Original Article

Double filtration plasmapheresis for children with different types of critical kidney diseases: a single-center retrospective cohort study

Yu Zhang^, Qing Xie^, Yaxian Chen^, Juanjuan Yang, Shi Huang, Linxia Deng, Jianhua Zhou^

Department of Pediatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Contributions: (I) Conception and design: Y Zhang; (II) Administrative support: J Zhou; (III) Provision of study materials or patients: Y Zhang, Y Chen; (IV) Collection and assembly of data: Q Xie, Y Chen, J Yang, S Huang; (V) Data analysis and interpretation: Y Zhang, Y Chen; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Jianhua Zhou. Department of Pediatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, No. 1095, Jiefang Ave., Wuhan 430030, China. Email: jhzhou99@qq.com.

Background: Double filtration plasmapheresis (DFPP) was initially used to facilitate the conduction of ABO-incompatible renal transplantation. The applicability of DFPP has recently expanded to cover the removal of various antibodies in adults with immune-mediated diseases. However, DFPP is seldom used in children, with few reports addressing its efficacy and safety in this population. This study aimed to explore the efficacy and adverse effects of DFPP for pediatric patients with renal indications.

Methods: Children who received DFPP between December 2017 and December 2020 at Tongji Hospital were retrospectively studied, and sub-grouped for analysis according to the types of disease. All children received 3 to 6 DFPP sessions within 2 to 3 weeks, and were assessed for clinical outcomes according to glomerular filtration rate, proteinuria and extra-renal symptoms. Pre- and post-DFPP plasma were collected to measure the levels of pathogenic autoantibodies, immunoglobulins, fibrinogen, albumin, calcium, etc. In-hospital complications were also recorded.

Results: Totally there were 10 children receiving 44 sessions of DFPP, including 2 males and 8 females, with a median age of 11.2 years old (5–13 years) and a median weight of 42.1 kg (20–59 kg). Five patients were treated for systemic lupus erythematosus (SLE), three patients for antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), one for C3 glomerulopathy and one for ABO-incompatible renal transplantation. Plasma autoantibodies decreased substantially by 93% and 89% in those with SLE and AAV after the last session, respectively. Complete or partial responses were achieved in 80%, 33.3%, 100% and 100% of patients with SLE, AAV, C3 glomerulopathy, and ABO-incompatible renal transplantation, respectively. The proportion of cumulative IgG, fibrinogen, and albumin removal at the end of the last sessions were 58.8%, 67.69%, and 14.05% respectively. The removal of calcium, potassium and creatinine were not statistically significant. A few episodes (4.55%) of hypotension were observed when fresh frozen plasma was used as the replacement fluid, and no bleeding nor severe anaphylaxis was noted.

Conclusions: The efficacy and safety of DFPP treatment in children with SLE, AAV, C3 glomerulopathy and ABO-incompatible renal transplantation were described in the present study. DFPP is proven to be a safe apheresis method for children weighing more than 20 kg.

Keywords: Double filtration plasmapheresis (DFPP); systemic lupus erythematosus (SLE); antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV); rapidly progressive glomerulonephritis (RPGN); ABO incompatible renal transplantation

^ ORCID: Yu Zhang, 0000-0002-0786-4368; Qing Xie, 0000-0001-6596-9662; Yaxian Chen, 0000-0002-9111-7612; Jianhua Zhou, 0000-0002-2468-4131.

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Introduction

Double filtration plasmapheresis (DFPP) is a membrane-based treatment modality that selectively removes large molecules through double filtration of the plasma of the patients. As a pioneer, Agishi *et al.* first used this technology in 1980s to desensitize patients receiving blood group incompatible renal transplantation (1). Afterwards, DFPP is proposed as a treatment option for the excessive production of abnormal immunoglobulins, or for the hyperviscosity syndrome as an adjunctive therapy. The procedure of DFPP requires two types of filters with different pore sizes. The blood of patients is drawn extracorporeally into a plasma separator, and filtrated plasma is then introduced to a plasma fractionator, in which the condensed plasma fraction containing molecules larger than fractionator pore size is partially discarded. On the other hand, the albumin-rich smaller molecules are allowed to filtrate and return to patients in combination with supplementation fluid of sufficient volume. As the filtration fraction of plasma fractionators is generally set at 0.8 in DFPP, nearly five-fold condensed immunoglobulins are discarded and one-fifth of the volume of supplementation fluid is used compared to single filtration plasmapheresis. However, limitations exist regarding the applicability of DFPP in children, due to the excessive extracorporeal volume within plasma fractionators (up to 150 mL). Consequently, there is a gap in knowledge on the efficiency of removal of various plasma components by DFPP procedure and the safety and tolerability of high-volume extracorporeal circulation in pediatric patients.

