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Efficacy of Two Combinations of Blood Purification Techniques for the Treatment of Multiple Organ Failure Induced by Wasp Stings

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Key Words

Wasp sting · Multiple organ failure syndrome · Hemoperfusion · Continuous veno-venous hemodiafiltration · Plasma exchange

Abstract

Background/Aims: The aim of this study was to explore the clinical efficacy of 2 combinations of blood purification techniques in patients with sting venom-induced multiple organ dysfunction syndrome (MODS). ***Methods:*** A total of 23 patients received 35 sessions of hemoperfusion (HP) + continuous veno-venous hemodiafiltration (CVVHDF) treatment and 22 sessions of plasma exchange (PE) + CVVHDF treatment, respectively. ***Results:*** Both HP + CVVHDF and PE + CVVHDF reduced the levels of inflammation, thus improving our patients' health condition. Moreover, PE + CVVHDF was found to be significantly more effective in reducing the levels of specific liver function markers and inflammatory mediators, as well as shortening prothrombin time and increasing the levels of serum albumin. ***Conclusion:*** Both combinations of blood purification techniques were capable of improving MODS. However, the PE + CVVHDF approach was more efficient for the removal of wasp venom and inflammatory mediators from the blood.

Introduction

Wasp stings are not uncommon worldwide, especially in rural areas in developing countries. The outcomes can range from a mild, self-limited anaphylactic reaction to a severe, systemic reaction with high risk of mortality. Multiple organ dysfunction syndrome (MODS) can occur as a consequence to a mass wasp attack. In developed countries, almost all patients who have suffered from a single or a few stings have had IgE-mediated allergic reactions of different degrees [1]. Thus, it is rare for them to develop renal failure and MODS [2]. In such cases, treatment is centered on controlling the allergic reaction and desensitization [3, 4]. However, in developing countries, especially in China, most patients are attacked by a swarm of wasps. The major clinical characteristics of these patients are toxic reactions, and the wasp venom toxicity is attributed to hemolytic, myotoxic, neurotoxic, nephrotoxic and hepatotoxic enzymes. Signs and symptoms include shock, rhabdomyolysis, intravascular hemolysis, coagulopathy, respiratory distress, cardiovascular abnormalities, hepatic damage, cerebral disturbances and acute kidney injury [5, 6]. The mechanisms underlying wasp sting injury may comprise the direct toxic effect of venom and immune inflammatory reaction to venom composi-

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tion. This immune inflammatory reaction involves both cellular (lymphocytes) and humoral (IgE and cytokines) immunity [2].

Currently, apart from hemodialysis sessions, the most prevalent nonspecific therapies used to treat victims of mass wasp attacks consist of the administration of antihistamines, corticosteroids, bronchodilators, vasodilators, bicarbonate, mannitol, adrenaline and mechanical ventilation. However, many of these measures seem to lack therapeutic efficacy [7]. Two isolated case reports in the literature described the successful outcomes after using plasma exchange (PE) or plasmapheresis combined with continuous veno-venous hemodiafiltration (CVVHDF) to treat MODS secondary to wasp attacks [8, 9]. Nevertheless, there is no specific and safe therapy currently available for the effective treatment of MODS resulting from mass wasp attacks. Therefore, there is an urgent need to explore an effective treatment for patients suffering from wasp venom-induced MODS.

The potential mechanism of wasp venom-induced MODS may be associated with the direct toxic effect of the venom and the immune inflammatory reaction to the venom's composition [10]. It is well known that blood purification is not only effective for the removal of toxic substances and inflammatory factors but also for the maintenance of hemodynamic stability. While the efficacy of single blood purification treatment is limited, the use of a combination of blood purification techniques for the treatment of MODS induced by wasp stings seems feasible. Thus, the aim of this study was to compare the clinical efficacy of 2 combinations of blood purifying techniques, hemoperfusion (HP) + CVVHDF and PE + CVVHDF, in terms of improvement of venom-induced MODS and to identify the most effective blood purification treatment for these patients.

