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Original Article

Effects of protein-supportive therapy on maternal and neonatal outcomes in patients with nephrotic syndrome during pregnancy

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Abstract: Objective: To investigate the clinical efficacy and safety of protein-supportive therapy in patients with nephrotic syndrome during pregnancy. Methods: This retrospective study included 314 women with moderate to severe preeclampsia, of whom 152 were diagnosed with nephrotic syndrome during pregnancy. Patients were divided into a treatment group (n=82) and a control group (n=70) according to treatment regimen. The treatment group received supplemental human albumin (daily dose < 15 g) in addition to blood pressure control, while the control group received only routine antihypertensive treatment. Blood pressure levels, 24-hour urinary protein, serum total protein, albumin, creatinine (Cr), uric acid (UA), blood urea nitrogen (BUN), estimated glomerular filtration rate (eGFR), lipid levels, liver function indicators, coagulation function, and inflammatory markers were compared between the two groups before and after treatment. Edema resolution time, length of hospital stay, pregnancy complications, and delivery method were observed; fetal birth weight, Apgar score, and perinatal mortality were also assessed. Adverse reactions during treatment were recorded. Results: Significant differences were observed in diastolic blood pressure, systolic blood pressure, 24-hour urinary protein, serum total protein levels, and renal function indicators before and after treatment in the treatment group (all $P < 0.05$). The control group mainly experienced decreased blood pressure and serum total protein levels (both $P < 0.05$). Post-treatment comparisons between groups showed that 24-hour urinary protein levels in the treatment group increased, significantly higher than in the control group, while serum total protein and albumin levels were significantly higher in the treatment group (all $P < 0.05$). Neonatal birth weight and Apgar scores were significantly higher in the treatment group ($P < 0.05$). Edema resolution time was longer in the treatment group than in the control group ($P < 0.05$). No serious allergic reactions or infections occurred during treatment. Conclusion: Protein-supportive therapy can improve hypoalbuminemia and fetal outcomes, but it may increase urinary protein excretion and edema resolution time. Thus, the benefits and risks should be carefully weighed in clinical practice.

Keywords: Protein-supportive therapy, pregnancy-associated nephropathy, nutritional status, renal function, pregnancy outcomes

Introduction

Pregnancy-associated nephropathy is a distinct type of kidney disease that occurs during pregnancy. Although its prevalence is less than 1%, it accounts for 20%-30% of the severe preeclampsia cases and has a perinatal mortality rate of approximately 25% [1]. Clinically, affected patients present primarily with edema, proteinuria, oliguria, hypertension, and hypoalbuminemia. If left untreated, this condition may lead to complications such as hypertensive encephalopathy, eclampsia, and heart failure, as well as adverse fetal outcomes such as premature birth, intrauterine growth restriction (IUGR), and neonatal asphyxia, thus seriously affecting maternal and neonatal outcomes [2]. In recent years, antihypertensive therapy has often been used as the basic treatment for pregnancy-associated nephropathy. By controlling blood pressure, it can partially reduce the burden on the kidneys and reduce proteinuria

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[3]. However, due to the large individual differences in the pathophysiological state of patients, some patients who only receive antihypertensive therapy cannot correct hypoalbuminemia and poor nutritional status, resulting in unsatisfactory maternal and neonatal outcomes [4]. Therefore, exploring more effective treatment strategies has become the focus of clinical practice. Protein-supportive therapy is a clinical nutritional support method that provides exogenous protein to correct hypoalbuminemia caused by massive proteinuria, thereby improving overall nutritional status. It can also increase plasma colloid osmotic pressure, promote interstitial fluid return, reduce edema, and enhance immune regulation [5]. In recent years, some experience has been accumulated in the application of protein-supportive therapy in patients with chronic kidney disease (CKD) and non-pregnant nephrotic syndrome, providing a preliminary theoretical basis for its use in pregnant patients with nephrotic syndrome [6]. However, the exact impact of protein-supportive therapy on renal function and maternal and neonatal outcomes in these patients remain unclear and require further clinical evidence. Against this background, this retrospective study aimed to investigate the clinical efficacy of protein-supportive therapy combined with conventional antihypertensive treatment in patients with nephrotic syndrome during pregnancy, and its impact on maternal and neonatal outcomes, in order to provide a more targeted basis for optimizing the clinical management of this disease.

