Int J Clin Exp Med 2020;13(9):7106-7112
www.ijcem.com /ISSN:1940-5901/IJCEM0113524

Original Article

Clinical efficacy of high-volume hemofiltration on severe acute pancreatitis combined with acute renal failure

Yihui Wang[1], Weisong Jiang[1], Chunyan Chen[2], Huiqiu Sheng[1], Enqiang Mao[1], Yuhua Zhou[1]

[1]*Department of Emergency Medicine, Rui Jin Hospital Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China;* [2]*Key Laboratory of Parasite and Vector Biology, Ministry of Health, Chinese Center for Tropical Disease Research, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China*

Received April 29, 2020; Accepted July 19, 2020; Epub September 15, 2020; Published September 30, 2020

Abstract: Objective: To explore the clinical efficacy of high-volume hemofiltration (HVHF) on patients with severe acute pancreatitis (SAP) combined with acute renal failure (ARF). Methods: 76 SAP patients combined with ARF admitted to our hospital from October 2016 to October 2017 were divided into two groups according to the random number table method. The control group (n = 38) was given conventional treatment, and the study group (n = 38) received HVHF in addition to conventional treatment. The following indicators were compared, including gastrointestinal function recovery time (GFRT), duration of abdominal pain (DAP), liver function indices [aspartate transaminase (AST), alanine transaminase (ALT)], renal function indices [blood urea nitrogen (BUN), serum creatinine (SCr)], serum amylase (AMS), white blood cell count (WBC), inflammation response indices [tumor necrosis factor-α (TNF-α), transforming growth factor-β (TGF-β), interleukin (IL)-6, IL-1β, IL-8)], acute physiology and chronic health status score (APACHE II) and quality of life. Results: The GFRT and DAP of the study group were significantly shorter than those of the control group (P<0.05). Compared with those before treatment, the serum AST, ALT, BUN, SCr, AMS, WBC, TNF-α, TGF-β, IL-6, IL-1β, IL-8 levels, and APACHE II scores of the two groups were significantly reduced after 3 months of treatment, while the quality of life scores were significantly increased, and the improvement of the above indicators in the study group were significantly better than those in the control group (P<0.05). Conclusion: HVHF can effectively improve electrolyte imbalance, reduce inflammation and improve the quality of life in patients with SAP combined with AFR.

Keywords: Acute renal failure, pancreatitis, hemofiltration, inflammatory response, quality of life

Introduction

Acute severe pancreatitis (SAP) combined with acute renal failure (ARF) is commonly diagnosed and its clinical symptoms are mostly characterized by systemic severe inflammatory response syndrome (SIRS), which seriously endangers human health [1]. It was clinically found that SAP combined ARF was caused by the massive release of pro-inflammatory cytokines and expression of the balanced plasma pro-inflammatory cytokines in pancreatic lesions, which leads to concurrent acute respiratory distress syndrome, shock and even multiple organ dysfunction syndrome (MODS) [2]. It was characterized by acute attack, severe symptoms, high mortality and violent reactions. On the basis of onset characteristics and symptoms of SAP, high-volume hemofiltration (HVHF) is primarily used as the main treatment method. HVHF mainly improves the clearance of middle and large molecule by increasing the replacement fluid flow rate and ultrafiltration rate, which can regulate the balance of anti-inflammatory and pro-inflammatory cytokines, maintain electrolyte balance and stable hemodynamics, so as to achieve symptom control and clinical efficacy in SAP patients [3]. This study aimed to explore the clinical efficacy of HVHF in the treatment of SAP patients combined with ARF.

