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ORIGINAL ARTICLE

Effects of hemoperfusion in the treatment of childhood Henoch-Schönlein purpura nephritis

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Purpose: *Immune mediators play a role in the pathogenesis of Henoch-Schönlein purpura (HSP) nephritis. Since hemoperfusion (HP) is able to eliminate the immune mediators in many diseases, we investigated the effects of HP in the treatment of HSP nephritis.*

Methods: *90 children with HSP nephritis were enrolled and followed up for 12 months. They were assigned to the HP group or the control group, respectively. Both groups were treated with corticosteroids and other supportive therapy. Patients in the HP group received HP for 3 consecutive days. The major outcomes included the percentage of patients with HSP nephritis, extrarenal symptoms, and recurrences and changes in serum levels of immune mediators.*

Results: *The percentage of patients with nephritis in the HP group was less than that in the control group at each visit; the differences for proportions at 1, 3, 6, 12 months were 16.7% (p = 0.133), 31.3% (p = 0.004), 10.8% (p = 0.283), and 20.6% (p = 0.003), respectively. The severity and duration of abdominal and joint pains in the acute phase were significantly improved in the HP group compared to those in the control group. Hemoperfusion also significantly reduced patients' serum levels of immune mediators including IgA, TNF-α, IL-6, and LTB4. However, recurrences between the two groups were not significantly different.*

Conclusions: *Hemoperfusion in combination with corticosteroid was more effective than corticosteroid alone in treating HSP nephritis. The effects may be achieved by eliminating immune mediators.*

Keywords: *Henoch-Schönlein purpura, Hemoperfusion, Nephritis, IgA, Cytokines*

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INTRODUCTION

Henoch-Schönlein purpura (HSP) is one of the most common types of systemic small vessel vasculitis in children (1). The severity of renal impairment determines the long-term prognosis of children with HSP. Those with HSP nephritis at onset may develop various renal impairments as adults many years after the initial HSP symptoms have resolved (2, 3). Although the exact pathogenic mechanisms have not been fully elucidated, HSP is regarded as a specific immune-mediated entity, with the involvement of IgA and many cytokines in its pathogenesis (4-10). HSP patients with nephritis have increased cytokine levels, such as TNF-α, than those without renal impairment (6). For this reason, we hypothesized that early removal of inflammatory mediators in the acute phase may help to alleviate renal impairment and improve clinical symptoms of HSP nephritis. At present, no drug therapy can directly eliminate circulating mediators. Hemoperfusion is one of the blood purification therapies which has been proven to efficiently eliminate inflammatory mediators during MODS, sepsis, and so forth (11-13). However, it remains unclear whether it is a beneficial therapy for HSP nephritis. The present study was therefore undertaken to explore the potential therapeutic effects of hemoperfusion in treating renal and extrarenal symptoms in HSP nephritis.

METHODS

Participants

A total of 128 children with a diagnosis of HSP nephritis who presented to West China Second University Hospital of Sichuan University from 2007 through 2009 were screened, of whom 90 eligible patients were enrolled in this study. All patients had acute onset. Inclusion criteria were aged between 4 and 16 years and a clinical diagnosis of HSP nephritis, based on typically distributed palpable purpura and established nephritis (defined as hematuria on microscopic urinalysis greater than 3 red blood cells per high power field, or proteinuria greater than or equal to 1+ with a dipstick test). Exclusion criteria were thrombocytopenia, other causes of nephritis, coagulation dysfunction, hemodynamic instability, and immunodeficiency. Those with a disease in which corticosteroids were contraindicated and with a life-threatening complication of HSP were also excluded. The parents or guardians of enrolled patients were informed about the procedures, possible benefits and risks of hemoperfusion. According to their choices, the children were divided into two groups: the hemoperfusion (HP) group and the control group. The protocol is shown in Figure 1.