Materials and Methods

Patients

Between January 2009 and December 2013, 23 patients with MODS induced by wasp stings admitted to the intensive care unit (ICU) at our hospital were enrolled in this study. Inclusion criteria were as follows: admission to the ICU, Acute Physiology and Chronic Health Evaluation (APACHE) II score ≥25 at admission [11], simultaneous failure of at least 2 organs, shock or allergy under control after treatment and cases in which treatment with drugs affecting immune function such as glucocorticoids were not used before and after admission. Patients were excluded from this study if they had any past medical history of acute infection, active inflammatory diseases, connective tissue disease, immune system disease, tumors, diabetes mellitus or hypertension. The study protocol was approved by the Medical Ethics Committee of Xiangyang Central Hospital, Xiangyang, China, and performed according to the recommendations of the Declaration of Helsinki. All subjects gave written informed consent before participating in the study.

Two Combinations of Blood Purification Treatments and Their Safety

Given the severity of multiple organ failure induced by wasp stings, and the mainly biologic toxic effects of these stings, CVVHDF alone is not a sufficient treatment. In addition to support treatment, the 23 patients received 2 blood purification treatments: HP + CVVHDF and PE + CVVHDF. In the HP + CVVHDF group, CVVHDF and HP were performed as tandem procedures. A temporary veno-venous vascular access was established with a flexible double-lumen catheter via the subclavian vein or the femoral vein. The CVVHDF was implemented at bedside using a PRISMA (Hospal) hemodialysis machine (Sweden), bicarbonate-based dialysis solution, synthetic low-flux polysulfone membranes (1.22) and a peristaltic blood pump with a blood flow of 250–280 ml/min. The dose of low molecular weight heparin was adjusted to 5,000 U for the first administration, followed by an additional 500 U every 2 h. For patients with a tendency to bleed (activated partial prothrombin time (PT) >120 s), we used an in vitro anticoagulant instead of heparin. The HP was performed by using a neutral macroporous resin (HA330, Zhuhai Lizhu Medical Bio-Material Co., Ltd., China) for 2 h. The HA330 resin cartridge is an extracorporeal HP device that uses neutral microporous resin, and it has been proven to remove inflammatory cytokines and improve organ dysfunction [12]. HA330 HP is being newly developed for use in the treatment of patients with sepsis. In the PE + CVVHDF group, the PE procedure was combined with CVVHDF. PE was implemented at bedside using standard plasma filters (Gambro PF 2000N, Switzerland). Then, the separated cells were returned back to the patient while their plasma was replaced with a total volume of 1,500–2,500 ml of fresh frozen plasma, lasting approximately 2–3 h during each session. The blood flow rate was 60–120 ml/min and PE rate was 25–30 ml/min. The interval between HP and PE was 2–3 days for a total of 2–3 sessions of therapy. The safety of the 2 methods was assessed according to the absence of the following complications: (1) hemorrhage, (2) infection, (3) allergy, (4) hypothermia, (5) hypotension and (6) blood coagulation.

Clinical Parameters and Laboratory Measurements

Patients were monitored continuously for changes in the level of consciousness, heart rate (HR) and mean arterial pressure (MAP). Leucocyte (LEU) count and levels of hemoglobin, platelets, C-reactive protein (CRP), albumin (ALB), alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum creatinine (SCR), blood urea nitrogen (BUN), creatine kinase (CK), lactate dehydrogenase (LDH), myoglobin, IgE, peripheral blood smear, PT, activated partial PT, interleukin-1 (IL-1), IL-6, IL-8, IL-10 and tumor necrosis factor α (TNF-α) in serum were collected and recorded before and after each session. Blood samples were centrifuged immediately and frozen in −70°C until analysis. All biochemical parameters were measured by standard auto-analyzers in the department of diagnosis at the Xiangyang Central Hospital. Concentrations of IL-1, IL-6, IL-8, IL-10 and TNF-α in serum were measured using a commercially available enzyme-linked immunosorbent assay kit (R&D Systems, Minneapolis, Minn., USA).

