

Hemoperfusion in Maintenance Hemodialysis Patients

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Keywords

Hemoperfusion · Maintenance hemodialysis · Appropriate patients · Treatment frequency · Shanghai consensus

Abstract

The accumulation of protein-bound uremic toxins and medium-large molecule toxins in maintenance hemodialysis (MHD) patients is one of the causes of long-term dialysis-related complications. Hemoperfusion can remove these uremic toxins and reduce the complications of MHD patients. Upon a review of the Chinese and international literature, combined with practical experience of clinical diagnosis and treatment, the Shanghai Medical Association Society of Nephrology reached a consensus on the clinical applications of hemoperfusion in MHD patients. This consensus included four aspects: selection of appropriate patients, treatment frequency, treatment methods, and adverse reactions and precautions and provided guidelines for the rational and standardized treatment of hemoperfusion in MHD patients.

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Introduction

Accumulation of protein-bound uremic toxins and large middle molecule toxins in maintenance hemodialysis (MHD) can cause hemodialysis-related complications such as pruritus, sleep disorders, peripheral neuropathy, dialysis-related amyloidosis, and refractory hypertension in MHD patients. Due to this correlation between uremia retention molecules and clinical signs and symptoms, the search for improved blood purification techniques in chronic patients undergoing renal replacement therapies should continue [1]. Treatments with increased convective transport such as hemodiafiltration (HDF) [2] or with use of medium cut off membranes such as expanded hemodialysis [3] have been proposed but adequacy issues are still present due to the high complexity of the techniques and to the intrinsic limitation of dialysis membranes permeability [4]. For this reason, we propose to explore further options and, in particular, the potential benefits in terms of clinical outcomes and patient's well-being of combining hemoperfusion with hemodialysis at least in one session per week. This proposal may be of particular interest in countries and centers where HDF and expanded hemodialysis are not feasible or in patients

where specific uremic toxins can only be removed by hemoperfusion.

According to the Chinese National Renal Data System (CNRDS), MHD patients in China at the end of 2019 are 633,000 with an increased dialytic age (31.5% >5 years, and 7.0% >10 years) [5]. With the increase of dialytic age of the MHD population, the incidence of dialysis-related long-term complications increases significantly resulting in poor quality of life and survival outcome. Many of these complications have been correlated with high level of retention protein-bound toxins and large middle molecules in blood [6].

Low flux dialysis (LFHD), high flux dialysis (HFHD), and HDF mainly remove toxins by diffusion and convection, but their ability to remove protein-bound uremic toxins and medium-large molecule toxins is limited. On the contrary, hemoperfusion (HP) can effectively remove such toxins by adsorption [7, 8]. Preliminary studies have shown that HP can improve severe uremic pruritus [9], sleep disorders [10], peripheral neuropathy [11], dialysis-related amyloidosis [12], and refractory hypertension [13] in MHD patients and improve the quality of life and survival rate of patients [14–16]. Since however standardized prescription and defined operational parameters are missing, the Shanghai Medical Association and the Shanghai Society of Nephrology convened in a consensus conference on the clinical applications of hemoperfusion in MHD patients.

Methods

The consensus process relied on evidence from the Chinese and international literature and combined with practical experience of clinical diagnosis and treatment. First, we identified the following themes that are central to the clinical applications of hemoperfusion in ESKD patients: selection of appropriate patients, treatment frequency, treatment methods, and adverse reactions and precautions. We selected these topics based on the level of possible clinical impact, the level of controversy, known or suspected variation in practice, potential importance for scientific outcome, potential for development of evidence-based medicine recommendations, and availability of evidence.

The consensus was then developed through a series of alternating breakout and plenary sessions. In the breakout session, members of the workgroups performed systematic literature reviews related to the topic questions via PubMed and Google Scholar database. Since hemoperfusion is more widely used in China, which resulting more evidence from China, literature reviews in Chinese were also performed via Chinese National Knowledge Infrastructure (CNKI) and Chinese Biomedical Literature Database (CBM). The first consensus conference was held in August 2020 in Shanghai, China. Clinicians and researchers representing Shanghai Medical Association Society of Nephrology attended the meeting

to discuss the issues relating to hemoperfusion in ESKD patients. The workgroup presented the drafts to conference participants for debate, discussion, and suggested revisions. The drafts were then revised based on the opinions and recommendations of the attendees. The second conference was conducted in October 2020 in Kunming, China. A total of 15 nephrologists from all over China were invited to get their nationwide experiences and opinions. Consensus statements were iteratively developed and refined in response to feedback by all attendees. The final product was assessed, aggregated, and agreed upon in the online-offline combined conference session in June 2020 in Shanghai, China.