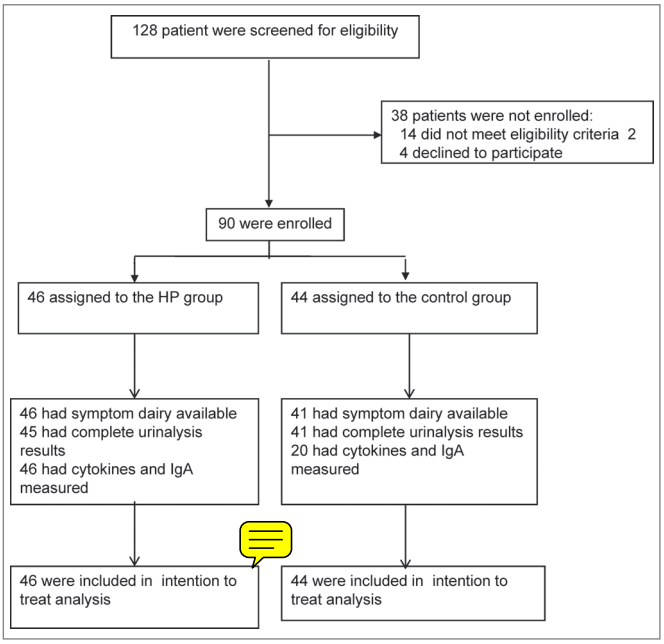

Fig. 1 - *Flowchart for inclusion and follow-up of patients.*

Clinical management

Both groups received supportive therapy and corticosteroid treatment. The protocol of corticosteroid therapy was as follows: dexamethasone 1 mg/kg•d (maximum 45 mg/d) pulse therapy once a day for 3 consecutive days followed by once every other day, 3 times in total; then oral prednisone 2 mg/kg•d (maximum 60 mg/d) was given for 2 weeks; after that, alternate-day prednisone therapy was administered, i.e., 2 mg/kg•d on odd-numbered days and 10 mg on even-numbered days at a tapering dose of 5 mg every 2 months until complete withdrawal when patients remained asymptomatic. If patients developed nephrotic-level proteinuria, then a full dose of oral prednisone was given for at least 4 weeks and immunosuppressants such as Tripterygium glycoside (a kind of Chinese herb with triptolide as one of its major active components with anti-proteinuric effects) (1 mg/kg, maximum 60 mg/d) was also administered appropriately.

Hemoperfusion was performed in the HP group using HA280, a resin cartridge made of polystyrene fibers (Zhuhai Lizhu Group, Biological Material Co, Zhuhai, China). Blood access was established via a double-lumen catheter inserted into the femoral vein using Seldinger's method. Treatment was carried out for 2 h at a blood flow rate of 3 to 5 ml/kg•min, once a day for 3 consecutive days. In order to maintain extracorporeal blood flow, nadroparin calcium (Fraxiparine, product of Glaxo Wellcome Production, Shanghai, China), was used as anticoagulant (40-60 u/kg). All side effects of hemoperfusion were collected and systematically recorded in detail on data sheets.

Laboratory investigations

Routine serum urea and creatinine levels were determined on Johnson Vitros 350 dry chemical autoanalyzer (Johnson & Johnson, New York, NY, USA). Freshly voided random urine was analyzed with a light microscope for hematuria and a dipstick test was used to test proteinuria qualitatively. Protein quantification in 24-h urine collection was measured on a Hitachi 7600 autoanalyzer (Hitachi Instrument Service, Tokyo, Japan) with turbidity method. The eGFR was calculated using the Schwartz formula (14). Occult blood in stool was investigated with BASO indicator paper on immune colloidal gold technique.

Blood samples of 46 patients in the HP group for the measurement of IgA and cytokines including TNF-α, IL-1β,

IL-6, and LTB4 were collected before and on 1, 2, and 3 days after hemoperfusion. Samples of the control group and the healthy control were also collected and measured (n = 20 and 32 respectively). Enzyme-linked immunosorbent technique was used to measure the levels of aforementioned mediators (Juying Bioscitech Ltd, Shenzhen, China) following the manufacturer's instructions. All samples were independently measured three times.

Symptom dairy and clinical evaluations

Enrolled patients were examined and evaluated by a doctor. The severity and duration of symptoms including skin lesions, abdominal and joint pains were recorded and scored. The severity of skin lesion was defined as follows: 1 = mild, scattered, sparse purpura, limited to both lower limbs; 2 = moderate, purpura mixed together, limited to both lower limbs; 3 = severe, purpura mixed together and distributed all over the body. The severity of abdominal and joint pains were classified as follows: 0 = no pain; 1 = mild pain, the child can move around and play; 2 = moderate pain, the child sometimes likes to stay still; 3 = severe pain, the child cannot move around or play or prefers to stay in bed (15). Renal laboratory findings were defined as hematuria on microscopy and/or proteinuria by dipstick test. Symptom dairies were given to parents or guardians at study inclusion and they were followed at 1, 3, 6, and 12 months. Urinalysis was performed at each visit. Clinical examinations and the laboratory results were collected and recorded on data sheet.

