood purifier. The single plasma exchange volume was 2800 mL, and each session lasted 100 minutes. Fresh frozen plasma was exchanged at a flow rate of 110 mL/min every 3 days. Following plasma exchange, 20-30 g of albumin was infused. The treatment period lasted 1 month. During plasma exchange, nursing staff closely monitored the patient's vital signs. Conventional heparin anticoagulation was administered, and the heparin dose was adjusted in a timely manner according to the patient's condition.

All treatment decisions were made by the attending physician team based on the patient's clinical condition and the wishes of their family members.

Data extraction

Data were extracted from the hospital's medical record system. The extracted and verified data included the following:

(1) General information. Age, sex, body mass index (BMI), smoking/alcohol use history, hypertension, diabetes, and family history of hepatitis B were recorded and comparatively analyzed.

(2) Therapeutic efficacy. Efficacy was evaluated one month post-treatment using the following criteria: Marked effect: disappearance of clinical symptoms such as bleeding, fatigue, and jaundice; Effective: improvement of the above clinical symptoms; Ineffective: no improvement in clinical symptoms. The total effective rate was calculated as the percentage of patients showing marked effect or effective response relative to the total number of cases.

(3) Complications. Adverse reactions occurring during treatment (e.g., allergy, infection, hypotension) were recorded, and the incidence rate was calculated.

(4) Hepatic function and hepatic fibrosis markers. Before and one month after intervention, 4 mL of fasting venous blood was collected from each patient in the early morning. Serum was separated by centrifugation and used to measure alanine aminotransferase (ALT), AST, and total bilirubin (TBIL) using an automated biochemical analyzer, as well as hyaluronic acid (HA), laminin (LN), and type IV collagen (IV-C) by chemiluminescence immunoassay.

(5) Serum biochemical indices and inflammatory factors. Enzyme-linked immunosorbent assays were performed to quantify serum levels of interleukin (IL)-18, intercellular adhesion molecule-1 (ICAM-1), procalcitonin (PCT), and IL-6 before and one month after intervention.

(6) Coagulation function. An automated blood cell analyzer was used to measure prothrombin time (PT), thrombin time (TT), and activated partial thromboplastin time (APTT) before intervention and at one month post-treatment.

Outcome measures

The outcome measures of this study included: (1) Clinical comparability between the two

Table 1. General information of the study participants

Characteristic	Control group (n=53)	Research group (n=58)	χ^2/t	P
Age (years)	65.89±7.39	65.36±7.88	0.365	0.716
Sex (male/female)	35/18	42/16	0.530	0.467
Body mass index (kg/m^2)	23.45±2.14	23.84±2.35	0.911	0.364
Smoking, n (yes/no)	25/28	32/26	0.710	0.400
Alcohol use, n (yes/no)	26/27	24/34	0.659	0.417
Hypertension, n (with/without)	12/41	10/48	0.508	0.476
Diabetes, n (with/without)	15/38	15/43	0.084	0.773
Family history of hepatitis B, n (with/without)	20/33	23/35	0.043	0.836

Note: Data are presented as mean ± standard deviation or n/n. P < 0.05 was considered statistically significant.

Table 2. Therapeutic efficacy

Curative effect	Control group (n=53)	Research group (n=58)	Fisher's exact	P
Marked effect	17 (32.08)	29 (50.00)		
Effective	20 (37.74)	26 (44.83)		
Ineffective	16 (30.19)	3 (5.17)		
Overall effectiveness	37 (69.81)	55 (94.83)		< 0.001

Note: Data are presented as n (%). P < 0.05 was considered significant.

groups at baseline. (2) Therapeutic efficacy of conventional treatment with or without PE-ALSS. (3) Clinical safety profile, assessed by the incidence of complications. (4) Hepatic function, measured by ALT, AST, and TBIL levels. (5) Hepatic fibrosis, assessed by HA, LN, and IV-C levels. (6) Serum biochemical indices, including IL-18 and ICAM-1. (7) Coagulation function, evaluated by PT, TT, and APTT. (8) Inflammation, quantified by PCT and IL-6 concentrations.