Materials and methods

Baseline data

76 SAP patients combined with ARF admitted to our hospital from October 2016 to October 2017 were included. The diagnosis of SAP was performed in accordance with the standards

issued by the Pancreatic Surgery Branch of the Chinese Medical Association Surgery Branch in 2001 [4] as well as the diagnostic criteria of ARF in *Diseology* [5]. The enrolled patients had no history of exposure to nephrotoxic drugs and poisons prior to the onset of ARF, and all patients or their families signed the written informed consent. Exclusion criteria: Patients who had acute or chronic infections or autoimmune diseases in other organs; those who underwent peripancreatic catheter drainage or pancreatic surgery during hospitalization; those who had poor compliance; and those who had malignant tumors or severe circulatory and respiratory diseases. This study was approved by the medical ethics committee of our hospital. 76 patients were equally divided into two groups according to the random number table. In the control group, there were 20 males and 18 females, aged 38-52 years old, with the average age of 44.58 ± 7.39 years, among which 22 had area of necrosis ≥67%, and 16 had area of necrosis = 33%. There were 16 cases graded as II and 22 cases graded as III on Balthazar CT. In the study group, there were 22 males and 16 females, aged 33-55 years, with the average age of 44.92 ± 7.84 years, among which 21 had area of necrosis ≥67%, and 17 had area of necrosis = 33%. There were 15 cases graded as II and 23 cases graded as III.

Methods

The control group was given conventional treatment, including fasting, early fluid resuscitation and gastrointestinal decompression, nutritional support, improving microcirculation, inhibiting pancreatic secretion, correcting acid and alkali and electrolyte disorders, *etc*. Surgical treatment and enteral nutrition support were performed when necessary. On the basis of conventional treatment, the study group was given HVHF: double-lumen central venous catheter was inserted using the Seldinger technique. In all, there were 4 cases of subclavian vein catheterization, 16 cases of femoral vein catheterization, and 18 cases of internal vein catheterization. 38 patients were treated with HVHF (Braun7106505, F60) for 6 hours per day. The concentrations of potassium and other electrolytes were adjusted according to the patient's condition. Post-dilution hemodiafiltration were 1000 to 4000 ml/h/1.73 m^2 and the blood flow was 250-300 mL/min. Anticoagulation regimen: patients without bleeding were treated with heparin anticoagulation (0.4-0.6 mg/kg, additional intravenous injection before blood filtration: 2-3 mg/h, and discontinued 0.5 h before the end of filtration). Those with bleeding tendency were treated with low molecular weight heparin calcium for anticoagulation (dose: 1500-2000U, continuous intravenous injection 100-200 U/h).

Gastrointestinal function recovery time (GFRT), duration of abdominal pain (DAP), aspartate transaminase (AST), alanine transaminase (ALT), blood urea nitrogen (BUN), serum creatinine (SCr), serum amylase (AMS), white blood cell count (WBC), tumor necrosis factor-α (TNF-α), transforming growth factor-β (TGF-β), interleukin (IL)-6, IL-1β, IL-8, APACHE II and quality of life scores were compared in two groups. The fasting venous blood was collected in the morning before treatment and 3 months after treatment, and the supernatant was extracted after centrifugation at 3000 r/min. AST, ALT, BUN, Scr, AMS and WBC were measured by an automatic biochemical analyzer, and TNF-α, TGF-β, IL-6, IL-1β and IL-8 were detected by enzyme-linked immunosorbent assay (ELISA). The operation method was strictly in accordance with the operation instructions of the ELISA kit. APACHE II scores were used to evaluate the patient's condition, including acute physiological score, age, and chronic health status. Higher score indicates worse physical condition of the patient. The SF-36 quality of life scale was used to assess the quality of life in terms of physical pain, physiological function, psychological function and social function. Higher score indicates better quality of life.

Statistical analysis

SPSS22.0 software was used for statistical analysis. The measurement data were expressed as x ± sd and compared by t test. The enumeration data were expressed as n (%) and compared by χ^2 test. The difference was statistically significant with $P<0.05$.

Results

Comparison of baseline data

There was no statistically significant difference between the two groups in terms of gender, age, pancreatic necrosis area and Balthazar CT grading ($P>0.05$, **Table 1**).