To address this issue, the study analyzed the efficiency and safety of DFPP in the treatment of children with different critical renal diseases, including systemic lupus erythematosus (SLE), antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), rapidly progressive glomerulonephritis (RPGN), and those receiving ABO incompatible renal transplantation. We present the following article in accordance with the STROBE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-22-322/rc).

Highlight box

Key findings

- Double filtration plasmapheresis (DFPP) is a safe and effective apheresis method for children (weight over 20 kg) with critical kidney diseases, such as systemic lupus erythematosus (SLE), ANCA-associated vasculitis (AAV), C3 glomerulopathy and ABO incompatible renal transplantation.

What is known and what is new?

- DFPP, as a membrane technology removing large molecules selectively, has been widely used for renal transplantation, autoimmune diseases, hyperviscosity syndrome and so on in adult patients.
- Plasma autoantibodies decrease substantially by 93% and 89% in children with SLE and AAV after the last session, respectively.
- The proportion of cumulative IgG, IgA, fibrinogen, and albumin removal at the end of the last sessions were 58.8%, 54.6%, 67.69%, and 14.05% respectively.
- Only hypotension (4.55%) and mild allergy were observed when fresh frozen plasma was used as the replacement fluid.
- The patient's lower weight limit for DFPP procedure is extended downward to 20 kg.

What is the implication, and what should change now?

- DFPP can be used for antibody-mediated kidney diseases in children (weight over 20 kg).

Methods

Patient identification

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethical Committee of Tongji Hospital (TJ-IRB20221290). Written informed consent was obtained from the parents of the patients before DFPP treatment.

This was a single-center retrospective cohort study of DFPP treatment in pediatric patients between December 2017 and December 2020. Patients were excluded if conventional plasmapheresis was applied prior to or during DFPP treatment. Identified patients were classified into four sub-groups as per the types of renal disease: SLE (group I), AAV (group II), RPGN (group III), and those receiving ABO-incompatible renal transplantation (group IV). The immunosuppressive regimens were recorded from patients of each group. For group I patients, their baseline data including Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score, renal function [serum creatinine, estimated glomerular filtration rate (eGFR), proteinuria,

and urinary sediment], antinuclear antibody (ANA), anti-double strand DNA antibody (Anti-dsDNA), complement C3 and extra-renal manifestations were recorded. For group II patients, the diagnosis of AAV was made according to the Chapel Hill 2012 definition (2). Their baseline data including renal function (serum creatinine, eGFR, proteinuria, and urinary sediment), renal biopsy category, ANCA, complement C3, neutrophils, hemoglobin, platelets, serum albumin and extra-renal manifestations were recorded. For groups III and IV patients, their clinical features and laboratory profiles were recorded. The pre- and post-DFPP serum levels of pathogenic autoantibodies, immunoglobulin G (IgG), IgA, IgM, C3, albumin, cholesterol, calcium, phosphate, potassium, magnesium, and fibrinogen were synchronously recorded. Post-DFPP sera were taken before intravenous immunoglobulin or fibrinogen/fresh frozen plasma (FFP) administration. Furthermore, the complications during DFPP treatment and the hospital stay were also monitored.

DFPP technique

In all patients, DFPP was performed using a plasma separator (Plasmaflow OP-08W Asahi Kasai) and a plasma fractionator (EC-20W Asahi Kasai). The plasma fractionator had a membrane with a cutoff value of around 200 KDa molecular weight. A double lumen catheter was inserted in the femoral vein and retained for 2 to 3 weeks. Each patient was treated with 3 to 6 sessions within two to three consecutive weeks. DFPP was performed by a continuous blood purification machine (Plasauto iQ21, Asahi Kasai). Blood and plasma flow were set at 100 to 120 mL/min and 20 to 24 mL/min, respectively. 600 to 800 mL of FFP were used as the replacement fluid. The arterial and venous pressure of two blood purification apparatuses were monitored during DFPP, and the duration of each session was 2 to 3 hours. Regional citrate anticoagulation or heparin anticoagulation was used for DFPP.