Among these, the primary endpoints were efficacy and clinical safety; general information, hepatic function, hepatic fibrosis, serum biochemical indices, coagulation function, and inflammatory factors were secondary measures.

Statistical analysis

Hepatic function, hepatic fibrosis markers, serum biochemical indices, coagulation function, and other continuous variables were expressed as mean ± standard deviation. The independent samples t-test was used to compare continuous data between groups, and the paired t-test was used to compare data before and after intervention within the same group. Counted data were presented as n (%); between-group comparisons were performed using the chi-square test, and Fisher's exact test was applied when expected frequencies were below 5. Univariate and multivariate logistic regression analyses were conducted to identify determinants of efficacy. All statistical analyses were performed using SPSS version 22.0. A *P*-value < 0.05 was considered significant.

Results

General information

Clinical comparability between the two patient cohorts was confirmed, as no statistically significant differences were observed in baseline general information. Specifically, there were no significant differences between the research group and the control group with respect to age, sex, BMI, smoking/alcohol use history, hypertension, diabetes, or family history of hepatitis B (all P > 0.05; **Table 1**).

Therapeutic efficacy

In the control group, the numbers of cases with marked effect, effective, and ineffective were 17, 20, and 16, respectively. In the research group, the corresponding numbers were 29, 26, and 3, respectively. The total effective rate was significantly higher in the research group than in the control group (94.83% vs. 69.81%, P < 0.001; **Table 2**).

Table 3. Complications

Complication	Control group (n=53)	Research group (n=58)	Fisher's exact	P
Allergy	2 (3.77)	0 (0.00)		
Infection	3 (5.66)	0 (0.00)		
Hypotension	2 (3.77)	1 (1.72)		
Total	7 (13.21)	1 (1.72)		0.027

Note: Data are presented as n (%). P < 0.05 was considered significant.

Table 4. Hepatic function before and after intervention

Indicator	Time point	Control group (n=53)	Research group (n=58)	t	P
ALT (U/L)	Before intervention	219.00±60.54	216.64±68.15	0.192	0.848
	After intervention	89.47±17.44	65.59±14.21	7.937	< 0.001
	t	14.968	16.525		
	P	< 0.001	< 0.001		
AST (U/L)	Before intervention	199.15±38.10	209.21±40.05	1.353	0.179
	After intervention	94.91±22.27	78.12±19.63	4.221	< 0.001
	t	17.196	22.384		
	P	< 0.001	< 0.001		
TBIL (μmol/L)	Before intervention	165.60±38.97	174.64±32.85	0.188	1.325
	After intervention	45.77±7.43	24.45±5.46	17.330	< 0.001
	t	21.990	34.348		
	P	< 0.001	< 0.001		

Data are presented as mean ± standard deviation. Note: ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin.

Complications

In the control group, cases of allergy, infection, and hypotension were 2, 3, and 2, respectively, compared to 0, 0, and 1 in the research group. The overall complication rate was significantly lower in the research group than in the control group (1.72% vs. 13.21%, P = 0.027; **Table 3**).

Hepatic function

Hepatic function was assessed by measuring serum levels of ALT, AST, and TBIL. No significant differences were observed between the two groups in any of these indicators at baseline (all P > 0.05). After intervention, all three indices decreased significantly in both groups (all P < 0.05), and post-treatment levels were significantly lower in the research group than in the control group (all P < 0.05; **Table 4**).

Hepatic fibrosis markers

Serum levels of HA, LN, and IV-C were measured before and after intervention. No significant differences were observed between the two groups at baseline (all P > 0.05). After treatment, all three markers decreased significantly in both groups, with significantly lower levels in the research group than in the control group (all P < 0.05; **Table 5**).

Serum biochemical indices

Serum levels of IL-18 and ICAM-1 were measured and compared between the two groups. No significant differences were observed in baseline IL-18 or ICAM-1 levels (both P > 0.05). After intervention, both markers decreased significantly in each group, with significantly lower concentrations in the research group than in the control group (all P < 0.05; **Table 6**).