HP Overview

HP is a blood purification treatment that circulates the patient's blood through an extracorporeal circulation system containing a hemoperfutor that adsorbs toxins, drugs, and metabolites to eliminate such substances. The basic principle of HP is adsorption. The hemoperfutor is cartridge containing an adsorbent. The adsorbent can consist of resin, activated carbon or polysaccharides. According to the nature of the force between the adsorbent surface and the adsorbate, adsorption can be divided into three basic types: physical, chemical, and biological.

Appropriate Patients

For MHD patients with the following clinical manifestations, HP treatment is recommended.

Severe Uremic Pruritus

If the modified Duo's pruritus score of the MHD patient is >12 or the VAS score is >8, HP treatment is recommended. In a study involving 90 MHD patients [9], the patients were randomly divided into a hemodialysis (HD) group, HD + HA130 group, and HD + HA330 group (HA130, HA330 cartridge, Jafron Biomedical Co.). After 8 weeks of treatment, the VAS score of the HD + HA130 group decreased from 8.46 ± 0.72 – 6.50 ± 0.82 , that of the HD + HA330 group decreased from 8.57 ± 0.76 – 4.63 ± 0.79 , and that of the HD group decreased slightly from 8.47 ± 0.82 – 7.89 ± 0.63 . The modified Duo's pruritus score in the HD + HA130 group and HD + HA330 group decreased significantly after treatment. Other studies of HD + HA130 [17] or HD + HA230 [18] have also shown that the pruritus symptoms of MHD patients were significantly improved after treatment. HFHD, HDF, and HD + HP treatment can improve uremic pruritus in elderly MHD patients. HFHD and HD + HA130

treatment was better than HDF treatment alone. The modified Duo's pruritus score of MHD patients with severe pruritus who underwent short-term high-frequency HD + HA130 treatment (three times a week) decreased from 24.9 ± 6.9 – 9.5 ± 6.2 after the first treatment; after six treatments, the score decreased to 2.9 ± 2.0 , and their pruritus symptoms rapidly improved [19]. The results of a prospective randomized, controlled, and multicenter study [7] of 440 MHD patients in 37 centers across the country showed that compared with LFHD, HFHD, LFHD + HP, and HFHD + HP, the modified Duo's pruritus score decreased by more than 50% after 1 year of LFHD and HFHD + HA130 treatment (once a week).

Severe Uremia-Related Sleep Disorders

If the Pittsburgh sleep quality index (PSQI) of the MHD patient is ≥ 10 , HP treatment is recommended. A prospective follow-up cohort study [10] of 158 MHD patients over 2 years showed that HD + HA130 treatment (once or twice every 2 weeks) significantly prolonged the sleep time and improved the sleep efficiency of patients compared with HD treatment alone. After 3 months of HD + HA130 treatment (once a week), the PSQI of MHD patients decreased from 10.7 ± 2.7 – 3.7 ± 2.0 [20], and the insomnia remission rate and quality of life scores were significantly higher than those in the HD group [21].

Protein-Energy Wasting

If the modified quantitative subjective global assessment (MQSGA) score is >20 [22] or the malnutrition-inflammation score (MIS) is >18 [23], HP treatment is recommended. After 6 months of HD + HA130 treatment, the MQSGA scores of patients decreased from 21.48 ± 3.95 – 17.71 ± 3.27 , which was significantly lower than those of the HDF group, and the scores of nutritional status and quality of life were better than those of the HDF group [24]. After 1 year of HD + HP treatment, patients' MIS decreased from 21.7 ± 3.4 – 10.7 ± 3.8 , which was significantly lower than those of the HD group, and patients' nutritional status improved [25]. After patients with end-stage diabetic nephropathy received 12 weeks of HD + HA130 treatment (once a week), BMI increased from 21.98 ± 2.28 kg/m² to 24.30 ± 1.51 kg/m², hemoglobin increased from 103.98 ± 12.76 g/L to 113.31 ± 12.94 g/L, and albumin increased from 32.75 ± 4.38 g/L to 35.73 ± 3.71 g/L, which were significantly greater than those levels in the HD and HFD groups [26].