Materials and methods

General information

This retrospective study included 314 women with moderate to severe preeclampsia admitted to the Department of Obstetrics and Gynecology of Suzhou Integrated Traditional Chinese and Western Medicine Hospital between December 2023 and December 2024. The diagnosis and classification of moderate to severe preeclampsia were based on the criteria from the International Society for the Study of Hypertension in Pregnancy. In addition, the 2020 Guidelines for the Diagnosis and Treatment of Hypertensive Disorders in Pregnancy were adopted, where severe preeclampsia was defined as systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg, with or without the involvement of vital organs [7]. Moderate preeclampsia was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg occurring after 20 weeks of gestation. Patients were included if they presented with proteinuria (≥0.3 g/24 h) but did not meet the severe criteria and had no significant involvement of vital organs. A final sample of 152 cases complicated with nephrotic syndrome of pregnancy was included in the analysis.

Inclusion criteria: meeting the diagnostic criteria for nephrotic syndrome during pregnancy, specifically as follows [8]: ① accompanied by symptoms such as lower extremity edema and morning eyelid edema; ② 24-hour urinary protein quantification ≥3.5 g, serum albumin concentration ≤30 g/L, hypercholesterolemia (> 7.7 mmol/L); ③ kidney injury was assessed according to the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines (2021 Clinical Practice Guidelines for Glomerular Diseases and the 2012 Acute kidney injury (AKI) diagnostic criteria). AKI was defined as a serum creatinine increase of ≥26.5 μmol/L within 48 hours, an increase to ≥1.5 times the baseline value within 7 days, or a urine output of < 0.5 mL/kg/h lasting for more than 6 hours; CKD was defined as kidney structural or functional abnormalities lasting for ≥3 months (e.g., estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 or persistent proteinuria); complete records of relevant clinical data such as prenatal check-ups and hospitalization records during pregnancy; singleton pregnancy; gestational age of onset between 24 and 34 weeks; age between 20 and 40 years.

Exclusion criteria: Allergic constitution; presence of other pregnancy complications that may affect the study results, such as gestational diabetes mellitus or thyroid dysfunction; premature termination of pregnancy; assessment showing severe dysfunction of major organs such as the heart, liver, or lungs, with specific quantitative criteria as follows: ① Liver dysfunction: Alanine aminotransferase (ALT) > 2 times the upper limit of normal or Aspartate aminotransferase (AST) > 2 times the upper limit of normal; ② Heart failure: New York Heart Association functional class III-IV, or echocardiographic left ventricular ejection fraction < 50%; ③ Resting arterial oxygen partial pres-

sure < 60 mmHg, or requiring continuous invasive/non-invasive mechanical ventilation.

It should be noted that the "nephrotic syndrome of pregnancy" defined in this study is a clinical syndrome specific to pregnancy, mainly manifested as nephrotic-range proteinuria (24-hour urinary protein ≥3.5 g) and hypoalbuminemia. Its diagnosis is not entirely equivalent to the independent disease entities of CKD or AKI as defined by KDIGO. In this study, the KDIGO criteria were primarily used for the objective assessment of the degree of renal function impairment, rather than for disease classification and diagnosis of pregnancy-related kidney diseases.

This study was approved by the Ethics Committee of Suzhou Integrated Traditional Chinese and Western Medicine Hospital. The study was conducted in strict accordance with the Declaration of Helsinki and related ethical guidelines. All research procedures complied with medical research ethics requirements and fully protected the privacy and legal rights of the participants.

Methods

In addition to controlling blood pressure, the treatment group received supplemental human serum albumin (Shanghai RAAS Blood Products Co., Ltd., National Drug Approval No. S10930020, specification: 5 g, 50 ml) administered via intravenous drip once daily. The actual dosage ranged from 10 to 14 g, with an average dosage of (12.52±0.38) g. The daily dosage was strictly controlled to be < 15 g. One course of treatment consisted of 5 consecutive days. Albumin dosage was individualized based on the patient's serum albumin level and the degree of edema. A higher dose (12-14 g/d) was administered when serum albumin was < 25 g/L or when significant edema was present, whereas a lower dose (10-12 g/d) was used when serum albumin was ≥25 g/L and edema was mild. The infusion rate was strictly controlled, with 50 mL administered over 1-2 hours by slow intravenous drip to avoid volume overload.