Coagulation function

Coagulation function was assessed by measuring PT, TT, and APTT. No significant differences were observed between the two groups in any of these indicators at baseline (all P > 0.05). After intervention, all three indicators decreased significantly in the research group and were significantly lower than those of the control group (all P < 0.05; **Figure 2**).

Table 5. Hepatic fibrosis markers before and after intervention

Indicator	Time point	Control group (n=53)	Research group (n=58)	t	P
HA (ng/mL)	Before intervention	150.06±17.05	155.53±21.08	1.494	0.138
	After intervention	100.47±10.41	84.83±7.00	9.360	< 0.001
	t	18.072	24.241		
	P	< 0.001	< 0.001		
LN (ng/mL)	Before intervention	118.96±13.99	122.40±13.40	1.323	0.189
	After intervention	80.81±8.71	69.90±8.18	6.805	< 0.001
	t	16.853	25.468		
	P	< 0.001	< 0.001		
IV-C (ng/mL)	Before intervention	173.51±17.59	173.97±22.65	0.906	0.119
	After intervention	85.21±7.97	76.21±5.52	6.965	< 0.001
	t	33.288	31.936		
	P	< 0.001	< 0.001		

Data are presented as mean ± standard deviation. Note: HA, hyaluronic acid; LN, laminin; IV-C, type IV collagen.

Table 6. Serum biochemical indices before and after intervention

Indicator	Time point	Control group (n = 53)	Research group (n = 58)	t	P
IL-18 (pg/mL)	Before intervention	698.42±113.47	745.10±151.66	1.822	0.071
	After intervention	543.92±138.18	343.34±108.30	8.550	< 0.001
	t	6.291	16.418		
	P	< 0.001	< 0.001		
ICAM-1 (μg/L)	Before intervention	558.30±155.28	526.88±137.29	1.131	0.260
	After intervention	406.30±158.26	282.57±128.80	4.534	< 0.001
	t	4.991	9.884		
	P	< 0.001	< 0.001		

Data are presented as mean ± standard deviation. Note: IL-18, interleukin-18; ICAM-1, intercellular adhesion molecule-1.

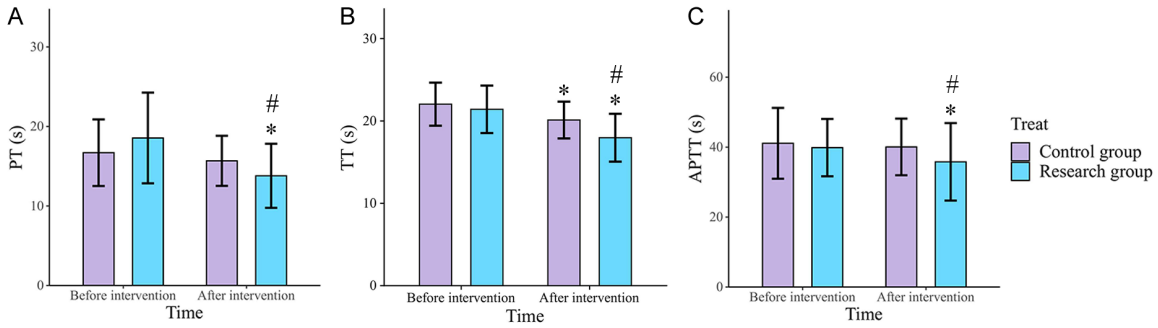

Figure 2. Coagulation function before and after intervention. A. Pre- and post-interventional PT in the two groups. B. Pre- and post-interventional TT in the two groups. C. Pre- and post-interventional APTT in the two groups. Note: *P < 0.05, versus before intervention; #P < 0.05 versus control group. PT, prothrombin time; TT, thrombin time; APTT, activated partial thromboplastin time.