Table 1. Comparison of baseline data between the two groups

Group	Gender (M/F)	Age (year)	Area of necrosis (≥67%/33%)	Balthazar CT grading (grading II/III)
Control group (n = 38)	20/18	44.58 ± 7.39	22/16	16/22
Study group (n = 38)	22/16	44.92 ± 7.84	21/17	15/23
t/χ^2	0.213	0.195	0.054	0.055
P	0.645	0.846	0.817	0.815

Table 2. Comparison of GFRT and DAP between the two groups ($\bar{x}$ ± sd)

Group	Gastrointestinal function recovery (d)	Abdominal pain relief (h)
Control group (n = 38)	6.74 ± 1.72	42.78 ± 6.34
Study group (n = 38)	4.83 ± 1.65	24.96 ± 5.27
t	4.940	13.324
P	0.000	0.000

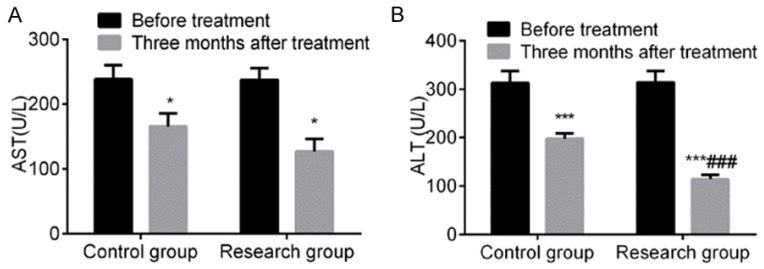

Figure 1. Comparison of liver function before and after treatment. Note: Compared with same group before treatment, ***P<0.001; compared with the control group, ###P<0.001.

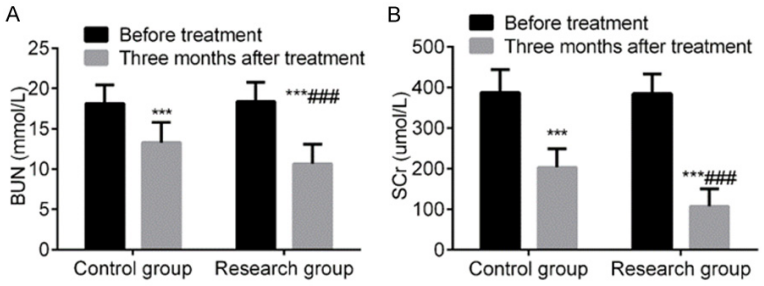

Figure 2. Comparative analysis of renal function before and after treatment with HVHF. Note: Compared with same group before treatment, ***P<0.001; compared with the control group, ###P<0.001.

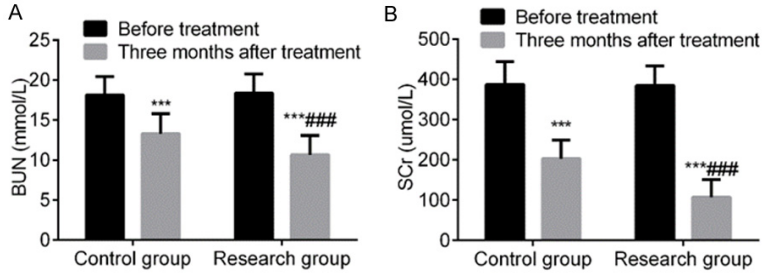

Figure 3. Comparative analysis of AMS and WBC levels before and after treatment with HVHF (x ± sd). Note: Compared with same group before treatment, ***P<0.001; compared with the control group, ###P<0.001.

GFRT and DAP

GFRT and DAP of the study group were significantly shorter than those of the control group (P<0.05), suggesting that HVHF can significantly improve the clinical symptoms and gastrointestinal function in SAP patients combined with ARF (**Table 2**).

Changes in liver function indices before and after treatment

Compared with those before treatment, AST and ALT of the two groups were significantly reduced after 3 months of treatment, and the improvement of AST and ALT in the study group was better than that in the control group (P<0.05), indicating that HVHF can improve the liver function in SAP patients combined with ARF (**Figure 1**).