Both groups of patients received standard antispasmodic and antihypertensive treatment, specifically as follows: Magnesium sulfate injection (Beijing Yimin Pharmaceutical Co., Ltd., National Drug Approval No. H11020319, specification: 10 mL:2.5 g) was administered. The initial dose was 4 g, which was diluted with 25 mL of 25% glucose injection and slowly injected intravenously within 5 minutes. Subsequently, 60 mL of magnesium sulfate injection was mixed with 1,000 mL of glucose solution (25% concentration) and administered intravenously at a rate of 2 g/h to maintain a stable blood drug concentration. The control group received only routine antihypertensive treatment, with the same dosage and administration of magnesium sulfate injection as the treatment group. The indications and administration regimens for diuretics and anticoagulants were completely identical between the two groups, and both groups followed a uniform low-salt, standardized protein diet. There were no other differences in systemic treatment except for albumin infusion. Diuretics were mainly used when significant edema or increased volume overload was present (e.g., furosemide 20-40 mg/day, intravenously or orally, adjusted according to urine output and edema). Anticoagulation therapy was mainly used for patients with hypercoagulable states or thrombotic risks (e.g., subcutaneous injection of low molecular weight heparin, with the usual dose administered according to body weight). All patients followed a uniform low-salt diet (< 5 g/day) and a standardized protein intake regimen.

Observational indicators

(1) Blood pressure, renal function, and protein indicators: Blood pressure, renal function, and protein levels were measured before treatment and at the end of treatment (prior to delivery). Systolic and diastolic blood pressure were measured at rest using a standard medical blood pressure monitor. Twenty-four hour urine samples were collected in sterile containers with preservatives. Patients were instructed to collect urine from 7:00 AM to 7:00 AM the following day, and the total urine volume was recorded. During collection, external contamination from perineal secretions and feces was avoided. The indicators were tested using a Hitachi 7600 fully automated biochemical analyzer, with all reagents manufactured by Roche Diagnostics GmbH, Germany. Serum creatinine (Cr), uric acid (UA), and blood urea nitrogen (BUN) levels were detected using an enzymatic method. The eGFR was calculated using the CKD Epidemiology Collaboration formula for creatinine. Twenty-four hour urinary protein qu-

antification was performed using the turbidimetric method with a fully automated biochemical analyzer. Internal quality control was implemented. The coefficient of variation (CV) for the same batch of tests was < 3.0%, and the CV for different batches was < 5.0%, with all quality control results within the allowable error range. Serum total protein levels were determined using the biuret reaction method, and serum albumin concentration was measured by the bromocresol green method. Considering the physiological characteristics of pregnancy, the eGFR reference range was ≥90 mL/min/1.73 m^2 for normal renal function, and < 90 mL/min/1.73 m^2 for decreased glomerular filtration function, excluding physiological hyperfiltration during pregnancy.

(2) Lipid indicators: Fasting venous blood was collected from patients before treatment and delivery. The levels of total cholesterol (TC) and triglyceride (TG) in both groups were measured using an enzymatic method with a fully automated biochemical analyzer to assess lipid metabolism.

(3) Liver function indicators: Venous blood samples were collected at the same time points. The activities of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured using an enzyme-coupled reaction assay with a Hitachi 7600 fully automated biochemical analyzer and Roche Diagnostics reagent kits. These were used as key indicators for assessing the degree of hepatocellular injury.

(4) Coagulation function indicators: Before and after treatment (before delivery), coagulation function was assessed using a Sysmex CS-5100 fully automated blood coagulation analyzer with commercially available reagents from Sysmex Corporation. Plasma D-dimer levels were detected using immunoturbidimetry. Simultaneously, prothrombin time (PT) and activated partial thromboplastin time (APTT) were accurately measured using the fully automated blood coagulation analyzer. Fibrinogen (FIB) concentration was measured using a coagulation method to assess coagulation function.