Table 1. Characteristics of patients and clinical scores at the time of therapy

Groups	Age, years	Number of wasps	APACHE II score	SOFA score	Time to treatment, h
HP + CVVHDF	43.3±13.2	10.3±3.4	25.9±3.7	13.7±4.8	26.5±8.1
PE + CVVHDF	40.5±12.6	9.8±2.9	27.5±3.4	14.9±4.6	24.3±7.5

Data in the table are presented as mean ± SD.

Data Analysis

The statistical software SPSS version 13.0 (SPSS Inc., Chicago, Ill., USA) was used for all statistical analyses. Continuous variables are expressed as mean ± standard deviation. Comparisons between groups were performed by the one-way analysis of variance. Comparisons of survival rates between groups were performed using the chi-square test. Values of $p < 0.05$ were considered statistically significant.

Results

Patients' Characteristics

Among the 23 patients included, 11 were men and 12 were women, with a mean age of 42.5 ± 11.4 (range 21–62) years. The mean value of APACHE II and Sequential Organ Failure Assessment (SOFA) scores were 26.9 ± 3.4 and 14.52 ± 4.56, respectively. There was no significant difference between the 2 groups in age, number of wasp attacks, APACHE II score, SOFA score and total time of treatment ($p > 0.05$; table 1).

Change in Hematology and Blood Chemistry

There was no significant difference between the data before treatment in the 2 groups ($p > 0.05$). Data presented in table 2 show that both HP + CVVHDF and PE + CVVHDF exerted an effect on LEU count, ALT, AST, SCR, BUN, CK, LDH, IgE and myoglobin ($p < 0.05$). Moreover, ALT, AST, CK and myoglobin levels were lower ($p < 0.05$) in the PE + CVVHDF group compared with the HP + CVVHDF group. A more significant decrease in CRP ($p < 0.01$) was observed in the PE + CVVHDF group compared with the HP + CVVHDF group. In the PE + CVVHDF groups, ALB levels and schistocytes on PBS were found to be significantly improved after the therapy ($p < 0.05$).

Change in Hemodynamics and Blood Coagulation

As shown in the table 3, HR and MAP were found to be significantly improved after the therapy in the both groups ($p < 0.05$). The PT was found to be significantly improved after the PE + CVVHDF therapy ($p < 0.05$).

Change in Cytokines

The baseline cytokine levels between the 2 groups were not significantly different ($p > 0.05$). There were no significant changes in the levels of IL-6 and IL-10 before and after treatment in both groups ($p > 0.05$). There was a significant decrease ($p < 0.05$) in the levels of IL-8 and TNF-α after treatment in both groups. The reduction in the level of TNF-α was significantly more marked in the CVVHDF + PE group compared with the HP + CVVHDF group ($p \leq 0.05$; table 4).

Clinical Outcomes

Among the 23 patients treated by the 2 different combinations of blood purification techniques, 11 patients survived in the HP + CVVHDF group and 7 patients survived in the PE + CVVHDF group. The survival rates were 31.43 and 31.82%, respectively. Baseline SOFA scores did not differ significantly between groups ($p > 0.05$; table 1). PE + CVVHDF significantly decreased the SOFA score compared with HP + CVVHDF (4.2 ± 1.1 vs. 6.8 ± 1.3). There were no significant differences in the survival rate between patients who underwent HP and PE treatments.

Discussion

In the present study, both combinations of blood purification techniques, HP + CVVHDF and PE + CVVHDF, were relatively effective for the management of patients with venom-induced MODS by reducing wasp venom and inflammatory cytokines, maintaining hemodynamic stability and improving our patients' health condition. However, the PE + CVVHDF combination was found to be significantly more effective in reducing the levels of specific liver function markers and inflammatory mediators, such as ALT, AST, CK, myoglobin, TNF-α and CRP, as well as shortening PT and increasing the levels of serum ALB. The PE + CVVHDF combination also reduced

Table 2. Change in hematology and blood laboratory parameters before and after therapy