Changes in renal function indices before and after treatment

In contrast to those before treatment, BUN and SCr of the two groups were significantly decreased after 3 months of treatment, and the study group showed higher improve-

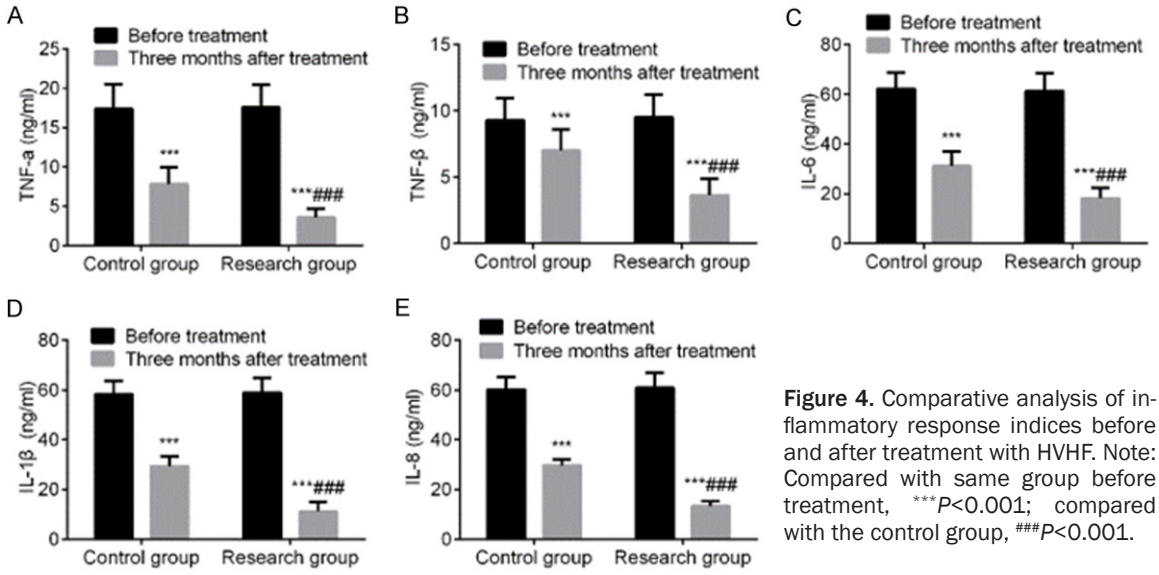

Figure 4. Comparative analysis of inflammatory response indices before and after treatment with HVHF. Note: Compared with same group before treatment, $^{***}P<0.001$; compared with the control group, $^{###}P<0.001$.

Table 3. Comparison analysis of APACHE II score before and after treatment (x ± sd, points)

Group	Before treatment	After treatment
Control group (n = 38)	24.26 ± 2.28	17.34 ± 1.89
Study group (n = 38)	24.13 ± 2.34	14.36 ± 1.74
t	0.245	7.151
P	0.807	0.000

ment of BUN and SCr than the control group ($P<0.05$), suggesting that HVHF can improve the renal function in SAP patients combined with ARF (**Figure 2**).

Changes in AMS and WBC before and after treatment

Compared with those before treatment, AMS and WBC in both groups were significantly reduced after 3 months of treatment, and the improvement of AMS and WBC in the study group was better than that in the control group ($P<0.05$), suggesting that HVHF treatment can significantly improve the level of AMS and WBC in SAP patients combined with ARF (**Figure 3**).

Changes in inflammatory response indices before and after treatment

In comparison with those before treatment, the serum levels of TNF-α, TGF-β, IL-6, IL-1β, and IL-8 in the two groups were significantly reduced after 3 months of treatment, and the study group showed significantly higher improvement than the control group ($P<0.05$), indicating that HVHF treatment can significantly reduce the degree of inflammatory response in SAP patients combined with ARF (**Figure 4**).

APACHE II score before and after treatment

After 3 months of treatment, APACHE II scores were significantly reduced in two groups, and the study group showed lower APACHE II scores than the control group ($P<0.05$), indicating that HVHF treatment can significantly improve the APACHE II score of SAP patients combined with ARF and speed up the rehabilitation of patients (**Table 3**).

Changes in quality of life before and after

The quality of life scores in both groups were significantly increased after 3 months of treatment, and the study group exhibited higher scores than the control group ($P<0.05$), suggesting that HVHF treatment can significantly improve the quality of life of SAP patients combined with ARF (**Figure 5**).