(5) Inflammatory indicators: Blood samples were collected from the median cubital vein under quiet and fasting conditions, with a volume of 5 mL, both before treatment and after treatment (before delivery). Serum biochemical parameters were determined using a Hitachi 7600 automatic biochemical analyzer with supporting kits from Roche Diagnostics GmbH, Germany. All specimens were centrifuged at 3,000 rpm for 10 minutes on a high-speed centrifuge with a radius of 6 cm. Serum was separated and stored at -80°C. C-reactive protein (CRP) levels in both groups were detected using immunoprecipitation, and white blood cell counts were determined using Microscope count method.

(6) Edema resolution time and length of hospital stay: The time required for complete resolution of lower extremity and systemic edema from the start of treatment was recorded and compared in detail for both groups (edema resolution time), as well as the total length of hospital stay from admission to discharge.

(7) Pregnancy complications and delivery method: The incidence of pregnancy complications in both groups was observed and statistically analyzed, including preeclampsia, postpartum hemorrhage, and preterm birth. The final delivery method was also documented, categorized as vaginal delivery (including natural delivery and assisted delivery) and cesarean section.

(8) Neonatal outcomes: Birth weight was measured immediately after delivery, and Apgar scores were calculated and recorded at 1 minute and 5 minutes after birth. The presence of intrauterine growth restriction (IUGR) was recorded, and the proportion of newborns transferred to the neonatal intensive care unit (NICU) and the perinatal mortality rate were statistically analyzed.

Statistical analysis

SPSS 23.0 software was used. All continuous variables underwent normality tests (Kolmogorov-Smirnov test) and homogeneity of variance tests (Levene test). This study included continuous variables such as systolic blood pressure, diastolic blood pressure, 24-hour urinary protein, serum total protein, albumin, Cr, UA, BUN, eGFR, blood lipids (TC, TG), liver function (ALT, AST), inflammatory markers (CRP, white blood cell count), edema resolution time, length of hospital stay, fetal birth weight, and Apgar score. All variables showed normality according to the Kolmogorov-Smirnov test (all

Table 1. Comparison of baseline data and combined treatment between the two groups

Data	Treatment group (n=82)	Control group (n=70)	χ^2/t	*P*
Age ($\bar{x}$±s, years)	24.79±2.10	25.32±3.05	1.262	0.209
Gestational age of onset ($\bar{x}$±s, weeks)	29.04±4.77	29.18±3.90	0.196	0.845
Proportion of first-time mothers (%)	68 (82.93)	56 (80.00)	0.215	0.643
Pregnancy times ($\bar{x}$±s, times)	1.57±0.77	1.66±0.59	0.889	0.376
Pre-pregnancy body mass index ($\bar{x}$±s, kg/m^2)	22.32±2.05	22.18±2.03	0.422	0.674
Preeclampsia grade (Moderate/Severe)	39/43	33/37	0.003	0.959
Diuretic use [n (%)]	56 (68.29)	38 (46.34)	0.052	0.820
Anticoagulant use [n (%)]	38 (46.34)	30 (42.86)	0.178	0.673

Note: The diagnosis and classification of moderate to severe preeclampsia were based on the criteria from the International Society for the Study of Hypertension in Pregnancy and the 2020 Guidelines for the Diagnosis and Treatment of Hypertensive Disorders in Pregnancy.

P > 0.05) and homogeneity of variance according to the Levene test (all P > 0.05). Continuous variables that were normally distributed and had homogeneity of variance were expressed as mean ± standard deviation ($\bar{x}$ ±sd), and independent samples t-tests were used for comparisons between groups. Categorical data were expressed as n (%), and analyzed with χ^2 tests. P < 0.05 was considered statistically significant.

Results

Baseline characteristics

No statistically significant differences were observed between the treatment and control groups in terms of key baseline data such as age, gestational age at onset, proportion of primiparous women, preeclampsia grade, and parity (all P > 0.05). Furthermore, there were no statistically significant differences between the two groups in the proportion of diuretics and anticoagulants used (both P > 0.05). See **Table 1**.