Outcome measures

The primary outcome was the percentage of patients with HSP nephritis at each visit. Secondary outcomes were: (1) the sum of scores during hospitalization and duration of symptoms in the acute phase; (2) recurrences and other extrarenal complications requiring operative intervention such as intracranial hemorrhage, gastrointestinal perforation or intussusception; (3) blood levels of IgA and other cytokines; (4) side effects of hemoperfusion.

Ethics

Approval of the Institutional Review Board (IRB)/Ethics Committee was obtained. This study was performed in accordance with the ethical standards of the Declaration of Helsinki. All the parents or guardians signed informed consent.

Statistical analysis

Data was managed using Microsoft office Excel; statistical analyses were performed with SPSS software (version 13.0). Sum of scores for abdominal pain, joint pain and purpura were compared using the *t*-test. Proportions were compared using Chi-square test or Fisher's Exact test as appropriate. The effects of therapy on HSP nephritis from the 1-month visit onward between the HP and the control groups were compared using the Kaplan-Meier method, with the difference evaluated using the log-rank test. ANOVA analysis was used to compare the levels of IgA and cytokines between multiple groups. P values less than 0.05 were considered significant.

All subjects were included in the analysis (intention to treat). The last available data was used for those subjects with incomplete data.

RESULTS

Study population

In all, 90 patients were enrolled in the study. Characteristics of both groups are shown in Table I. There were no significant differences of baseline characteristics between the two groups.

Efficacy of hemoperfusion in relieving abdominal and joint symptoms and purpura in the acute phase

Hemoperfusion was effective in relieving abdominal and joint pains in the acute phase. Within the first 2 weeks of diagnosis the duration of abdominal and joint pains were significantly ~~more~~ shortened in the HP group than in the control group (for abdominal pain and joint pain respectively: mean difference, 1.2 and 2.2 days, p = 0.03, p = 0.000). The mean sum of severity scores for abdominal and joint pains in the first week after diagnosis were also significantly less in the HP group (mean difference, 1.5 and 1.2, p = 0.04 and 0.04 respectively for abdominal pain and joint pain).

However, hemoperfusion did not improve purpura, there were no significant differences between the severity scores,

TABLE I - CLINICAL AND LABORATORY FEATURES OF PARTICIPANTS AT BASELINE

Characteristic	HP group (n = 46)	Control group (n = 44)
Male/female	30/16	25/19
Mean age at diagnosis (years)	10.2 (6 to 16)	10.3 (5 to 16)
Mean time (days) to diagnosis*	17.1 (2 to 90)	15.5(1 to 60)
Purpura	46 (100%)	44 (100%)
Abdominal pain	31(67.4%)	27 (61.4%)
Joint pain	22 (47.8%)	26 (59.1%)
Renal laboratory findings	46 (100%)	44 (100%)
Proteinuria†	42 (91.3%)	37 (84.1%)
1+	17 (36.9%)	13 (29.5%)
2+	9 (19.6%)	5 (11.4%)
3+	7 (15.2%)	8 (18.2%)
4+	9 (19.6%)	11 (25.0%)
Hematuria‡	34 (73.9%)	38 (86.4%)
3-10	6 (13.0%)	7 (15.9%)
1+	15 (32.6%)	8 (18.2%)
2+	2 (4.4%)	5 (11.4%)
3+	8 (17.4%)	11 (25.0%)
4+	3 (6.5%)	7 (15.9%)
Proteinuria† & hematuria‡	28 (60.9%)	31 (70.5%)
WBC in urine	3.3 (0 to 11)	2.4 (0 to10)
Crystalluria	None	None
Cast		
Granular cast	19 (41.3%)	14 (31.8%)
Cellular cast	5 (10.8%)	1 (0.2%)
24 h urine protein (mg/kg)	43.5 (0.4 to 214.2)	45.4 (0.0 to 224.1)
BUN (in mmol/L)	4.12 (2.2 to 10.8, n = 36)	4.4 (2.2 to 9.9, n = 36)
CREA (in μmol/L)	37.4 (24 to 58, n = 36)	34.6(17 to 66, n = 36)
eGFR (mL/min/ 1.73 m^2)$	142.9 (98.2 to 208.2, n = 36)	147.8 (92.4 to 200.1, n = 36)
Renal pathology§	8 (15.2%)	6 (13.6%)
Class I	4 (50.0%)	5 (83.3%)
Class II	3 (37.5%)	1 (16.7%)
Class III	1 (12.5%)	0 (0.0%)
Other laboratory test		
Occult blood in stool	14 (46.7%, n = 30)	4 (23.5%, n = 17)