Discussion

SAP is an acute inflammatory state of the pancreas caused by premature activation of human pancreatic enzymes system. After a large number of inflammatory cells are activated, they begin to release cytokines. Therefore, the "cytokine storm" occurs and aggravates SAP [6,

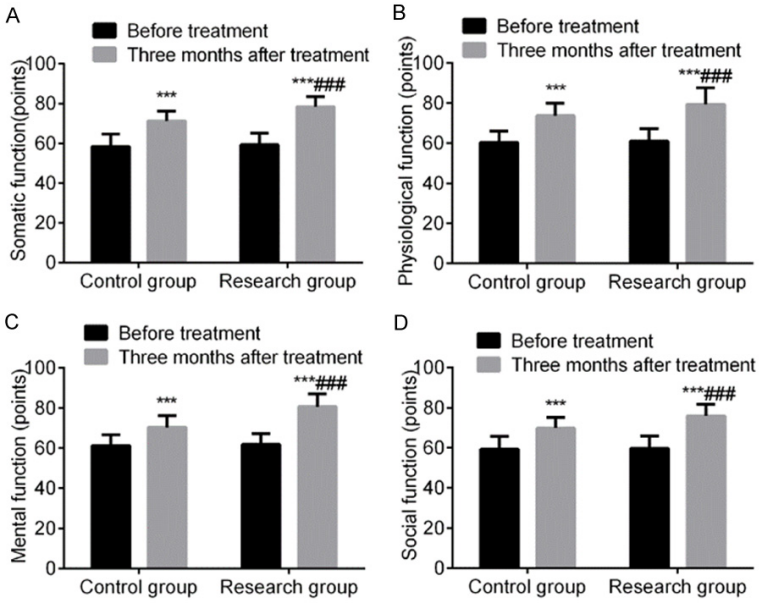

Figure 5. Comparative analysis of quality of life before and after treatment with HVHF. Note: Compared with same group before treatment, $^{***}P<0.001$; compared with the control group, $^{###}P<0.001$.

7]. In 1988, Rindeknecht proposed the hypothesis of the pathogenesis of SAP, believing that SAP is caused by the excessive activation of WBC, which triggers the inflammatory response of the pancreas and leads to life-threatening SAP. SAP can cause the activation of inflammatory factors such as human mononuclear macrophages, lymphocytes and neutrophils, thereby promoting the release of inflammatory cytokines such as IL-6, TNF-α, IL-8, and stimulating the synthesis of acute-phase proteins such as CRP in the liver of patients. The above factors are released in large quantities when the body's immune system reacts violently. It can cause the uncontrolled inflammation, leading to systemic inflammatory syndrome (SIRS), and ultimately the occurrence of MODS [8-10]. Clinical studies have shown that MODS is a risk factor for death of SAP patients during hospitalization [11]. The degree and scale of inflammatory responses in SAP patients should be minimized to improve the patient's condition and reduce mortality.

With the continuous development of medical technology, HVHF technology has become the first treatment option for SAP patients combined with ARF [12]. The key to increase the success rate of SAP treatment is to prevent the early occurrence of MODS, so hemofiltration is a promising therapy [13-15]. HVHF is commonly used in blood purification therapy, which simulates the glomerular filtration to slowly, massively and effectively remove toxic and harmful solutes from the blood [16-18]. HVHF uses high-volume filters and pipelines with high degree of biocompatibility and a fluid balancing system to remove nitrogen-containing metabolic wastes and correct salt, water and acid-base flocculation to ensure homeostasis. HVHF is also effective in eliminating inflammatory mediators from the blood, including TNF-α, IL-1β, TGF-β, IL-6 and IL-8 and other cytokines, reducing SIRS, and preventing the development of MODS [19-22]. This study showed that the GFRT and DAP of the study group were shorter than those of the control group; the serum AST, ALT, BUN, SCr, AMS, WBC, TNF-α, TGF-β, IL-6, IL-1β, IL-8 levels, and the APACHE II scores were significantly reduced after treatment, whereas the quality of life scores were significantly increased. The improvement of these indices in the study group was better than those in the control group, demonstrating that HVHF has very good treatment efficacy for SAP patients, which helps to improve the systemic inflammatory response and organ failure symptoms, liver and kidney function, and promote physical recovery as well as the quality of life [23]. The underlying mechanism may be that HVHF reabsorbs excess water and solutes in the blood and corrects the disordered anti-inflammatory factors and electrolytes, so as to reduce the influence of inflammatory factors on various organ functions and thus improve organ functions, especially liver and kidney functions [24, 25]. In the clinical treatment of SAP, although there was no significant difference in patients undergoing conventional emergency treatment before hemofiltration, HVHF may lead to differences in the final outcomes.