Blood pressure, renal function, and protein indicators

Before treatment, there were no statistically significant differences in blood pressure, renal function, or protein indicators between the two groups (all P > 0.05). After treatment, both diastolic and systolic blood pressure in the two groups decreased significantly compared to before treatment (both P < 0.05), but there was no statistically significant difference in blood pressure levels between the treatment and control groups (both P > 0.05). The control group mainly showed a decrease in blood pressure and serum total protein levels (both P < 0.05). Post-treatment intergroup comparisons showed that the 24-hour urinary protein in the treatment group was significantly higher than that in the control group and baseline levels in the same group, whereas serum total protein and albumin levels were significantly higher in the treatment group than in the control group (all P < 0.05). In the treatment group, serum Cr and BUN levels were significantly higher than before treatment, while eGFR was significantly lower (all P < 0.05). In the control group, these indicators showed no significant changes before and after treatment (P > 0.05). See **Table 2**.

Lipid indicators

Before treatment, there were no statistically significant differences in TC and TG levels between the two groups (both P > 0.05). After treatment, there were no statistically significant differences in TC or TG levels between the two groups (both P > 0.05). See **Figure 1**.

Liver function indicators

Before treatment, there were no statistically significant differences in ALT and AST levels between the two groups (both P > 0.05). After treatment, no statistically significant differences were found in the above levels (P > 0.05). See **Table 3**.

Coagulation function indicators

Before treatment, PT, APTT, and fibrinogen levels did not differ significantly between the two

Table 2. Comparison of related indicators between groups ($\bar{x}\pm s$)

Indicator		Treatment group (n=82)	Control group (n=70)	*t*	*P*
Diastolic blood pressure (mmHg)	Before treatment	105.11±8.45	104.36±7.21	0.583	0.561
	After treatment	93.12±6.72*	94.44±6.21*	1.249	0.213
Systolic blood pressure (mmHg)	Before treatment	166.32±15.62	165.11±13.24	0.510	0.611
	After treatment	144.32±8.77*	145.78±7.20*	0.686	0.494
24-hour urine protein (g)	Before treatment	6.20±1.33	6.31±1.20	0.532	0.596
	After treatment	8.11±1.45*	6.68±1.06	7.003	<0.001
Serum total protein (g/L)	Before treatment	50.32±7.15	51.46±6.20	1.041	0.300
	After treatment	55.11±5.79*	47.20±4.84*	9.045	<0.001
Albumin (g/L)	Before treatment	25.37±4.20	24.66±3.77	1.089	0.278
	After treatment	26.63±5.05	23.68±4.06	4.082	<0.001
Cr (μmol/L)	Before treatment	82.55±8.30	82.02±7.33	0.414	0.680
	After treatment	88.30±7.55*	84.17±6.40	3.603	<0.001
UA (μmol/L)	Before treatment	441.52±64.20	457.12±72.10	1.411	0.160
	After treatment	482.32±47.36*	477.20±56.98	0.605	0.546
BUN (μmol/L)	Before treatment	4.67±0.80	4.52±0.73	1.199	0.232
	After treatment	5.30±0.75*	4.71±0.90	4.409	<0.001
eGFR (mL/min/1.73 m²)	Before treatment	86.21±12.21	86.39±9.63	0.100	0.921
	After treatment	79.26±8.65*	83.48±7.90	3.119	0.002

Note: Compared with before treatment in this group, *P<0.05. creatinine (Cr), uric acid (UA), blood urea nitrogen (BUN), filtration rate (eGFR).

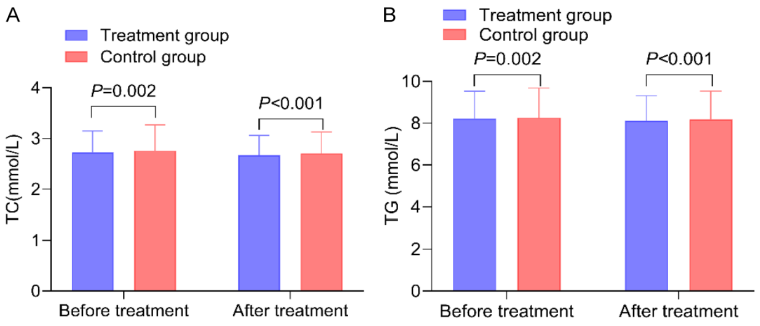

Figure 1. Comparison of lipid indicators between the two groups ($\bar{x}\pm s$, mmol/L). A: Comparison of TC; B: Comparison of TG. total cholesterol (TC) and triglyceride (TG).