Data are number of patients (%) or mean (range).
*Time from first manifestations observed at home to diagnosis.
†U-protein ≥1+ with a dipstick test.
‡U-erythrocytes >3 per high power field (HPF), renal erythrocytes were counted.
$The eGFR was estimated using the Schwartz formula.
§The biopsy findings were graded according to the classification developed by the International Study of Kidney Disease in Children (ISKDC).

TABLE II - INFLUENCE OF HEMOPERFUSION ON ABDOMINAL AND JOINT PAINS, PURPURA IN THE ACUTE PHASE

Characteristic	HP	Control	Mean difference	95% CI	*p*
Abdominal pain duration†	2.9	4.1	1.2	0.1 to 2.4	0.03
Abdominal pain severity‡	3.9	5.4	1.5	0.0 to 3.1	0.04
Joint pain duration†	3.3	5.5	2.2	1.0 to 3.2	0.000
Joint pain severity‡	3.6	4.8	1.2	0.1 to 2.4	0.04
Days before no new purpura observed*	5.5	5.8	0.3	-0.72 to 1.4	0.52
Purpura severity‡	8.5	9.2	0.7	-0.53 to 1.8	0.28

†Mean sum of days with pain within the first 2 weeks (for abdominal pain: HP n = 31, control n = 27; for joint pain: HP n = 22; control n = 26).
‡Mean sum of scores for pain and purpura within the first 2 week.
*Time from which no new purpura occurred during hospitalization.

and the time from which no new purpura occurred during hospitalization between the two groups. Table II showed the influence of hemoperfusion on abdominal and joint pains, and purpura in the acute phase.

Efficacy of hemoperfusion in treating HSP nephritis

Among 90 patients, 11 children (6 in the HP group and 5 in the control group) received Tripterygium glycoside during follow-ups because of persistent nephritis symptoms and were not included in the comparison. Hemoperfusion was effective in treating HSP nephritis. The disappearance of nephritis between the 2 groups during the 12 months of follow-up was shown in Figure 2 (log rank p = 0.000). The percentage of patients with nephritis in the HP group was less than that in the control group at each visit, differences for proportions (p values) at 1, 3, 6, and 12 months were 16.7% (p = 0.133), 31.3% (p = 0.004), 10.8% (p = 0.283), 20.6% (p = 0.003) respectively (Tab. III). The number and percentage of patients with nephritis at each time point according to different grades of renal laboratory findings at onset in the two groups were shown in Table III.

A total of 17 patients (7 in the HP group and 10 in the control group) had nephrotic level proteinuria at inclusion, during 12 months of follow-ups none in the HP group

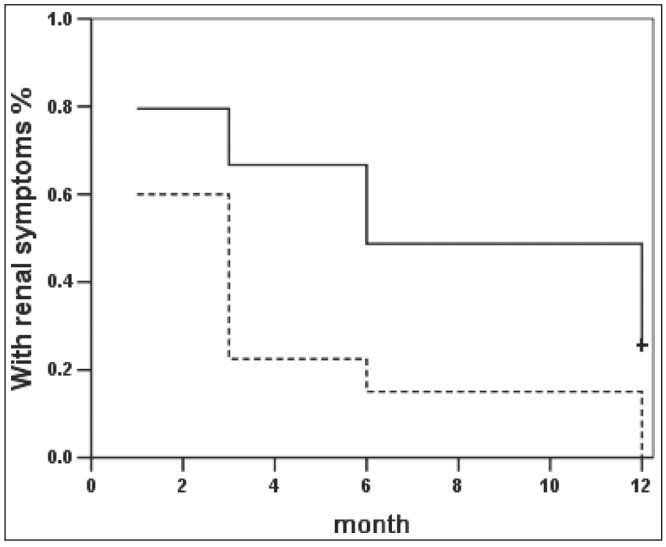

Fig. 2 - *Disappearance of HSP nephritis after treatment. Survival analysis of patients with HSP nephritis during 12 months of follow-up. Dashed line, the HP group (n = 40); solid line, the control group (n = 39; log rank p = 0.000).*

(0/7, 0.0%) and 1 in the control group (1/10, 10.0%) still had nephritis, but the difference was not significant (Fisher's Exact Test p = 0.58).
No patients in either group developed renal inadequacy during the 12-month follow-up.