In summary, early application of HVHF in the treatment of SAP combined with AFR can effectively eliminate inflammatory response, improve

cardiopulmonary, renal and liver functions as well as quality of life, and prevent the conversion from SIRS to MODS and MOF. However, this is a single-center, small-sample study, which may affect the accuracy of the results. Large-scale, multi-center studies are expected to be performed in the future.

Acknowledgements

This work was supported by Medical Guidance Project of Shanghai Science and Technology Commission (No. 18411966400; No. 164119-70700) and National Natural Science Foundation Youth Project (No. 81601665).

Disclosure of conflict of interest

None.

Address correspondence to: Yuhua Zhou, Department of Emergency Medicine, Rui Jin Hospital Shanghai Jiao Tong University School of Medicine, No. 197, Rui Jin Er Road, Shanghai 200025, China. Tel: +86-13916115155; E-mail: yhuazzz@163.com

References

[1] He WH, Yu M, Zhu Y, Xia L, Liu P, Zeng H, Zhu Y and Lv NH. Emergent triglyceride-lowering therapy with early high-volume hemofiltration against low-molecular-weight heparin combined with insulin in hypertriglyceridemic pancreatitis: a prospective randomized controlled trial. J Clin Gastroenterol 2016; 50: 772-778.

[2] Abulimiti A, Husaiyin A and Sailai Y. Evaluation of HVHF for the treatment of severe acute pancreatitis accompanying MODS. Medicine (Baltimore) 2018; 97: e9417.

[3] Zhao M, Zhou Y, Liu S, Li L, Chen Y, Cheng J, Lu Y and Liu J. Control release of mitochondria-targeted antioxidant by injectable self-assembling peptide hydrogel ameliorated persistent mitochondrial dysfunction and inflammation after acute kidney injury. Drug Deliv 2018; 25: 546-554.

[4] Pancreatic Surgery Group SBoCMA. Draft for diagnosis and treatment of severe acute pancreatitis. Chinese Journal of Practical Surgery 2001; 21: 513-517.

[5] Wang H. Nephrology (3rd Edition) Beijing: People 's Medical Publishing House; 2008.

[6] Kaplan M, Ates I, Akpinar MY, Yuksel M, Kuzu UB, Kacar S, Coskun O and Kayacetin E. Predictive value of C-reactive protein/albumin ratio in acute pancreatitis. Hepatobiliary Pancreat Dis Int 2017; 16: 424-430.

[7] Thorsen A, Borch AM, Novovic S, Schmidt PN and Gluud LL. Endoscopic necrosectomy through percutaneous self-expanding metal stents may be a promising additive in treatment of necrotizing pancreatitis. Dig Dis Sci 2018; 63: 2456-2465.

[8] Nakaharai K, Morita K, Jo T, Matsui H, Fushimi K and Yasunaga H. Early prophylactic antibiotics for severe acute pancreatitis: a population-based cohort study using a nationwide database in Japan. J Infect Chemother 2018; 24: 753-758.

[9] Spiliopoulos S, Inchingolo R, Lucatelli P, Iezzi R, Diamantopoulos A, Posa A, Barry B, Ricci C, Cini M, Konstantos C, Palialexis K, Reppas L, Trikola A, Nardella M, Adam A and Brountzos E. Transcatheter arterial embolization for bleeding peptic ulcers: a multicenter study. Cardiovasc Intervent Radiol 2018; 41: 1333-1339.

[10] Wang Y and Chen M. Fentanyl ameliorates severe acute pancreatitis-induced myocardial injury in rats by regulating NF-κB signaling pathway. Med Sci Monit 2017; 23: 3276-3283.

[11] Ren YC, Huang CL, Chen SM, Zhao QY, Wan XJ and Li BW. Dilation catheter-guided mini-forceps biopsy improves the diagnostic accuracy of malignant biliary strictures. Endoscopy 2018; 50: 809-812.