Inflammatory factors

Serum levels of of PCT and IL-6 were measured as inflammatory factors. No significant differences were observed between the two groups in either marker at baseline (both P > 0.05). After treatment, PCT decreased significantly in both groups, and IL-6 decreased significantly in the research group but not in the control group (all P < 0.05). Post-treatment levels of

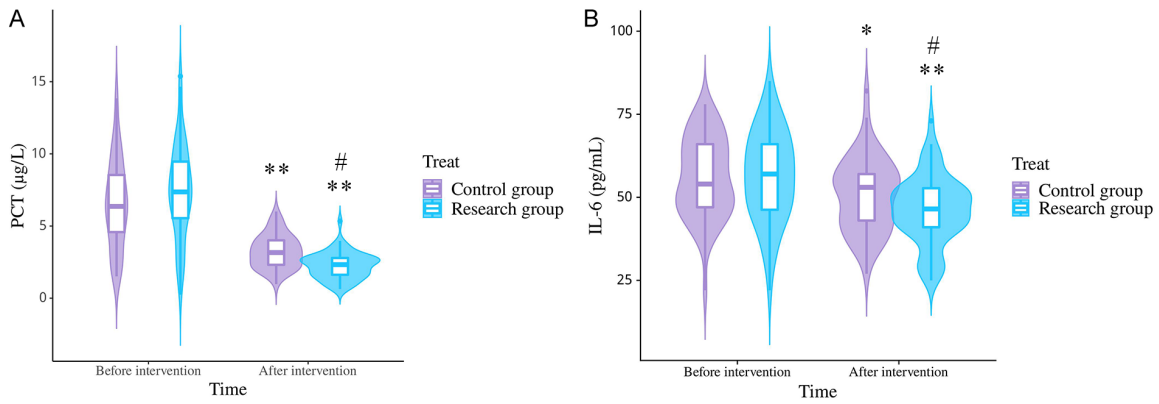

Figure 3. Inflammatory factors before and after intervention. A. Pre- and post-interventional PCT in two groups. B. Pre- and post-interventional IL-6 in two groups. Note: **P < 0.01 versus before intervention; #P < 0.05 versus control group. PCT, procalcitonin; IL-6, interleukin-6.

both markers were significantly lower in the research group than in the control group (both P < 0.05; **Figure 3**).

Analysis of factors affecting efficacy

Patients were further divided into two groups based on treatment outcome: the ineffective group (n=19) and the effective group (n=92). Univariate analysis was first performed to screen for potential determinants of efficacy. Age, sex, smoking/alcohol use history, diabetes, family history of hepatitis B, and pre-treatment levels of ALT, AST, TBIL, HA, LN, IV-C, IL-18, ICAM-1, TT, APTT, and PCT were not significantly associated with efficacy (all P > 0.05). In contrast, BMI, hypertension, pre-treatment PT, pre-treatment IL-6, and treatment modality were identified as significant correlates of therapeutic efficacy (all P < 0.05; **Table 7**).

Factors showing significant differences by the univariate analysis were entered as independent variables in the multivariate logistic regression model, with treatment outcome (effective vs. ineffective) as the dependent variable (**Table 8**). Multivariate analysis revealed that BMI, hypertension, pre-treatment PT, and pre-treatment IL-6 were not independent predictors of treatment efficacy (all P > 0.05). However, treatment modality (B = -1.865, odds ratio = 0.155, 95% confidence interval: 0.038-0.628) remained an independent determinant (P=0.009; **Table 9**).