Statistical analysis

The data were described as median (if continuous variables) and frequency or percentage (if categorical variables). For continuous variables, statistical analyses were performed with GraphPad Prism 5.0 software using paired Wilcoxon rank tests for comparing parameters with baseline values. For categorical variables, paired Chi-squared test was used to evaluate the differences between before and after DFPP treatment. Significance test with two sides was applied, and a P value ≤0.05 was considered statistically significant.

Results

Clinical response to treatments

Ten patients were identified and enrolled in this study. In group I, five female children were included, with their data shown in *Table 1*. All of the patients in group 1 showed a deterioration of renal function. Renal pathologies showed that three had class IV lupus nephritis (LN) and two had mixed classes (V+VI). Patients in Group I were first put on methylprednisolone pulse therapy (0.5 g/day) for three days, and then treated with DFPP combined with prednisone (2.0 mg/kg/day). They continued to receive prednisone plus immunosuppressive agents as cyclophosphamide or calcineurin inhibitors (CNIs) for induction therapy for six months. All had a clinical response to induction therapy (*Figure 1*). Unfortunately, one passed away within two months of initiating DFPP due to intracerebral hemorrhage secondary to lupus encephalopathy. Three shifted to maintenance with oral prednisone plus oral cyclosporine A or mycophenolate mofetil (MMF). The other one received tacrolimus plus MMF in addition to prednisone. After more than two years of follow-up, there was no relapse, no renal function deterioration, and prednisone and immunosuppressive agents were gradually reduced.

As shown in *Table 2*, three children with AAV were included in group II, among whom one showed crescentic glomerulonephritis with glomerulosclerosis. All patients in group II initially received methylprednisolone pulse therapy (0.5 g/day) for three days, followed by DFPP and oral prednisone (2.0 mg/kg/day). They later received intravenous cyclophosphamide (IV-CTX) plus prednisone for further induction, and maintenance regimens with oral prednisone plus CNIs and/or MMF. Some of them had a clinical response to induction therapy (*Figure 2*). After induction therapy for six months, one dialysis-dependent child prior to enrollment remained on dialysis, while of the two dialysis-independent patients prior to enrollment, one showed improvement in renal function and proteinuria level, and another required maintenance dialysis. Improvements in extra-renal symptoms were noted in all group II patients.

In group III, one 12-year-old boy with C3 glomerulopathy was included. His body weight was 45 kg initially, and he presented with acute renal failure (creatinine 202 μmol/L),

Table 1 Baseline characteristics of the five group I patients with SLE

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age at SLE diagnosis (years)	10	11	9	12	13
Sex	F	F	F	F	F
Body weight (kg)	32	59	36.5	47.3	53.5
SLEDAI score	30	22	20	20	28
Renal involvement at SLE diagnosis	Yes	Yes	Yes	Yes	Yes
Renal biopsy category	IV	IV	IV+V	IV	IV+V
Other organ involvement at SLE diagnosis	Heart, lung	Lung	Lung, intestinal tract	No	Heart, lung
ANA	1:1,000	1:3,200	1:3,200	1:3,200	1:1,000
Anti-dsDNA	1:320	1:320	>1:1,000	1:100	1:1,000
Complement C3 (g/L)	0.31	0.35	0.27	0.22	0.21
Serum creatinine (μmol/L)	103	82	94	146	102
Albumin (g/L)	27.5	28.2	37.4	25.7	21.4
Urinary protein (g/24 h)	3.267	3.165	0.46	2.875	3.18
eGFR at SLE diagnosis (mL/min/1.73 m^2)	52.1	68.5	57.9	40.5	55.4

SLE, systemic lupus erythematosus; F, female; SLEDAI, systemic lupus erythematosus disease activity index; ANA, Anti-nuclear antibody; Anti-dsDNA, anti-double-stranded DNA antibody; eGFR, estimated glomerular filtration rate. eGFR (mL/min/1.73 m^2) =0.413× height (cm)/Scr (mg/dL).