Microinflammatory State

Excluding infection, history of malignant tumors and any active rheumatic immune disease, if a patient's levels of high-sensitivity C-reactive protein (hs-CRP) is >3 mg/L, CRP is >8 mg/L [27], IL-6 is ≥ 16.2 pg/mL [28], or TNF- α is ≥ 41.22 pg/mL [29], HP treatment is recommended. After 1 year of HDF + HA130 treatment, the CRP level of patients was significantly lower than that of patients in the HD and HDF group, the diversity of intestinal flora was significantly increased, as was the level of intestinal probiotics (*Lactobacillus acidophilus*), and the level of pathogenic bacteria (*Escherichia coli*) was significantly reduced [30]. Three studies [14, 31, 32] have shown that the hs-CRP, IL-6, and TNF- α of patients administered HD + HA130 treatment for 1–2 years were significantly reduced.

Severe Secondary Hyperparathyroidism

For patients with severe secondary hyperparathyroidism that cannot be controlled by drug treatment and intact parathyroid hormone (iPTH) that is constantly >600 pg/mL, HP treatment is recommended. After 1 year of HFHD + HA130 treatment, the average iPTH of patients decreased from 459.74 pg/mL to 411.46 pg/mL and that of patients in the LFHD + HA130 group decreased from 417.58 pg/mL to 327.34 pg/mL, which demonstrates a better treatment effect of HA130 than that of HFHD and HD [7]. After 2 years of HD + HA130 treatment, the level of iPTH decreased by 12.77% [14]. The once-a-week treatment of HA130 + paricalcitol effectively reduced the levels of iPTH and alkaline phosphatase the blood calcium-phosphorus product and the dosage of paricalcitol in MHD patients [33].

Severe Hyper β_2 -Microglobulin

For patients with persistent elevation of β_2 -microglobulin (β_2 -MG) >30 mg/L [34] or with dialysis-related amyloidosis such as carpal tunnel syndrome, HP treatment is recommended. HD + HA130 treatment significantly reduced the blood β_2 -MG level of MHD patients, thereby preventing or improving dialysis-related amyloidosis [14, 31]. After 1 year of HFHD + HA130 treatment, the blood β_2 -MG levels of patients decreased from 40.8 ± 13.4 mg/L to 27.8 ± 8.6 mg/L and that of patients in the LFHD group decreased from 44.6 ± 14.5 mg/L to 37.1 ± 11.1 mg/L [7]. After 1 year of HD + Lixelle S15 (a model of perfusion device) treatment 3 times a week, 17 patients with dialysis-related amyloidosis had decreased blood β_2 -MG levels, from 29.3 ± 9.6 mg/L to 24.7 ± 5.1 mg/L, and increased activities of daily living scores [12].

Refractory Hypertension

For MHD patients who are fully dialyzed, whose dry body weight reaches the target, and who maintain systolic blood pressure (SBP) > 160 mm Hg (1 mm Hg = 0.133 kPa) after taking the maximum dose or maximum tolerance of three or more different types of antihypertensive drugs [35], HP treatment is recommended. After 1 year of HD + HA130 treatment (once every 2 weeks), 75 MHD patients with refractory hypertension had SBP decrease from 176.38 ± 10.07 mm Hg to 152.93 ± 7.08 mm Hg, diastolic blood pressure (DBP) decrease from 98.51 ± 6.70 mm Hg to 87.73 ± 5.60 mm Hg, plasma renin, angiotensin II and aldosterone levels decrease significantly, and their dosage of antihypertensive drugs decrease significantly [13]. The above research results are consistent with those of MHD patients with refractory hypertension receiving HD + HP treatment (once a week) [36–38]. HD + HDF treatment (once every 2 weeks) and HD + HP treatment (once a week) improved the blood pressure variation rate of MHD patients, decreased their SBP variation rate from $4.11 \pm 0.52\%$ to $3.12 \pm 0.44\%$, and decreased the DBP variation rate from $2.14 \pm 0.43\%$ to $1.48 \pm 1.31\%$ [39].

Restless Legs Syndrome

For patients with RLS severity scale scores ≥ 11 , HP treatment is recommended. After 3 months of HD + HA130 treatment (once a week), patient RLS scores decreased from 13.5 ± 6.2 to 3.6 ± 1.4 , and sleep quality significantly improved [20]. After HD + HP treatment (once a week), the patients' RLS scores decreased from 25.13 ± 6.24 – 7.56 ± 1.21 , and the effective treatment rate was 97.78% [40].