Discussion

In the present study, the total treatment efficacy rate was significantly lower in the control group than in the research group (69.81% versus 94.83%), suggesting that PE-ALSS is more effective than conventional treatment alone in improving short-term outcome in patients with CSHB. This benefit may be attributable to the ability of PE-ALSS to remove circulating toxins and metabolic waste products, correct acid-base and electrolyte imbalances, optimize the internal environment, and promote the repair of damaged hepatocytes, thereby maximizing therapeutic efficacy. In a study by Bai et al. [16], PE-ALSS significantly improved treatment efficacy and enhanced liver and coagulation functions in patients with acute-on-chronic liver failure, which is consistent with our findings. Regarding safety, the overall incidence of complications (e.g., allergy, infection, and hypotension) was significantly lower in the research group than in the control group (1.72% vs. 13.21%), indicating that PE-ALSS can substantially reduce the complication rate for CSHB patients. This may be explained by the fact that PE-ALSS acts primarily on plasma components without directly interfering with cellular metabolism or pharmacokinetics, thereby avoiding the risk of drug-induced liver injury and systemic toxicity. In addition, by partially replacing the liver's detoxification function, PE-ALSS facilitates the elimination of drug metabolites and other potentially harmful substances, which may further reduce the risk of drug-related adverse reactions such as hepatotoxicity. In a retrospective single-center study by Yang et al. [17], PE-ALSS was shown to reverse organ failure and reduce the risk of complications and death in 480 patients with HBV-related acute-on-chronic liver failure, supporting the findings of the present study. Similarly, a prospective

Table 7. Univariate analysis of potential factors affecting treatment efficacy

Characteristic	Ineffective group (n = 19)	Effective group (n = 92)	χ^2/Fisher's exact	P
Age (years)			0.130	0.718
< 65 (n = 45)	7 (36.84)	38 (41.30)		
≥ 65 (n = 66)	12 (63.16)	54 (58.70)		
Sex			3.022	0.082
Male (n = 77)	10 (52.63)	67 (72.83)		
Female (n = 34)	9 (47.37)	25 (27.17)		
Body mass index (kg/m^2)			5.370	0.021
< 24 (n = 52)	6 (31.58)	46 (50.00)		
≥ 24 (n = 59)	13 (68.42)	46 (50.00)		
Smoking history			0.015	0.902
Yes (n = 57)	10 (52.63)	47 (51.09)		
No (n = 54)	9 (47.37)	45 (48.91)		
Alcohol use history			1.529	0.216
Yes (n = 50)	11 (57.89)	39 (42.39)		
No (n = 61)	8 (42.11)	53 (57.61)		
Hypertension			4.180	0.041
Yes (n = 22)	7 (36.84)	15 (16.30)		
No (n = 89)	12 (63.16)	77 (83.70)		
Diabetes			2.643	0.104
Yes (n = 30)	8 (42.11)	22 (23.91)		
No (n = 81)	11 (57.89)	70 (76.09)		
Family history of hepatitis B			0.035	0.852
Yes (n = 43)	7 (36.84)	36 (39.13)		
No (n = 68)	12 (63.16)	56 (60.87)		
Pre-treatment ALT (U/L)			0.508	0.476
< 220 (n = 56)	11 (57.89)	45 (48.91)		
≥ 220 (n = 55)	8 (42.11)	47 (51.09)		
Pre-treatment AST (U/L)			2.182	0.140
< 200 (n = 53)	12 (63.16)	41 (44.57)		
≥ 200 (n = 58)	7 (36.84)	51 (55.43)		
Pre-treatment TBIL (μmol/L)			0.413	0.521
< 170 (n = 51)	10 (52.63)	41 (44.57)		
≥ 170 (n = 60)	9 (47.37)	51 (55.43)		
Pre-treatment HA (ng/mL)			-	0.072
< 150 (n = 46)	4 (21.05)	42 (45.65)		
≥ 150 (n = 65)	15 (78.95)	50 (54.35)		
Pre-treatment LN (ng/mL)			0.413	0.521
< 120 (n = 51)	10 (52.63)	41 (44.57)		
≥ 120 (n = 60)	9 (47.37)	51 (55.43)		
Pre-treatment IV-C (ng/mL)			2.449	0.118
< 173 (n = 52)	12 (63.16)	40 (43.48)		
≥ 173 (n = 59)	7 (36.84)	52 (56.52)		
Pre-treatment IL-18 (pg/mL)			1.758	0.185
< 720 (n = 49)	11 (57.89)	38 (41.30)		
≥ 720 (n = 62)	8 (42.11)	54 (58.70)		