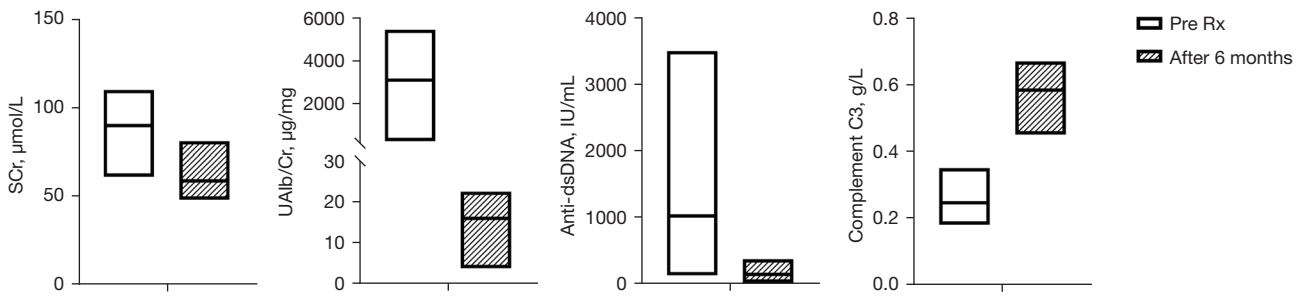

Figure 1 Clinical efficacy of DFPP in patients with SLE. DFPP, double filtration plasmapheresis; SLE, systemic lupus erythematosus; SCr, serum creatinine; UAlb/Cr, urinary albumin creatinine ratio; Anti-dsDNA, anti-double-stranded DNA antibody.

malignant hypertension, severe proteinuria (1,250 mg/day), hematuria, hypocomplementemia (C3 0.47 mg/L), hypergammaglobulinemia (15.2 g/L), hypoalbuminemia (24.7 g/L) and anemia (Hb 78 g/L). Renal biopsy showed crescentic glomerulonephritis with predominant mesangial and glomerular basement membrane C3 deposits. The child received methylprednisolone (500 mg once daily for three days intravenously, followed by 2 mg/kg/day orally) plus IV-CTX monthly. He simultaneously received DFPP for 4 sessions as an adjuvant induction therapy within two weeks. After five months, the child achieved partial remission with a normal renal function (serum creatinine 84 μmol/L), with 960 mg of daily proteinuria and a serum C3 of 0.89 g/L (*Figure 3*).

In group IV, one 5-year-old boy (body weight: 20 kg) with CKD stage 5D due to PAX2 mutation-associated nephrotic syndrome was included. His blood group was O+, and received ABO-incompatible renal transplantation with his grandmother as the donor (blood group AB+). The degree of HLA mismatch was 4/8, and the initial anti-A/

Table 2 Baseline characteristics of the 3 group II patients with ANCA-associated glomerulonephritis

	Patient 1	Patient 2	Patient 3
Age at ANCA-GN diagnosis (years)	12	12	11
Sex	F	F	F
Body weight (kg)	37	47.5	42
Diagnosis	MPA	MPA	MPA
Renal involvement at ANCA-GN diagnosis	Yes	Yes	Yes
Need for dialysis at ANCA-GN diagnosis	No	No	Yes (HD: 2 or 3 times per week)
Other organ involvement at ANCA-GN diagnosis	DAH	DAH	No
ANCA IF	c-ANCA	p-ANCA	p-ANCA
ANCA specificity	PR3	MPO	MPO, PR3
ANCA titer (IU/mL)	358.59	129.21	99.29, 68.38
Renal biopsy category	Crescentic GN	Crescentic GN	Crescentic GN
Serum creatinine (μmol/L)	91	162	836
Albumin (g/L)	43.2	33.8	24.2
Complement C3 (g/L)	1.0	NA	0.72
Neutrophils ($\times 10^9$/L)	11.66	5.72	5.01
Hemoglobin (g/L)	84	93	67
Platelets ($\times 10^9$/L)	312	273	104
Urinary protein (g/24 h)	0.2	2.3	0.4
eGFR at ANCA-GN diagnosis (mL/min/1.73 m^2)	61.4	34.7	6.4 (pre-dialysis)

ANCA, antineutrophil cytoplasmic antibody; ANCA-GN, ANCA-associated glomerulonephritis; F, female; MPA, microscopic polyangiitis; HD, hemodialysis; IF, immunofluorescence; DAH, diffuse alveolar hemorrhage; PR3, particular proteinase 3; MPO, myeloperoxidase; eGFR, estimated glomerular filtration rate; NA, not available.