	HP + CVVHDF (n = 35)		PE + CVVHDF (n = 22)	
	pre-therapy	post-therapy	pre-therapy	post-therapy
LEU, $\times 10^9$/l	18.6±8.1	14.3±6.5[a]	19.1±8.7	14.7±7.0[a]
Hemoglobin, g/l	65.1±20.3	69.6±19.5	69.7±18.4	69.2±19.1
Platelet, $\times 10^9$/l	79.2±26.3	78.6±24.5	78.9±25.2	78.3±26.7
CRP, mg/l	45.4±21.3	28.5±15.6[b]	47.8±24.7	28.9±15.8[b]
ALB, g/l	25.8±6.2	27.1±6.4	25.2±5.8	29.9±6.1[a]
ALT, IU/l	312.6±104.5	230.7±145.2[a]	320.1±110.3	170.3±105.1[a, c]
AST, IU/l	435.7±258.9	342.5±261.8[a]	440.6±160.1	276.4±159.2[a, c]
SCR, μmol/l	385.6±121.7	237.6±110.5[a]	378.4±126.3	242.3±117.4[a]
BUN, mmol/l	15.6±10.7	9.8±8.6[a]	16.1±11.2	9.4±8.1[a]
CK, IU/l	1,120.4±825.7	867.6±578.1[a]	1,198.2±853.6	690.4±560.3[a, c]
LDH, IU/l	863.2±620.1	641.7±560.8[a]	875.4±629.3	659.5±572.1[a]
Myoglobin, μg/l	412.7±215.3	324.6±205.1[a]	420.4±210.2	269.2±208.7[a, c]
IgE, IU/ml	342.3±135.1	258.9±106.2[a]	348.6±141.7	250.6±110.8[a]
PBF (schistocytes), %	3.5	2.9	3.4	1.1[a]

Data in the table are presented as mean ± SD, except where indicated.
PBF = Peripheral blood smear.
[a] Before vs. after therapy $p < 0.05$.
[b] Before vs. after therapy $p < 0.01$.
[c] PE + CVVHDF group vs. HP + CVVHDF group ($p < 0.05$).

Table 3. Change in hemodynamics and blood coagulation before and after therapy

	HP + CVVHDF		PE + CVVHDF	
	pre-therapy	post-therapy	pre-therapy	post-therapy
HR	120.15±35.24	90.21±30.12[a]	121.27±34.56	92.18±31.65[a]
MAP	82.25±20.43	98.41±22.36[a]	82.44±21.12	99.52±23.26[a]
PT	23.4±10.1	20.6±11.4	24.7±11.3	17.8±10.6[a]
Activated partial PT	101.6±48.3	95.7±47.2	103.6±50.4	96.9±48.8

Data in the table are presented as mean ± SD.
[a] Post- vs. pre-therapy ($p < 0.05$).

Table 4. Changes in cytokines before and after therapy

	HP + CVVHDF		PE + CVVHDF	
	pre-therapy	post-therapy	pre-therapy	post-therapy
IL-1, pg/ml	35.3±6.1	34.5±4.3	34.7±5.6	34.6±4.8
IL-6, pg/ml	120.7±45.2	112.3±39.4	123.6±44.9	116.7±38.1
IL-8, pg/ml	65.2±23.7	24.8±9.5[a]	67.5±24.1	23.1±10.9[a]
IL-10, pg/ml	48.1±4.3	40.6±3.8	47.9±5.1	42.1±5.6
TNF-α, pg/ml	6.8±0.7	4.7±0.4[a]	6.4±0.5	3.6±0.2[a, b]

Data in the table are presented as mean ± SD.
[a] Before vs. after therapy ($p < 0.05$).
[b] PE + CVVHDF group vs. HP + CVVHDF group ($p < 0.05$).

the SOFA score significantly compared with HP + CVVHDF.

A definitive treatment for venom-induced MODS has not been established yet. Many therapeutic procedures, including specific honey bee anti-venom, adrenaline, hydrocortisone, optimal hydration and alkaline diuresis, have been evaluated and found to have limited benefits [13, 14]. However, only a few studies have reported the use of blood purification for venom-induced MODS treatment. In the medical literature, the largest case series reporting the treatment with blood purification on venom-induced MODS included 119 patients [2]. Notably, there was no data regarding the effect of blood purification on mortality or disease progression of venom-induced MODS. Most of the reports on the subject consist of case presentations in which PE and plasmapheresis combined with CVVHDF were used successfully [8, 9]. The present study results not only indicated that both combinations of blood purification techniques played an important role in the management of venom-induced MODS, but also that PE + CVVHDF was the most effective blood purification therapy of the 2 combinations assessed.