Efficacy of hemoperfusion in reducing recurrences and extrarenal complications

Hemoperfusion did not reduce the recurrences of HSP. During the 12 months of follow-up, 15 recurrences (primarily purpura) were seen in both groups, among them 8 in the HP group (8/46, 17.4%) and 7 in the control group (7/44, 15.9%) (Pearson Chi square p = 0.85). Four children were readmitted to the hospital because of severe purpura and abdominal pain, 1 in the HP group and 3 in the control group (p = 0.32 by Fisher's Exact test).
No patients in either group developed severe complications such as intracranial hemorrhage, gastrointestinal symptoms needing operative intervention, or renal insufficiency.

Effects of hemoperfusion in reducing IgA and cytokines

On day 0, the serum levels of IgA and the cytokines including TNF-α, IL-1β, IL-6, and LTB4 were significantly increased in HSP patients compared to the healthy control, while the levels of the mediators between the control and the HP group were not significantly different. Corticosteroids alone did not efficiently reduce the levels of IgA and cytokines: on day 3 the levels of tested mediators were reduced compared with that on day 0 in the control group, but the differences were not significant ($p>0.05$) (Tab. IV).
Hemoperfusion demonstrated efficacy in reducing the levels of IgA and cytokines. The levels of mediators decreased quickly after hemoperfusion: on day 3 the levels of IgA, TNF-α, and LTB4 in the HP group were significantly lower than that seen in the control ($p = 0.004$, <0.001, and 0.009 respectively). Except for IL-1β, the levels of the other four mediators in the HP group decreased significantly on day 3 compared to those on day 0 (Tab. IV).

Side effects of hemoperfusion

In general, 90 patients received 270 periods of hemoperfusion, side effects observed included hypotension during hemoperfusion (22/270, 8.1%), urticaria (7/270, 2.5%), blood clotting of cartridge (2/270, 0.7%). The most common side effect was hypotension which was treated by reducing the blood flow rate and fluid infusion. Urticaria was treated by an antihistamine medicine such as chlorphenamine. Blood clotting of the cartridge was corrected by removing the catheter. No severe complications were observed such as anaphylaxis, fever, or a massive hemorrhage of the gastrointestinal tract and other locations, and so on.

DISCUSSION

Although HSP is generally a self-limited process, 1/3 of patients have recurrent symptoms and 40% to 50% of patients develop nephritis within 4 to 6 weeks (16), late deterioration of renal function has been reported many years after the nephritis (2). Since the long-term prognosis of HSP is heavily dependent on the severity of nephritis, early and effective treatment of this most serious complication of HSP could improve its prognosis. At present, drugs including corticosteroid and immunosuppressants are the mainstay of therapy, but for the time being there is little evidence to indicate the best treatment for HSP nephritis (17). Since IgA and many other cytokines are implicated in its pathogenesis, early removal of such mediators may

TABLE III - EFFICACY OF HEMOPERFUSION IN TREATING HSP NEPHRITIS

Category	Acute phase		1 month		3 month		6 month		12 month	
	HP	Control	HP	Control	HP	Control	HP	Control	HP	Control
Mild hematuria†	4 (10.0%)	6 (15.4%)	0 (0.0%)	2 (5.1%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	2 (5.1%)	0 (0.0%)	1 (2.6%)
Severe hematuria‡	1 (2.5%)	1 (2.6%)	1 (2.5%)	1 (2.6%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mild proteinuria*	10 (25.0%)	3 (7.7%)	5 (12.5%)	2 (5.1%)	1 (2.5%)	0 (0.0%)	1 (2.5%)	1 (2.6%)	0 (0.0%)	0 (0.0%)
Severe proteinuria**	2 (5.0%)	3 (7.7%)	2 (5.0%)	1 (2.6%)	1 (2.5%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Mild hematuria & Mild proteinuria	9 (22.5%)	10 (25.6%)	4 (10.0%)	5 (12.8%)	1 (2.5%)	3 (7.7%)	3 (7.5%)	2 (5.1%)	1 (2.5%)	2 (5.1%)
Mild hematuria & Severe proteinuria	6 (15.0%)	4 (10.3%)	2 (5.0%)	3 (7.7%)	0 (0.0%)	3 (7.7%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)
Severe hematuria & Mild proteinuria	2 (5.0%)	4 (10.3%)	1 (2.5%)	3 (7.7%)	1 (2.5%)	3 (7.7%)	1 (2.5%)	2 (5.1%)	0 (0.0%)	2 (5.1%)
Severe hematuria & Severe proteinuria	6 (15.0%)	8 (20.5%)	5 (12.5%)	9 (23.1%)	4 (10.0%)	10 (25.6%)	2 (5.0%)	5 (12.8%)	0 (0.0%)	3 (7.7%)
Total	40 (100%)	39 (100%)	20 (50%)	26 (66.7%)	8 (20%)	20 (51.3%)	9 (22.5%)	13 (33.3%)	1 (2.5%)	9 (23.1%)
p	NS		0.13		0.004		0.283		0.003	