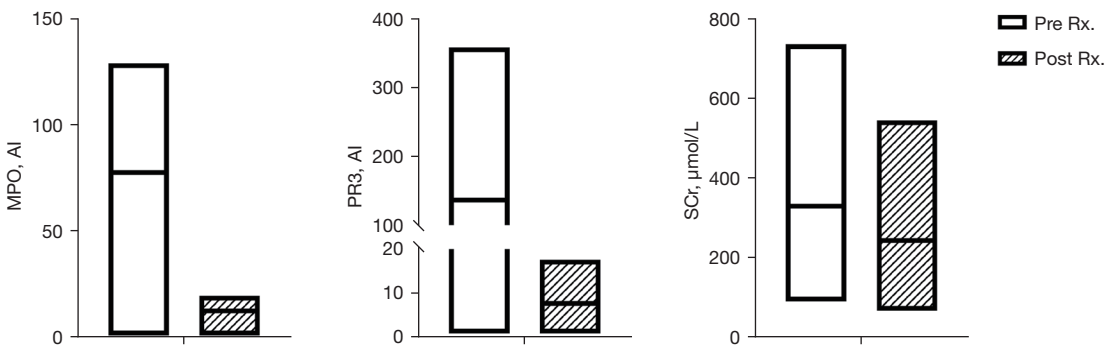

Figure 2 Clinical efficacy of DFPP in patients with AAV. DFPP, double filtration plasmapheresis; AAV, antineutrophil cytoplasmic antibody-associated vasculitis; MPO, myeloperoxidase; PR3, proteinase 3; AI, antibody intensity; SCr, serum creatinine.

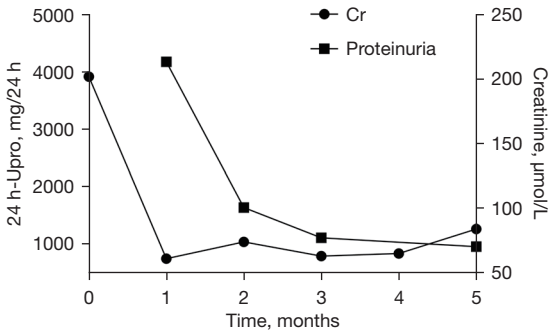

Figure 3 Biochemical parameters of the patient with C3 glomerulopathy during induction and maintenance therapies. 24 h-Upro, 24-hour urinary protein quantity; Cr, creatinine.

anti-B antibody titer was 1:4 (IgG), 1:256 (IgM) and 1:2 (IgG), 1:128 (IgM) respectively, without any anti-HLA antibodies detected. He received one dose of rituximab (375 mg/m^2) and tacrolimus, MMF and prednisolone starting one week pre-operatively. He also received DFPP in order to achieve an anti-A and anti-B IgG titers lower than 1:16 pre- and post-operatively. The anti-A and anti-B antibody titers fell progressively with each DFPP session, reaching less than 1:16 on the day of operation. Pre-operative coagulation abnormalities were ameliorated with fibrinogen infusion. His surgery was uneventful without post-operative complications. Graft kidney functioned well post-operatively, and his serum creatinine stabilized at 30 to 50 μmol/L since post-operative day two. Post-operative anti-A IgM titers remained at 1:64 during the second week and rose to 1:128 one week later, necessitating another 3 DFPP sessions. His anti-A IgM and IgG titers stabilized at 1:8 since four weeks after operation, and he did not receive DFPP thereafter.

Immunokinetics response to DFPP

The study found that the proportion of serum IgG removed by DFPP was statistically significant (P=0.028) (*Figure 4*), with a cumulative proportional removal rate after the entire treatment period of 58.8%. The proportional removal rate of IgA removal was similar to that of IgG (54.6%). The removal rate of IgM, whose molecular weight was larger than IgA and IgG, was more than 74.6% at the end of last session. On the other hand, the cumulative removal rate of C3 was at 39.1% at the end of DFPP treatment.