Table 3. Comparison of liver function indicators between the two groups ($\bar{x}\pm s$, U/L)

Indicator		Treatment group (n=82)	Control group (n=70)	*t*	*P*
ALT	Before treatment	39.72±6.11	40.16±4.89	0.484	0.629
	After treatment	38.89±5.32	39.33±4.41	0.549	0.584
AST	Before treatment	29.45±4.12	28.77±3.90	1.039	0.300
	After treatment	28.31±5.20	28.11±4.16	0.259	0.796

Alanine aminotransferase (ALT), aspartate aminotransferase (AST).

groups (all P > 0.05). After treatment, there were no statistically significant differences in PT, APTT, and FIB levels between the two groups (all P > 0.05). See **Figure 2**.

Inflammatory indicators

Before treatment, C-reactive protein (CRP) and white blood cell counts were comparable between the groups (both P > 0.05). After treatment, no significant differences were observed between the groups in CRP levels or white blood cell counts (both P > 0.05). See **Table 4**.

Edema resolution time and hospital stay

The edema resolution time in the treatment group was significantly longer than that in

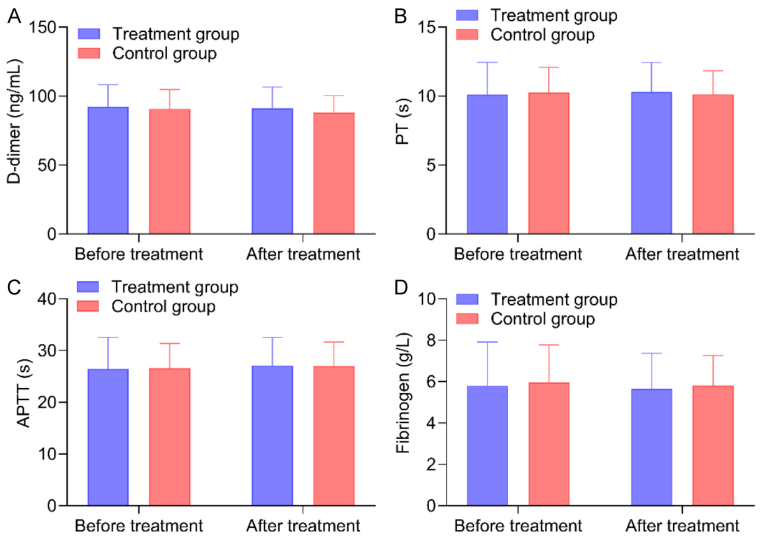

Figure 2. Comparison of coagulation function indicators between the two groups ($\bar{x}\pm s$). A: Comparison of D-dimer; B: Comparison of PT; C: Comparison of APTT; D: Comparison of Fibrinogen. prothrombin time (PT), activated partial thromboplastin time (APTT).

the control group (P < 0.05). However, there was no significant difference in hospital stay between the two groups (P > 0.05). See **Table 5**.

Pregnancy complications and delivery methods

The incidence of preterm birth in the treatment group (60.98%) was lower than that in the control group (77.14%) (P < 0.05). There were no statistically significant differences between the two groups in the incidence of preeclampsia, postpartum hemorrhage, and the ratio of vaginal delivery to cesarean section (all P > 0.05). See **Table 6**.

Neonatal outcomes

The mean birth weight and Apgar scores at 1 min and 5 min after birth were significantly better in the treatment group than in the control group (both P < 0.05). The proportion of neonates admitted to the NICU in the treatment group (64.63%) was significantly lower than that in the control group (80.00%) (P < 0.05). No significant differences were observed between the groups in the incidence of intrauterine growth restriction (IUGR), perinatal mortality or gestational age distribution of premature infants (P > 0.05). See **Table 7**.