†U-erythrocytes ≤2+ per high power field (HPF), only renal erythrocytes were counted.
‡U-erythrocytes ≥3+ per high power field (HPF), only renal erythrocytes were counted.
*U-protein ≤2+ with a dipstick test.
**U-protein ≥3+ with a dipstick test.

TABLE IV - SERUM LEVELS OF IGA AND CYTOKINES AFTER TREATMENT

	Healthy control (n = 32)	Control Day 0 (n = 20)	Control Day 3 (n = 20)	HP Day 0 (n = 46)	HP Day 1 (n = 46)	HP Day 2 (n = 46)	HP Day 3 (n = 46)
IgA (mg/L)	22.3 ± 5.7	55.2 ± 16.3*	51.3 ± 13.5‖	56.4 ± 19.9*‖	49.9 ± 15.6	42.7 ± 12.3‡	37.1 ± 8.7†‡
TNF-α (pg/ml)	29.9 ± 13.3	38.5 ± 10.1**	33.5 ± 7.4‖	36.8 ± 14.4**‖	30.9 ± 13.5§	22.9 ± 11.7†‡	20.8 ± 11.2†‡
IL-1β (pg/ml)	29.8 ± 9.4	49.3 ± 8.7*	45.9 ± 6.5‖	51.4 ± 22.8*‖	47.9 ± 14.8	40.3 ± 14.9	37.9 ± 21.4
IL-6 (pg/ml)	12.1 ± 3.5	20.5 ± 5.5*	17.2 ± 5.9‖	20.4 ± 7.5*‖	17.5 ± 4.8	15.9 ± 5.6§	14.6 ± 6.2‡
LTB4 (pg/ml)	50.6 ± 10.3	144.1 ± 34.8*	139.8 ± 26.8‖	148.9 ± 78.5*‖	130.3 ± 6.9.0	118.0 ± 63.2	100.9 ± 58.1†§

**p*<0.01 (compared with Healthy control).
***p*<0.05 (compared with Healthy control).
†*p*<0.01 (compared with control on day 3).
‡*p*<0.01 (compared with HP on day 0).
§*p*<0.05 (compared with HP on day 0).
‖*p*<0.05 (compared with control on day 0).

help to alleviate the disease. To this effect, we utilized a new technique – hemoperfusion – to treat HSP nephritis. The results demonstrated that compared with those treated with corticosteroids alone, patients receiving hemoperfusion had quicker relief of HSP nephritis and abdominal and joint pains. These effects may be attributed to IgA and cytokine reduction after hemoperfusion.

It has been suggested that early corticosteroid treatment was effective in reducing abdominal and joint symptoms (15, 18-20). In our practice we also found its efficacy. Moreover, we found that hemoperfusion in combination with corticosteroids was more effective than corticosteroids alone in treating these symptoms. Compared to the control group, patients in the hemoperfusion group had

shorter duration and less severe abdominal and joint pains in the acute phase. Since those symptoms are usually most disturbing in the acute phase of HSP, hemoperfusion remains to be a good add-on treatment especially for those patients with severe abdominal and joint pains.