Impact of DFPP on hemoglobin level, platelets, prothrombin time (PT), activated partial thromboplastin time (aPTT), international normalized ratio (INR) and fibrinogen over a series of sessions

Hemoglobin levels and platelet counts were not affected by DFPP (*Figure 5*), reflecting an absence of hemodilution. PT and INR increased after the last DFPP session. The cumulative proportional removal rate of fibrinogen was similar to that of IgM, at 67.69%. One of the weaknesses of DFPP is the massive removal of fibrinogen, which could lead to elevated PT and INR and even spontaneous bleeding episode. Therefore, if the fibrinogen level is too low, fibrinogen or FFP infusion is necessary.

Impact of DFPP on other plasma components

Through the use of FFP as the replacement fluids, the cumulative proportional removal rate of serum albumin was 14.05% (*Figure 6*), while that of serum cholesterol was 53.1%. No significant change in serum creatinine, potassium (P=0.263), magnesium (P=0.932), or phosphate (P=0.150) was observed, and none required magnesium or potassium supplementation throughout the hospital stay. Mild hypocalcemia after DFPP treatment occurred, possibly related to the use of regional citrate anticoagulation and sodium citrate contained in FFP. Even if 10% calcium gluconate injection (0.5 mL/kg, Max 20 mL) supplementation was used before each DFPP session for preventing hypocalcemia.

Adverse effects associated with DFPP

The study found few complications in the total of 44 DFPP sessions. Traditionally, the most dreadful adverse effect is bleeding tendency related to fibrinogen and factor VIII removal. Transient hypotension is also one of the most common adverse effects of plasmapheresis in children. However, the patients included in this study did not have any spontaneous bleeding, likely due to the use of FFP as the replacement fluid and using fibrinogen infusion. There were two hypotensive episodes during 44 DFPP sessions, equivalent to 4.55% incidence of having symptomatic hypotension. Finally, there were two episodes of mild allergic reactions presenting as pruritus. None of the patients had bloodstream infection, significant post-operative drop of hemoglobin or platelets, or access failure during their hospital stay.

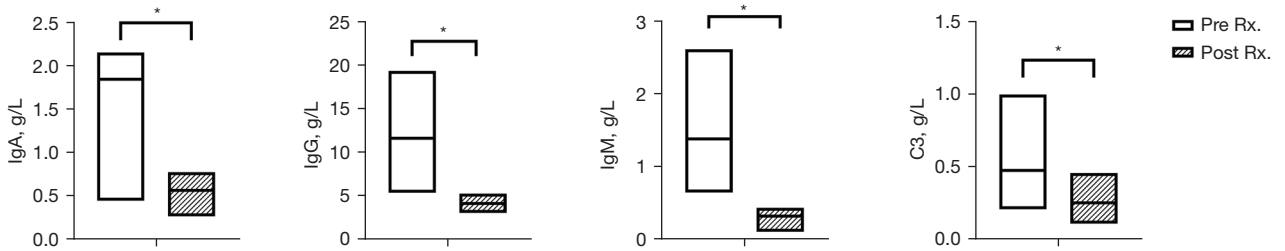

Figure 4 Removal of immunoglobulins and complements. P values were calculated according to the model described in the Method section. *, P<0.05. IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; C3, complement C3.