In the case of MODS induced by wasp stings, the free myoglobin and hemoglobin generated by rhabdomyolysis and hemolysis, as well as venom toxins and inflammatory factors, can be removed from circulation by blood purification therapy [15, 16]. The HP approach is effective for the removal of medium and large molecules and toxins bound to proteins, which is why HP is widely applied to manage cases of drug overdose and intoxications. Moreover, the HA330 macroporous adsorption resin used in HP has a relative specificity for systemic inflammatory response syndrome, acute respiratory distress syndrome, sepsis and acute necrotic pancreatitis; thus, it can be used to remove the protein-bound toxins and toxic factors. PE is another blood purification modality that can remove antibodies, immune complexes, and toxins as well as replenish coagulation factors and other bioactive substances by using fresh frozen plasma [17, 18]. However, PE alone cannot efficiently remove the medium and small toxin particles. Unlike PE, CVVHDF is effective for the removal of small molecules, such as urea and amino acid metabolites, and substances of intermediate molecular weight, including proinflammatory cytokines [19]. Moreover, CVVHDF is associated with significant improvement in hemodynamic instability and nutritional support in patients with MODS [19, 20]. However, CVVHDF does not allow large molecules to pass through the hemofilter. Therefore, the combination of these 2 blood purification techniques was considered and has been used as a therapeutic procedure for many medical conditions [21–24]. Tang et al. [25] reported a case of severe acute pancreatitis in a pregnant woman who developed MODS. The combination of HP (HA330) and CVVHDF was also used to manage MODS with a successful outcome. In the present study, the levels of LEU, CRP, ALT, AST, SCR, BUN, CK, LDH, myoglobin, HR and TNF were significantly decreased after HP + CVVHDF treatment.

Furthermore, PE + CVVHDF may be effective in the removal of circulating endotoxins and inflammatory factors, replacement of normal coagulation factors and proteins, interruption of coagulopathy, as well as improvement in hemodynamic instability and nutritional support. All these effects may translate into a potential improvement of MODS. Chu et al. [26] reported 11 cases of acute fatty liver of pregnancy complicated by MODS treated with PE + CVVHDF. They showed that this treatment could effectively reduce the serum levels of total bilirubin and lactic acid, shorten PT, increase the oxygenation index (PaO_2/FiO_2) and facilitate hepatic and renal recovery without apparent adverse effects during severe acute fatty liver of pregnancy. In this study, ALT, AST, CK, myoglobin and TNF-α levels were lower after PE + CVVHDF treatment compared with HP + CVVHDF treatment. Additionally, PT was shortened, and ALB and MAP levels were higher after PE + CVVHDF treatment.

The potential mechanism of wasp venom-induced MODS may be associated with the direct toxic effect of the venom and the immune inflammatory reaction to the venom composition, which seem to be associated with the development of MODS separately. Zhang et al. [27] reported a case of MODS secondary to mass wasp stings and concluded, based on the autopsy report, that the wasp venom-induced systemic effect was a possible underlying mechanism of MODS development. In this study, the level of cytokines IL-1, IL-6, IL-10 and TNF-α in serum increased, suggesting the induction of an immune-mediated inflammatory reaction. Thus, it is possible that the release of large amounts of inflammatory mediators was attributable to the multiple organ injury. We found no relationship between the levels of cytokines (IL-1, IL-6, IL-8, IL-10, TNF-α) to wasp venom and the therapeutic response. One possible reason is that wasp venom contains several different antigens and is very complex; many cytokine levels change in this inflammatory response, and those measured in this study may not be sensitive markers of the therapeutic response. Additional studies are needed to identify sensitive biomarkers.