Uremic Peripheral Neuropathy

For patients with numbness, abnormal sensation or retardation of nerve transmission in the limbs, weakening or disappearance of muscle tension or tendon reflex, and whose peripheral nerve electrophysiological examination shows more than 2 nerves are involved, HP treatment is recommended. HD + HA130 treatment (once a week) effectively improved the symptoms of peripheral neuropathy in patients with end-stage renal disease and significantly accelerated the sensory conduction velocity (SCV) of the median nerve, tibial nerve and lateral popliteal nerve, with a treatment effect equivalent to that of peritoneal dialysis and better than that of single HD treatment [11]. HFHD, HDF, HD + HP treatment significantly accelerated SCV and improved uremic neuropathy [41]. The effective rate of HD + HA130 treatment in improving the symptoms of peripheral neuropathy was 90.91% [42].

It is recommended that MHD patients undergo HP treatment to prevent the occurrence of various dialysis-related long-term complications when conditions permit. A multicenter, open, randomized, parallel controlled study on the effect of HD + HP treatment on the survival rate of MHD patients [16] showed that 1,407 MHD patients treated with HD or HDF + HA130 (at least once every 2 weeks) and followed up for 96 weeks had a 37% reduction in all-cause mortality and cardiovascular mortality, and the mortality of cardiovascular disease of the HP group decreased from the 24th week.

Treatment Frequency

Individualized HP treatment frequency should be determined according to patients' complications and severity.

Severe Uremic Pruritus

For MHD patients with a modified Duo's pruritus score > 12 or VAS score > 8, HP treatment should be performed once or twice every 2 weeks. After 8 weeks of HD + HA130 or + HA330 treatment (once every 2 weeks), both the VAS score and modified Duo's pruritus score of patients in the two groups had decreased significantly compared with those before treatment. The improvement of pruritus symptoms in the HA330 group was better than that in the HA130 group [9]. An 8-week HD + HA130 or + HA230 treatment also significantly improved patients' pruritus symptoms [17, 18], and the treatment effect was better than that of HDF alone. The remission rate of pruritus in patients who underwent short-term high-frequency HD + HA130 treatment (3 times/week for two consecutive weeks) was 100% [19].

Severe Uremia-Related Sleep Disorders

For MHD patients with PSQI scores ≥ 10 , HP treatment at a frequency of once a week is recommended; for patients with PSQI scores greater than 5 but less than 10 ($5 < \text{PSQI scores} < 10$), HP treatment at a frequency of once or twice every 2 weeks is recommended. HD + HA130 treatment (once or twice every 2 weeks) significantly prolonged patients' sleep duration and improved their sleep quality [10]. After 3 months of HD + HA130 treatment (once a week), the PSQI scores of MHD patients was significantly reduced, and the remission rate of insomnia was significantly higher than that of the HD group [20, 21].

Protein-Energy Wasting

For patients with MQSGA scores >20 [22] or MIS >18 [23], HP treatment is recommended once a week. HD + HA130 treatment (once a week) significantly improved the nutritional and microinflammatory state of MHD patients while significantly reducing their MQSGA score and MIS; a better treatment effect than that of a single HD treatment but still equivocal compared with HDF treatment [24, 25]. For patients with end-stage diabetic nephropathy, HD + HA130 treatment is recommended once a week. After treatment, patients' BMI increased from $21.98 \pm 2.28 \text{ kg/m}^2$ to $24.30 \pm 1.51 \text{ kg/m}^2$, and their hemoglobin and albumin levels were significantly higher than those in the HD and HDF groups [26].

Microinflammatory State

After excluding infection, history of malignant tumors, active rheumatic immune disease, etc., patients that constantly have levels of hs-CRP >3 mg/L, CRP >8 mg/L [27], IL-6 $\geq 16.2 \text{ pg/mL}$ [28], or TNF- $\alpha \geq 41.22 \text{ pg/mL}$ [29], HP treatment is recommended once or twice every 2 weeks. Compared with patients in the HD or HDF groups, patients who underwent HDF + HA130 treatment (once a week) had significantly lower CRP levels and *E. coli* levels and significantly higher *L. acidophilus* levels [30]. HD + HP treatment (once or twice every 2 weeks) significantly improved the microinflammatory state of patients [31, 32].

Severe Secondary Hyperparathyroidism

For patients with severe secondary hyperparathyroidism that cannot be controlled by drug treatment and iPTH constantly >600 pg/mL, HP treatment is recommended once a week. HFHD or LFHD + HA130 treatment (once a week) reduced the level of iPTH in MHD patients [7]. Paricalcitol + HA130 treatment (once a week) effectively reduced patients' iPTH and alkaline phosphatase levels as well as the necessary dosage of paricalcitol [33].