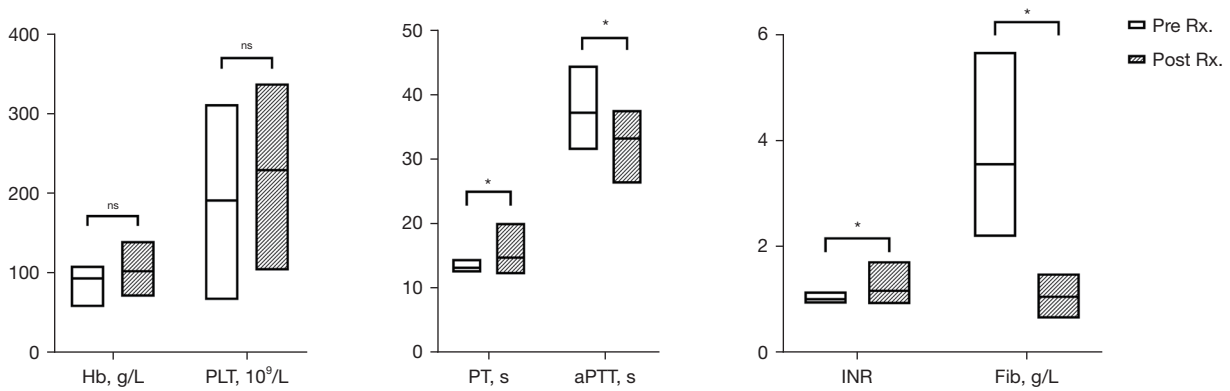

Figure 5 The course of hemoglobin level, platelet count, PT, aPTT, INR, and fibrinogen. Hemogram and coagulation tests were assessed before the first DFPP session and after the last DFPP session. P values were calculated according to the model described in the Method section. *, P<0.05. Hb, hemoglobin; PLT, platelet; PT, prothrombin time; aPTT, activated partial thromboplastin time; INR, international normalized ratio; Fib, fibrinogen; ns, no significance.

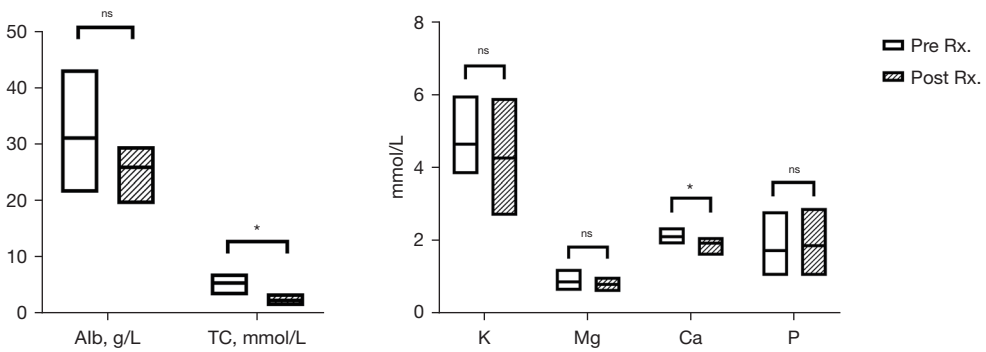

Figure 6 Removal of albumin, cholesterol and electrolytes. P values were calculated according to the model described in the Method section. *, P<0.05. Alb, albumin; TC, total cholesterol; K, potassium; Mg, magnesium; Ca, calcium; P, phosphorus; ns, no significance.

Discussion

Although apheresis is a widely established therapeutic option in pediatric patients, reports involving the use of DFPP in this population are scarce regarding the indications, technical details, and procedural outcomes. This study described a group of children with different renal indications treated by DFPP from December 2017 to December 2020. With regard to the indications, as per the 2019 American Society for Apheresis (ASFA) guideline (3), 70% and 20% patients in this study received plasmapheresis for category I/II and category III diseases, respectively, while one (10%) received apheresis due to RPGN (C3 glomerulonephritis), which was not included in the ASFA guideline. According to the guideline, clinical outcomes of these specified diseases were associated with the degree of disease-specific antibodies removal. The present study found that after the last DFPP session, plasma autoantibodies decreased substantially by 93% and 89% in patients with SLE and AAV, respectively. The rate of achieving complete or partial responses to apheresis-based regimens was 80%, 33.3%, 100% and 100% in children with SLE, AAV, RPGN, and those receiving ABO-incompatible renal transplantation, respectively.

Few studies have evaluated the efficacy of DFPP to remove serum immunoglobulins to date. Hebibi *et al.* showed that the percentage removal of IgG, IgA and IgM was 37.8%, 52.8% and 61.5%, respectively, without using replacement solutions (4). Jagdish *et al.* found that the proportional removal rate of IgG, IgA, and IgM after 4 sessions were 72%, 89%, and 96%, respectively, with the use of either 5% albumin or effluent albumin concentration as replacement solution which is roughly 1.75 to 2 times the serum albumin (5). This study also found the cumulative removal rate of serum IgG, IgA, IgM and C3 at the end of DFPP sessions at 58.8%, 54.6%, 74.6% and 39.1%, respectively, using FFP as the replacement fluid. However, a significant decrease in immunoglobulin levels could increase patients' susceptibility to infection. If patients' serum IgG level is too low, supplemental post-DFPP IVIG will be necessary.