In the present study, all patients were treated with 1 of the 2 different combinations of blood purification therapies, and 18 out of the 23 patients survived. The overall survival rate was 78.3%. Furthermore, there were no significant differences in survival rates between the 2 treatment groups. The levels of AST, ALT, CK, myoglobin and TNF-α were found to be lower in patients treated with PE + CVVHDF, which may be associated with the direct removal of toxic venom particles and inflammatory mediators. The significant improvement in ALB levels and PT reduction after PE + CVVHDF therapy could be attributed to the replacement of normal coagulation factors and proteins, interruption of coagulopathy and reduction of the thrombotic process. Furthermore, we did not observe any apparent adverse effects of PE + CVVHDF.

This study has several limitations. First, the sample size was relatively small because such cases were uncommon; therefore, further multicenter studies with larger samples are required to confirm these findings. Second, given that these findings are applicable mainly to the populations in rural areas in developing countries exposed to wasp swarms, especially in China, these results may not be applicable to the populations in developed countries.

Conclusion

The present study results indicated that both PE + CVVHDF and HP + CVVHDF combinations were effective in treating MODS caused by mass wasp stings and that the PE + CVVHDF approach was more effective for the removal of toxic substances and inflammatory mediators. Although further randomized clinical trials are warranted to confirm these preliminary findings, our results suggest that both PE + CVVHDF and HP + CVVHDF approaches can be used in the ICU setting in China for the successful management of patients suffering from wasp venom-induced MODS.

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Conflicts of Interest

The authors report no conflicts of interest.

References

1 Bilo BM, Rueff F, Mosbech H, Bonifazi F, Oude-Elberink JN; EAACI Interest Group on Insect Venom Hypersensitivity: Diagnosis of hymenoptera venom allergy. Allergy 2005;60:1339–1349.
2 Xie C, Xu S, Ding F, Xie M, Lv J, Yao J, Pan D, Sun Q, Liu C, Chen T, Li S, Wang W: Clinical features of severe wasp sting patients with dominantly toxic reaction: analysis of 1091 cases. PLoS One 2013;8:e83164.
3 Hamilton RG: Diagnosis and treatment of allergy to hymenoptera venoms. Curr Opin Allergy Clin Immunol 2010;10:323–329.
4 Muller UR: New developments in the diagnosis and treatment of hymenoptera venom allergy. Int Arch Allergy Immunol 2001;124:447–453.
5 Kim YO, Yoon SA, Kim KJ, Lee BO, Kim BS, Chang YS, Bang BK: Severe rhabdomyolysis and acute renal failure due to multiple wasp stings. Nephrol Dial Transplant 2003;18:1235.
6 Taggar JS, Watson T, Musarrat K, Millane T: Kounis syndrome presenting as ST-segment elevation myocardial infarction following a hymenoptera (bee) sting. Int J Cardiol 2009;136:e29–e30.
7 Franca FO, Benvenuti LA, Fan HW, Dos Santos DR, Hain SH, Picchi-Martins FR, Cardoso JL, Kamiguti AS, Theakston RD, Warrell DA: Severe and fatal mass attacks by 'killer' bees (Africanized honey bees – apis mellifera scutellata) in brazil: clinicopathological studies with measurement of serum venom concentrations. Q J Med 1994;87:269–282.
8 Masako M, Hisako H, Eisuke Y, et al: A case of wasp sting disease complicated by multiple organopathy: capability of lifesaving by early diagnosis for continuous blood filtration and exchange of plasma. Jpn J Exp Med 1999;76:1355–1358.
9 Zhang L, Li Z, Fu P, Cao Y, Shi Y, Liu F, Su B, Xu H: Hybrid renal replacement treatment in acute pulmonary edema with acute kidney injury following multiple wasp stings: a report of 3 cases. Blood Purif 2010;30:106–107.
10 Burns D: Diseases caused by arthropods and other noxious animals; in Rook's Textbook of Dermatology, Seventh Edition, 1992, pp 1555–1618.
11 Schmidt H, Hoyer D, Rauchhaus M, Prondzinsky R, Hennen R, Schlitt A, Carter J, Hottenrott K, Müller-Werdan U, Werdan K, Buerke M: ACE-inhibitor therapy and survival among patients with multiorgan dysfunction syndrome (MODS) of cardiac and non-cardiac origin. Int J Cardiol 2010;140:296–303.
12 Huang Z, Wang SR, Su W, Liu JY: Removal of humoral mediators and the effect on the survival of septic patients by hemoperfusion with neutral microporous resin column. Ther Apher Dial 2010;14:596–602.
13 George P, Pawar B, Calton N, Mathew P: Wasp sting: an unusual fatal outcome. Saudi J Kidney Dis Transpl 2008;19:969–972.
14 Santos KS, Stephano MA, Marcelino JR, Ferreira VM, Rocha T, Caricati C, Higashi HG, Moro AM, Kalil JE, Malaspina O, et al: Production of the first effective hyperimmune equine serum antivenom against Africanized bees. PLoS One 2013;8:e79971.
15 Brown SG, Blackman KE, Stenlake V, Heddle RJ: Insect sting anaphylaxis; prospective evaluation of treatment with intravenous adrenaline and volume resuscitation. Emerg Med J 2004;21:149–154.
16 Goodman JW, Goldfarb DS: The role of continuous renal replacement therapy in the treatment of poisoning. Semin Dial 2006;19:402–407.
17 Eser B, Guven M, Unal A, Coskun R, Altuntas F, Sungur M, Serin IS, Sari I, Cetin M: The role of plasma exchange in HELLP syndrome. Clin Appl Thromb Hemost 2005;11:211–217.
18 Li MQ, Li JQ, Zhi ZX, Xu JY, Zhang Z, Lu F, Li L, Xu YJ, Mo X, Lu B, et al: Efficacy of various combined blood purification techniques for treating patients with non-viral acute liver failure. Cell Biochem Biophys 2014;68:571–575.