Severe Hyper β_2 -MG

For patients whose β_2 -MG levels in serum are higher than 30 mg/L [34] or patients with dialysis-related amyloidosis such as carpal tunnel syndrome, HP treatment is recommended 1–3 times each week. HFHD or LFHD + HA130 (once a week) significantly reduced blood β_2 -MG levels in MHD patients [7, 14]. After patients with dialysis-related amyloidosis received 1-year HD treatment (3 times a week) and Lixelle S15, their serum β_2 -MG levels significantly decreased, and their Activities of Daily Living scores significantly increased [12].

Refractory Hypertension

For MHD patients whose dry weight reaches the target, who are on the maximum dosage or maximum tolerated dosage of 3 or more different types of antihypertensive drugs, and whose SBP is higher than 160 mm Hg [35], HP treatment is recommended once or twice every 2 weeks. HD + HP (once or twice every 2 weeks) significantly reduced the levels of SBP, DBP, plasma renin, angiotensin II, and aldosterone and the dosage of antihypertensive drugs [13, 36–38]. HD + alternating HDF (once every 2 weeks) and HP (once every 2 weeks) improved the rate of blood pressure variation in MHD patients and reduced the risk of cardiovascular events [39].

Restless Legs Syndrome

For patients with severity scale scores ≥ 11 , HP treatment is recommended every week. After 3 months of HD + HA130 treatment (once a week), patients' RLS severity scale scores decreased from 13.5 ± 6.2 to 3.6 ± 1.4 , and their sleep quality significantly improved [20]. After HD + HP treatment (once a week), the RLS severity scale scores of the patients were also significantly reduced [40].

Uremic Peripheral Neuropathy

For patients with limb numbness or paresthesia, weakened or absent muscle tension or tendon reflex or whose peripheral nerve electrophysiological examination shows more than 2 nerves involved, weekly HP treatment is recommended. HD + HA130 treatment (once a week) effectively improved the symptoms of peripheral neuropathy in end-stage renal disease patients, and the SCV of the median nerve, anterior tibial nerve, and common peroneal nerve was significantly accelerated [11]. HFHD or HDF or HD + HA130 (once a week) effectively accelerated patients' SCV and thus improved uremic neuropathy outcomes [41, 42].

For patients without dialysis-related complications, HP treatment is recommended once or twice every 2 weeks to prevent long-term dialysis-related complications. A 2-year follow-up study of 1,407 MHD patients from 30 centers [16] found that HD or HDF + HA130 significantly reduced all-cause mortality and cardiovascular mortality, reduced the occurrence of cardiovascular events, and improved the patients' quality of life.

Treatment Methods

According to the Standard Operating Procedures for Blood Purification (Chinese Edition, 2021) [43], the general operational method of combined hemoperfusion with hemodialysis in China shows as follows.

Either one cap of the cartridge is unscrewed. 2–5 mL syringe (without needle) is used to inject 12,500 U (100 mg) of heparin into the cartridge. The cartridge is recapped. The cartridge is shaken and rotated 180° for 10 times to fully mix the heparin with adsorbents and put for 20–30 min statically. Hemoperfusion cartridge, dialyser, and dialysis conduits are installed in turn according to the blood flow direction. The arterial tube of the circuit is filled with saline, and then connected with the arterial end of the cartridge to fill the cartridge with saline. The venous end of the cartridge is connected with the intravenous tube of blood circuit. The whole set is rinsed with 1,000 mL saline. The cartridge and intravenous tube of blood circuit are disconnected. The venous end of the dialyser is connected with the intravenous tube of blood circuit, and the arterial end of the dialyser with the venous end of the cartridge. The whole set is rinsed with 2,000 mL saline and the air is removed completely. The treatment parameters of hemodialysis machines are set according to the prescription. Heparinization or low molecular weight heparin is usually adopted for anticoagulation. The anticoagulant dosage should depend on patient's condition. When the hemoperfusion treatment is completed, the cartridge is rinsed with 200 mL saline at a flow rate of 50–100 mL/min until the color in the cartridge becomes shallow. The cartridge is removed and the hemodialysis treatment is continued. The recommendation of key operational parameters shows as follows.

Treatment Mode

HP can be combined with three blood purification methods, i.e., LFHD, HFHD, and HDF.

Each HP Treatment Duration

The recommended HP treatment duration is 2.0–2.5 h each time. In practice, it should be the treatment duration recommended in the product manual of each brand of perfusion device.