Pre-treatment ICAM-1 (μg/L)			0.003	0.960
< 535 (n = 52)	9 (47.37)	43 (46.74)		
≥ 535 (n = 59)	10 (52.63)	49 (53.26)		
Pre-treatment PT (s)			-	0.037
< 17 (n = 42)	3 (15.79)	39 (42.39)		
≥ 17 (n = 69)	16 (84.21)	53 (57.61)		
Pre-treatment TT (s)			0.219	0.640
< 22 (n = 53)	10 (52.63)	43 (46.74)		
≥ 22 (n = 58)	9 (47.37)	49 (53.26)		
Pre-treatment APTT (s)			1.124	0.289
< 40 (n = 52)	11 (57.89)	41 (44.57)		
≥ 40 (n = 59)	8 (42.11)	51 (55.43)		
Pre-treatment PCT (μg/L)			3.266	0.071
< 7 (n = 55)	13 (68.42)	42 (45.65)		
≥ 7 (n = 56)	6 (31.58)	50 (54.35)		
Pre-treatment IL-6 (pg/mL)			-	0.041
< 53 (n = 49)	4 (21.05)	45 (48.91)		
≥ 53 (n = 62)	15 (78.95)	47 (51.09)		
Treatment modality			-	< 0.001
Conventional treatment (n = 53)	16 (84.21)	37 (40.22)		
Conventional treatment+PE-ALSS (n = 58)	3 (15.79)	55 (59.78)		

Data are presented as n (%). Note: ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; HA, hyaluronic acid; LN, laminin; IV-C, type IV collagen; IL-18, interleukin-18; ICAM-1, intercellular adhesion molecule-1; PT, prothrombin time; TT, thrombin time; APTT, activated partial thromboplastin time; PCT, procalcitonin; IL-6, interleukin-6; PE-ALSS, plasma exchange-based artificial liver support system.

Table 8. Assignment of variables for multivariate logistic regression analysis

Variable	Code	Assignment
Body mass index (kg/m^2)	X1	< 24 = 0, ≥ 24 = 1
Hypertension	X2	No = 0, Yes = 1
Pre-treatment PT (s)	X3	< 17 = 0, ≥ 17 = 1
Pre-treatment IL-6 (pg/mL)	X4	< 53 = 0, ≥ 53 = 1
Treatment modality	X5	Conventional treatment = 0, Conventional treatment+PE-ALSS = 1
Therapeutic efficacy	Y	Effective = 0, Ineffective = 1

Note: PT, prothrombin time; IL-6, interleukin-6; PE-ALSS, plasma exchange-based artificial liver support system.

Table 9. Multivariate logistic regression analysis of independent predictors of patient efficacy

Variable	B	SE	Wald	P	OR	95% CI
Body mass index (kg/m^2)	1.199	0.625	3.680	0.055	3.315	0.974-11.280
Hypertension	0.723	0.647	1.247	0.264	2.060	0.580-7.321
Pre-treatment PT (s)	0.888	0.721	1.519	0.218	2.430	0.592-9.980
Pre-treatment IL-6 (pg/mL)	1.177	0.681	2.987	0.084	3.244	0.854-12.320
Treatment modality	-1.865	0.714	6.823	0.009	0.155	0.038-0.628

Note: PT, prothrombin time; IL-6, interleukin-6; OR, odds ratio; CI, confidence interval.

multicenter study by Chen et al. [18] reported that PE-ALSS significantly improved clinical outcomes and prolonged survival in patients with HBV-related acute-on-chronic liver failure. Furthermore, a case-control matched analysis by Yang et al. [19] demonstrated that PE-ALSS

significantly improved short-term survival and reduced the risk of short-term mortality in this patient population.