19 Hongliang T, Rong Z, Xiaojing W, Rao S, Lun L, Jinhui T, Nong C, Kehu Y: The effects of continuous blood purification for SIRS/MODS patients: a systematic review and meta-analysis of randomized controlled trials. ISRN Hematol 2012;2012:986795.
20 Saito A: Current progress in blood purification methods used in critical care medicine. Contrib Nephrol 2010;166:100–111.
21 Ozdemir FN, Tutal E, Sezer S, Gür G, Bilgic A, Haberal M: Effect of supportive extracorporeal treatment in liver transplantation recipients and advanced liver failure patients. Hemodial Int 2006;10(suppl 2):S28–S32.
22 Yorgin PD, Eklund DK, Al-Uzri A, Whitesell L, Theodorou AA: Concurrent centrifugation plasmapheresis and continuous venovenous hemodiafiltration. Pediatr Nephrol 2000;14:18–21.
23 Li LJ, Yang Q, Huang JR, Xu XW, Chen YM, Fu SZ: Effect of artificial liver support system on patients with severe viral hepatitis: a study of four hundred cases. World J Gastroenterol 2004;10:2984–2988.
24 Nasa P, Singh A, Juneja D, Singh O, Javeri Y: Continuous venovenous hemodiafiltration along with charcoal hemoperfusion for the management of life-threatening lercanidipine and amlodipine overdose. Saudi J Kidney Dis Transpl 2014;25:1255–1258.
25 Tang Y, Zhang L, Fu P, Kang Y, Liu F: Hemoperfusion plus continuous veno-venous hemofiltration in a pregnant woman with severe acute pancreatitis: a case report. Int Urol Nephrol 2012;44:987–990.
26 Chu YF, Meng M, Zeng J, Zhou HY, Jiang JJ, Ren HS, Zhang JC, Zhu WY, Wang CT: Effectiveness of combining plasma exchange with continuous hemodiafiltration on acute fatty liver of pregnancy complicated by multiple organ dysfunction. Artif Organs 2012;36:530–534.
27 Zhang L, Tang Y, Liu F, Shi YY, Cao Y, Xu H, Fu P: Multiple organ dysfunction syndrome due to massive wasp stings: an autopsy case report. Chin Med J (Engl) 2012;125:2070–2072.