Blood Flow during HP Treatment

When HP is combined with HD or HDF, the blood flow should be controlled at 150–250 mL/min.

Hemoperfutor Connection with Dialyzer or Filter in Group Treatment

It is recommended that the hemoperfutors be connected in series, in front of a dialyzer or filter.

Start Time of HP Treatment in the Treatment Group

For group treatment, HD and HP devices should be combined in series. After 2.0–2.5 h of the first group treatment, the HP device should be removed, but HD treatment should continue; alternatively, 2.0 h–2.5 h before the end of HD treatment (the second group treatment), the HP device should be installed, and the group treatment should be performed again. Notes: (1) during the first group treatment, little-to-no ultrafiltration is recommended to prevent blood coagulation; (2) the second group treatment may improve the clearance rate of medium-large molecules and protein-bound toxoids, but it will increase the risk of blood coagulation and cause hypotension. Clinically, different choices can be made according to the actual conditions.

No significant difference was reported in the clearance effect of serum creatinine and blood urea nitrogen between the two treatment groups for MHD patients. The second group treatment had a better clearance effect on iPTH, fibroblast growth factor 23 (FGF-23), blood β_2 -MG, IL-1, IL-6, and TNF- α levels and did not cause more adverse events, such as hypotension or blood coagulation [44, 45].

Adverse Reactions in HP Treatment and Notes

Adverse Reactions in HP Treatment and Management **Abnormal Biocompatibility**

After 0.5–1.0 h HP treatment, patients may experience chills, fever, chest tightness, dyspnea, or transient reductions in white blood cell or platelet counts. Intravenous injections of dexamethasone, oxygen inhalation, and other treatments should be performed immediately; if the symptoms are not alleviated after the above treatments, HP treatment should be discontinued.

Adsorbent Particle Embolization

During treatment, patients may experience chest tightness, progressive dyspnea, and decreased blood pressure. If so, it should be determined whether the patient has adsorbent particle embolization. Once embolism occurs, the treatment should be stopped immediately, and oxygen inhalation or hyperbaric oxygen treatment should be performed. In the meantime, active symptomatic treatment is required.

Air Embolism

Patients may experience symptoms such as cough, chest tightness, shortness of breath, sudden dyspnea or cyanosis, decreased blood pressure, and even coma. This

is due to a failure to completely clear the gas in the extracorporeal circulation pipeline before perfusion treatment, air return to the blood, or issues with the pipeline such that the connection is not firm during the treatment or that gas enters the body. Once the diagnosis of air embolism is confirmed, HP treatment must be stopped immediately, and the left lateral position should be adopted with the head low and feet high; pure oxygen inhalation, mask oxygen inhalation or endotracheal intubation, and other cardiopulmonary support treatments should be performed. If the amount of air in the embolism is large, puncture gas extraction in the right atrium or right ventricle can be performed as necessary.

Blood Coagulation Dysfunction

Adsorption treatment may be accompanied by blood coagulation factor adsorption, or a large amount of platelet aggregation and activation occur during HP treatment, resulting in blood coagulation. Insufficient heparin dosage, insufficient blood flow, and low ambient temperature can all lead to blood coagulation. Attention should be given to these factors during treatment, and timely action should be taken.

Hypotension

Hypotension may occur due to the reduced blood volume in the initial stage of HP treatment or excessive ultrafiltration or allergic reaction during treatment. Active prevention, early detection, rapid treatment, and appropriate volume expansion are required, and HP treatment should be ended as necessary. Notes on HP treatment patients' vital signs such as blood pressure, respiration, and heart rate should be observed during treatment; circulation pipelines should be observed for blood coagulation and leakage; and blood routine, coagulation, and other indicators should be examined regularly.

HP Is Not Recommended, or HP Treatment Should Be Suspended, in the following Circumstances

(1) Platelet count $<60 \times 10^9/L$; (2) white blood cell count $<4 \times 10^9/L$; (3) hypotension (predialysis blood pressure $<90/60$ mm Hg); (4) active hemorrhage; and (5) unstable hemodynamics or vital signs.

Conclusion

Hemoperfusion therapy has proven effective for MHD patients. Combining HD/HDF and HA130 hemoperfusion therapy can prevent maintenance dialysis-related

complications and improve patient quality of life and prognosis. However, more high-quality evidence-based studies are needed to clarify the timing and frequency of HP to provide a basis for the application of HP in MHD patients.

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Wei Lu and Gengru Jiang researched all the data for the article, wrote the text, and reviewed the manuscript before submission.

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