In terms of hepatic function, ALT, AST, and TBIL in the research group were statistically reduced after intervention, and were lower than those of the control group, suggesting that PE-ALSS for CSHB can significantly improve patients' hepatic function. This could reflect the effective inhibition of hepatic fibrosis-related indices and inflammatory markers by PE-ALSS, thus reducing further hepatocyte damage and effectively ameliorating hepatic function. In the prospective study by Wu et al. [20], the intervention of PE-ALSS in patients with HBV-related acute-on-chronic liver failure contributed to an evidently enhanced 28-day treatment effectiveness rate and 90-day survival rate and significantly improved hepatic function, with certain cost-effectiveness, which supports our findings. The above-mentioned clinical advantages of PE-ALSS may be attributed to its effective restoration of the patient's internal environment, helping not only to correct the body's acid-base balance and electrolyte disorders but also to repaire damaged liver cells [21, 22], which is conducive to the improvement in patients' hepatic function and the effective play of therapeutic effects. As far as hepatic fibrosis is concerned, the research group showed evident decreases in HA, LN, and IV-C after intervention that were significantly lower than those of the control group, indicating that PE-ALSS can significantly alleviate hepatic fibrosis in CSHB patients. This may be realized through PE-ALSS-enabled elimination of profibrosis factors, optimization of the microenvironment within the liver, and prevention of progressive hepatocyte damage, thus effectively preventing the liver fibrosis process. Besides, serum biochemical indices such as IL-18 and ICAM-1, as well as inflammatory factors such as PCT and IL-6, dropped significantly in the research group after intervention, and were lower compared to those of the control group, suggesting that PE-ALSS for CSHB patients can significantly address the abnormally high IL-18 and ICAM-1 levels and help suppress abnormal inflammatory reactions. IL-18 is known to aggravate hepatocyte damage by inducing hepatocyte inflammatory necrosis or apoptosis; the high expression of ICAM-1 not only activates and promotes the secretion of inflammatory cytokines but also intensifies hepatocyte damage and necrosis [23, 24]. Serum PCT is closely related to renal insufficiency in patients with HBV-related acute-on-chronic liver failure, and IL-6, as a signal molecule in the immune response against pathogens, mediates the pathogenesis of CHB, liver cirrhosis, and hepatocellular carcinoma to some extent [25, 26]. The underlying mechanism may involve PE-ALSS-mediated immune status enhancement by regulating the Th1/Th2 balance, thereby effectively eliminating inflammatory indicators. In terms of coagulation function, we observed a notable drop in PT, TT, and APTT in the research group after intervention, also lower than those in the control group, which indicates that the treatment of CSHB patients with PE-ALSS is conducive to improving coagulation function. This might be because PE-ALSS, by infusing fresh frozen plasma, rapidly replenishes all the crucial clotting factors and fibrinogen that the patient is severely lacking due to liver synthesis disorders, thereby quickly correcting the coagulation imbalance. Finally, regression analysis confirmed the role of conventional treatment+ PE-ALSS as a protective factor for efficacy among SCHB patients, suggesting the positive effect of this therapy on reducing the risk of ineffective treatment in such patients.

There are some limitations in this study that need to be addressed in the future. First, the cases were limited in sample size and restricted to a single-center source, which may affect sample representativeness. In the future, multi-center data from different regions should be included to improve the accuracy of the research results. Second, as this was a retrospective study, there are inherent limitations in data collection. Future studies should supplement the levels of indicators at different time points as much as possible to dynamically assess changes in these indicators. Finally, the treatment cost of PE-ALSS has not been evaluated; future cost-benefit analyses may help to further promote this therapy.

To sum up, for patients with CSHB, treatment with PE-ALSS can significantly enhance short-term curative efficacy with a relatively low total complication rate. It also markedly improves hepatic function, suppresses hepatic fibrosis progression, down-regulates abnormally elevated IL-18, ICAM-1, PCT, and IL-6 levels, and ameliorates inflammation and coagulation function, deserving clinical promotion. Also, this therapy

is associated with a reduced risk of treatment ineffectiveness in CSHB patients. Our research can provide reliable insight and new treatment strategies for the clinical application of PE-ALSS in CSHB patients.

Disclosure of conflict of interest

None.

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