There is no firm evidence to indicate that the use of corticosteroids alone is the best treatment for HSP nephritis, especially for those with nephrotic level proteinuria (17). Corticosteroids may reduce the production of inflammatory mediators by inhibiting immune responses, but it is not effective in eliminating existing mediators such as IgA and cytokines. Hemoperfusion has been reported to efficiently eliminate inflammatory mediators. In our study we used the HA280 type resin cartridge to perform hemoperfusion. The HA type resin cartridge is an extracorporeal hemoperfusion device which has been proven to efficiently adsorb different cytokines (12, 13). The HA280 cartridge uses neutral microporous resin (5-15 nm in diameter) and is designed specifically, but not exclusively, to adsorb cytokines whose molecular weights are between 10-50 kDa, such as TNF-α (17KD) and IL-6 (26KD). TNF-α, IL-1β, IL-6, and LTB4 are reported to be implicated in the pathogenesis of HSP, their levels were high in the tissues, plasma, or urine of HSP patients. They are pro-inflammatory cytokines produced by many cell types and promote glomerular mesangial proliferation, glomerular fibrosis, and angiogenesis, among other conditions (5-8). Furthermore, cytokine levels may reflect the severity of HSP; for example, the serum levels of TNF-α in patients with renal involvement is significantly higher than those without nephritis (5). IgA plays a vital role in the pathogenesis of HSP. It was reported that IgA increased in serum and deposited on the small vessel walls of HSP patients (16, 17). IgA derived during acute HSP binds to endothelial cells and may modulate the functional and survival of these cells (9); moreover, IgA can enhance cytokines such as IL-8 production thus worsening HSP (4). Since IgA and cytokines participate in the pathogenesis of HSP, early removal of these mediators may help to abate renal impairments. In our study, hemoperfusion significantly reduced patients' serum levels of IgA and most of the aforementioned cytokines, which may contribute to the improvement of renal impairments: by the 12-month follow-up only 2.5% children still had nephritis in the HP group compared to 23.1% in the control group.

It is worth noting, however, that the therapeutic effects of treatment in relieving HSP nephritis, and abdominal and joint pains are not attributable entirely to hemoperfusion. They resulted from the combination therapy of hemoperfusion, corticosteroids, and other supportive therapies. Hemoperfusion is an effective add-on treatment for HSP nephritis, and abdominal and joint symptoms, but its therapeutic effects are limited. Hemoperfusion failed to significantly decrease the renal involvement of patients with nephrotic level proteinuria at onset, and the recurrences and readmission to hospital between the two groups were not significantly different. What is more, 11 patients in the cohort still received immunosuppressants during follow-ups, which indicates corticosteroid and immunosuppressant remain to be the main treatments for severe HSP nephritis. However, we only performed hemoperfusion 2 hours a day for 3 consecutive days. The course of this treatment may be too short to completely eliminate the mediators in circulation, so the therapeutic effects are limited.

In addition to hemoperfusion, other blood purification techniques have been used to treat HSP. For example, plasmapheresis demonstrated efficacy in treating HSP patients with various complications such as gastrointestinal involvement, renal impairment, and intracerebral hemorrhage (21-23), but several problems remain. Plasma exchange may lead to blood transfusion transmitted diseases; the amount of plasma needed is large (usually 30-40 ml/kg), which is not always available. What is more, it is so expensive that many patients cannot afford the treatment. On the contrary, hemoperfusion is less costly and more feasible. There is no risk of transmitting diseases since all the tubing and the cartridge are disposable. What is more, hemoperfusion is safe: the most common side effect seen in our practice is hypotension, which is endurable, easy to correct, and disappears quickly once hemoperfusion is completed.

This study has certain limitations. First, it is a non-randomized, concurrent control study: blinding was not used in the acute phase when doctors evaluated the patients during hospitalization because the catheters inserted in patients' femoral veins easily revealed their grouping. Second, the data on renal pathological characteristics is limited: though we performed renal biopsies on some patients, the data was not enough to make a comparison, therefore the standard for renal impairments is rough since we failed to correlate the improvement of clinical symptoms, and the reduction of IgA and cytokines with pathological changes of the kidney. Third, some data were missing among responses to the symptom dairy. Finally, the time of observation was short: long-term follow-up is needed to

make a more complete evaluation of the effects of hemoperfusion.

CONCLUSIONS

In conclusion, this study demonstrates that hemoperfusion with the HA280 cartridge in combination with corticosteroids is more effective than corticosteroids alone in treating HSP nephritis. The effects may be achieved by reducing the circulating IgA and cytokines. However, many questions such as the timing and duration of hemoperfusion still remain. For this reason, further studies involving larger, better powered, multicenter clinical trials should be carried out to address those questions and to assess the benefits of hemoperfusion in the treatment of HSP nephritis more accurately.

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Conflict of Interest Statement: The authors declare no conflict of interest.

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