Adverse reactions

No serious allergic reactions or infections occurred in either group during treatment. In the treatment group, 3 cases (3.66%) experienced mild adverse events, including 2 cases of fever (body temperature 37.5-38.0°C, possibly related to infusion reaction, which subsided spontaneously 1-2 hours after drug discontinuation) and 1 case of redness and swelling at the infusion site (which subsided 24 hours after local hot compress). In the control group, 4 cases (5.71%) experienced mild adverse events, including 2 cases of headache and 2 cases of nausea and vomiting, all of which were relieved after symptomatic treatment. There was no significant difference in the number of mild adverse events between the two groups (P > 0.05). See **Table 8**.

Discussion

The pathogenesis of nephrotic syndrome during pregnancy is complex, involving multiple factors such as immune-mediated glomerular damage, pregnancy-specific hyperfiltration, hormonal changes, and hypercoagulable states. Ultimately, this leads to damage to the glomerular filtration barrier, manifesting as massive proteinuria, hypoalbuminemia, and edema, severely impacting maternal and infant outcomes [9, 10].

Antihypertensive therapy is a fundamental measure, effectively controlling blood pressure and partially alleviating symptoms, but its intervention on glomerular damage is limited [11, 12]. This study showed that blood pressure significantly decreased in both groups after treatment, but there was no difference between the groups, suggesting that blood pressure control mainly came from standardized antihypertensive therapy, while protein-supportive therapy did not produce an additional antihypertensive effect. Protein-supportive therapy, by supplementing exogenous albumin, increases plasma colloid osmotic pressure, improving circulation and nutritional status, whose main effect is

Table 4. Comparison of inflammatory indicators between the two groups ($\bar{x}\pm s$)

Indicator		Treatment group (n=82)	Control group (n=70)	*t*	*P*
CRP (mg/L)	Before treatment	18.33±6.20	18.12±4.80	0.231	0.818
	After treatment	17.89±5.66	17.75±4.30	0.169	0.866
White blood cell count ($\times10^9$/L)	Before treatment	20.15±4.12	21.03±3.77	1.365	0.174
	After treatment	19.32±5.04	20.22±4.25	1.179	0.241

CRP: C-reactive protein.

Table 5. Comparison of edema regression time and hospital stay between the two groups ($\bar{x}\pm s$, d)

Indicator	Treatment group (n=82)	Control group (n=70)	*t*	*P*
Time for edema to subside	20.12±4.10	13.57±3.15	10.898	<0.001
Hospital stays	23.42±3.04	23.79±2.77	0.779	0.437

Table 6. Comparison of pregnancy complications and delivery methods between the two groups [n (%)]

Group	Pregnancy complications			Mode of delivery	
	Preeclampsia	Postpartum hemorrhage	Premature birth	Vaginal delivery	Cesarean section
Treatment group (n=82)	8 (9.76)	6 (7.32)	50 (60.98)	18 (21.95)	64 (78.05)
Control group (n=70)	9 (12.86)	8 (11.43)	54 (77.14)	14 (20.00)	56 (80.00)
χ^2	0.366	0.763	4.568	0.087	
P	0.545	0.382	0.033	0.769	

Table 7. Comparison of the conditions of the two groups of newborns

Indicator	Treatment group (n=82)	Control group (n=70)	χ^2/t	*P*
Fetal birth weight ($\bar{x}\pm s$, kg)	2.33±0.25	2.16±0.22	4.414	<0.001
Apgar score ($\bar{x}\pm s$, points)				
1 min after birth	7.60±0.65	7.33±0.50	2.832	0.005
5 min after birth	8.34±0.71	8.01±0.68	2.912	0.004
IUGR (%)	14 (17.07)	15 (21.43)	0.464	0.496
NICU occupancy rate (%)	53 (64.63)	56 (80.00)	4.395	0.036
Perinatal mortality rate (%)	12 (14.63)	10 (14.29)	0.004	0.952
Gestational age distribution [n (%)]			0.050	0.820
<32 weeks	12 (24.00)	14 (25.93)		
32-34 weeks	38 (76.00)	40 (74.07)		

Note: NICU: neonatal intensive care unit, IUGR: intrauterine growth restriction.