Fibrinogen is a high molecular weight protein and has a cumulative removal rate of 67.69% in this study, similar to that of IgM. Yeh *et al.* described that after one DFPP session, it took 3 to 4 days for fibrinogen to return to the pre-procedure level (6). Jouve *et al.* also showed that fibrinogen reconstitution was depending on the time between two apheresis sessions and reached 1 g/L in the best-case scenario with a 2-day interval using albumin as the replacement fluid (7,8). In this sense, sufficient interval between each DFPP session is required to allow patients' fibrinogen levels to recover. In this study, each DFPP session was undertaken with an interval of 3 days, and FFP was routinely used as the replacement fluid. This may be the reason why there were no active bleeding episodes observed during DFPP, although patients' PT and INR increased. However, if the fibrinogen level becomes too low, fibrinogen or FFP infusion would become necessary.

With regard to the apheretic complications, only mild adverse events including symptomatic hypotension and mild allergy were observed during 9.1% of all the DFPP sessions. This incidence is similar to those reported in previously published reports (9,10). During DFPP treatment, serum albumin decreases as well as globulin. The sieving coefficient of DFPP membranes for albumin is 0.2 to 0.6, as suggested by most manufacturers, which means that 80% to 40% of albumin will be removed during each DFPP session. This drop of colloidal oncotic pressure due to albumin removal can lead to intravascular dehydration-associated complications such as hypotension. Therefore, symptomatic hypotension is common during DFPP treatment, but this can be mitigated by restoring serum albumin concentrations. Agishi *et al.* (1) initially performed DFPP without using the replacement fluid, but others started to use albumin-containing replacement fluid to improve hypoalbuminemia later. In this study, 0.5 to 0.8 L FFP was used as the replacement fluid, leading to a serum albumin reduction of 14.05% and only 2 episodes of symptomatic hypotension observed during 44 DFPP sessions. Nishi *et al.* reported that if using 12.5% albumin as the replacement fluid, a significant decline in globulins with a higher post-DFPP serum albumin was observed, without any hypotensive episode (11). Undoubtedly, a lower incidence of hypotension can accompany a higher albumin concentration in the replacement fluid. However, albumin is rather expensive, and albumin-containing replacement fluid (1–2 times concentration compared to serum albumin) was usually use. During this practice, the incidence of symptomatic hypotension was much lower than practices without using any replacement fluid [the former *vs.* the latter, 4.55% *vs.* 100% (4)].

Two episodes of mild allergy occurred in group I and IV patients, presenting as pruritus quickly relievable by intravenous dexamethasone. Paglialonga *et al.* described that DFPP and plasma adsorption carried the advantage of reducing the risk of allergic reactions (such as pruritus,

urticaria, dyspnea) in PE (9). In addition, any electrolyte imbalance was not observed during treatment. The calcium supplement was given only once at pre-procedure, even though regional citrate anticoagulation was used routinely for DFPP.

The limitations of this study included its retrospective design, the low number of patients included, and the absence of a control arm receiving conventional plasmapheresis. In addition, all children received immunosuppression simultaneously, and the exact therapeutic efficacy of DFPP could not be ascertained.

Conclusions

In conclusion, this report showed that DFPP could efficiently remove macromolecular pathogens from blood with reduced plasma or albumin supplements in pediatric patients with different critical kidney diseases including SLE, AAV, RPGN due to C3 glomerulopathy, and those receiving ABO-incompatible renal transplantation. Based on the findings of this study, DFPP in children is feasible and safe. Except for hypotension and mild allergy, other serious adverse effects such as abnormal bleeding were not observed in the patients included in the study. Nonetheless, serum fibrinogen and immunoglobulins levels should still be monitored.

Acknowledgments

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-22-322/rc

Data Sharing Statement: Available at https://tp.amegroups.com/article/view/10.21037/tp-22-322/dss

Peer Review File: Available at https://tp.amegroups.com/article/view/10.21037/tp-22-322/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-22-322/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Tongji Hospital. Written informed consent was obtained from patients' father or mother before DFPP treatment.

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