[12] Yamabe A, Irisawa A, Shibukawa G, Sato A, Fujisawa M, Arakawa N, Yoshida Y, Igarashi R, Maki T, Yamamoto S, Ikeda T, Abe Y and Hoshi K. Inflammatory bile duct obstruction during the healing stage of severe acute pancreatitis. Intern Med 2017; 56: 1037-1040.

[13] Konończuk T, Łukaszuk B, Mikłosz A, Chabowski A, Żendzian-Piotrowska M and Kurek K. Cerulein-induced acute pancreatitis affects sphingomyelin signaling pathway in rats. Pancreas 2018; 47: 898-903.

[14] Zhang FH, Sun YH, Fan KL, Dong XB, Han N, Zhao H and Kong L. Protective effects of heme oxygenase-1 against severe acute pancreatitis via inhibition of tumor necrosis factor-α and augmentation of interleukin-10. BMC Gastroenterol 2017; 17: 100.

[15] Owusu L, Xu C, Chen H, Liu G, Zhang G, Zhang J, Tang Z, Sun Z and Yi X. Gamma-enolase predicts lung damage in severe acute pancreatitis-induced acute lung injury. J Mol Histol 2018; 49: 347-356.

[16] Hu J, Li P and Zhang T. Rhubarb combined with trypsin inhibitor for severe acute pancreatitis: a systematic review and meta-analysis. Phytother Res 2018; 32: 1450-1458.

[17] Minkov GA, Yovtchev YP and Halacheva KS. Increased circulating CD4+CD25+CD127low/neg regulatory t-cells as a prognostic biomarker in acute pancreatitis. Pancreas 2017; 46: 1003-1010.

[18] Kang X, Lu XG, Zhan LB, Liang ZK, Guo WX, Ma Q, Wang Y, Song JB, Feng JY, Wang CH, Bai LZ, Song Y and Liu GH. Dai-Huang-Fu-Zi-Tang alleviates pulmonary and intestinal injury with severe acute pancreatitis via regulating aquaporins in rats. BMC Complement Altern Med 2017; 17: 288.

[19] Chen J, Huang C, Wang J, Zhou H, Lu Y, Lou L, Zheng J, Tian L, Wang X, Cao Z and Zeng Y. Dysbiosis of intestinal microbiota and decrease in paneth cell antimicrobial peptide level during acute necrotizing pancreatitis in rats. PLoS One 2017; 12: e0176583.

[20] Katoch M, Paul A, Singh G and Sridhar SNC. Fungal endophytes associated with viola odorata linn. as bioresource for pancreatic lipase inhibitors. BMC Complement Altern Med 2017; 17: 385.

[21] Sugimoto M, Sonntag DP, Flint GS, Boyce CJ, Kirkham JC, Harris TJ, Carr SM, Nelson BD, Bell DA, Barton JG and Traverso LW. Biliary stenosis and gastric outlet obstruction: late complications after acute pancreatitis with pancreatic duct disruption. Pancreas 2018; 47: 772-777.

[22] Jeon TJ and Park JY. Clinical significance of the neutrophil-lymphocyte ratio as an early predictive marker for adverse outcomes in patients with acute pancreatitis. World J Gastroenterol 2017; 23: 3883-3889.

[23] Lee SH, Yun SJ, Ryu S, Choi SW, Kim HJ, Kang TK, Oh SC and Cho SJ. Massive bleeding from inferior mesenteric vein with hypovolemic shock: a rare complication of acute pancreatitis. J Emerg Med 2018; 55: e5-e8.

[24] Yogendranathan N, Herath H, Sivasundaram T, Constantine R and Kulatunga A. A case report of zinc phosphide poisoning: complicated by acute renal failure and tubulo interstitial nephritis. BMC Pharmacol Toxicol 2017; 18: 37.

[25] Si X, Li J, Bi X, Wu L and Wu X. Clinical evaluation of high-volume hemofiltration with hemoperfusion followed by intermittent hemodialysis in the treatment of acute wasp stings complicated by multiple organ dysfunction syndrome. PLoS One 2015; 10: e0132708.