Table 8. Comparison of adverse reaction incidence in the two groups [n (%)]

Group	Fever	Redness and swelling at the infusion site	Headache	Nausea and vomiting	Overall adverse reaction
Treatment group (n=82)	2 (2.44)	1 (1.22)	0 (0.00)	0 (0.00)	3 (3.66)
Control group (n=70)	0 (0.00)	0 (0.00)	2 (2.86)	2 (2.86)	4 (5.71)
χ^2					0.360
P					0.550

volume and nutritional support, rather than directly affecting blood pressure [13, 14].

The results of this study indicated that protein-supportive therapy had a "dual effect". On the one hand, the serum total protein and albumin levels of patients increased significantly after treatment, suggesting that the therapy can effectively correct hypoalbuminemia and thus improve nutritional status; at the same time, the birth weight and Apgar score of newborns increased, and the preterm birth rate and NICU admission rate decreased, suggesting that it had a positive impact on perinatal outcomes. This effect may not be achieved by improving renal function, but is related to increasing plasma colloid osmotic pressure and improving systemic and uteroplacental circulation [15]. Related studies suggest that albumin infusion can indirectly optimize placental perfusion by improving blood volume status, but this study did not include placental hemodynamic parameters, and there is still a lack of direct evidence to support it [16]. The relevant mechanism needs further verification. On the other hand, this study also found that the 24-hour urinary protein, Cr and BUN levels increased, eGFR decreased, and the edema resolution time was prolonged in the treatment group, suggesting that protein-supportive therapy did not improve maternal renal function and may even increase the burden on the kidneys. This may be related to the fact that albumin infusion expands blood volume and increases intraglomerular pressure, thereby exacerbating protein filtration [17]; meanwhile, this therapy failed to repair the fundamental damage to the glomerular filtration barrier [18]. Delayed edema resolution may be related to increased volume and insufficient excretion, suggesting that diuretic therapy should be combined to optimize volume management.

Based on the KDIGO criteria and the characteristics of renal function during pregnancy, the changes in renal function indicators in the treatment group did not reach the diagnostic threshold for acute kidney injury, which were mostly due to the decline from the hyperfiltration state during pregnancy and changes in volume load, and had a certain degree of reversibility, with overall renal safety being controllable. This study did not find that protein-supportive therapy had a significant effect on blood lipids, liver function, coagulation and inflammatory indicators, suggesting that its short-term impact on other system functions is limited. This may be related to the fact that albumin mainly participates in volume and nutritional regulation, but does not directly participate in lipid metabolism, coagulation factor synthesis and inflammatory response [19-23].

Regarding maternal and infant outcomes, protein-supportive therapy showed a positive effect, but the NICU admission rate was still high, suggesting that nephrotic syndrome during pregnancy itself poses an independent risk to newborns, and more aggressive monitoring strategies are often adopted clinically. Regarding adverse reactions, only a few mild events were observed, and there was no difference between groups, indicating that the therapy has a certain degree of safety.

In clinical application, protein-supportive therapy is not suitable for all patients. It is more suitable for patients with significantly reduced serum albumin (e.g., < 25 g/L), moderate to severe edema, and no volume overload [24]. For patients with eGFR < 60 mL/min/1.73 m^2 or volume overload, it should be used with caution and close monitoring is necessary. During treatment, nutritional status, volume overload, and renal function should be comprehensively assessed to implement individualized treatment.

This was a single-center retrospective study and did not use propensity score matching. Therefore, there was still a risk of confounding bias. Furthermore, lacking postpartum renal function follow-up data made it impossible to assess long-term effects. In addition, although the distribution of preterm gestational age was supplemented, a more refined stratified analysis was not performed; diuretic use and changes in urine volume were not systematically recorded, which may affect the interpretation of the results. Future prospective studies are needed to improve follow-up and stratified analysis to further validate the conclusions of this study.

In conclusion, protein-supportive therapy has the advantage of improving hypoalbuminemia and neonatal outcomes in nephrotic syndrome during pregnancy, but it may increase protein-

uria and delay edema resolution, suggesting that it places a certain burden on the kidneys. Clinical practice should weigh the benefits and risks and implement individualized application.

Disclosure of conflict of interest

None.

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