Original Article

Effect of hemoperfusion cartridge on different internal environmental indicators

Li-jun Wang¹, Nyirimigabo Eric^{2,3}, Mu-ming Yu¹, Yan-fen Chai¹

¹ Department of Emergency Medicine, Tianjin Medical University General Hospital, Tianjin 300052, China

² Tianjin University of Traditional Chinese Medicine, Tianjin 300193, China

³ Rwanda Bureau of Standards, The Republic of Rwanda

Corresponding Author: Yan-fen Chai, Email: chaiyanfen2000@yahoo.com.cn

BACKGROUND: This study aimed to observe the effect of hemoperfusion (HP) cartridge on different internal environment indicators at different time points in patients with acute blood poisoning and to find alternative indicators for the detection of blood poisoning.

METHODS: The levels of internal environment indicators (blood pH, P_vCO_2 , P_vO_2 , blood lactate, potassium, free calcium, bicarbonate, and blood glucose) before and after HP treatment were recorded for patients with acute poisoning at time points of 30 minutes and 120 minutes. After calculating the difference value δ , the statistical software was used to analyze the statistical difference of the influence caused by HP cartridge at two time points. According to the formula, adsorption rate % = $\frac{a-v}{a} \times 100$, the adsorption rate of each indicator was calculated respectively.

RESULTS: The difference of indicators at different time points in inlet and outlet such as blood glucose, free-calcium, and lactate was statistically significant ($P < 0.05$), but the difference in indicators such as pH, P_vCO_2 , P_vO_2 , potassium, sodium, and bicarbonate was not statistically significant ($P > 0.05$).

CONCLUSION: During HP treatment, the indicators of blood glucose, free-calcium and lactate were significantly affected by HP cartridge, and the effect varies with time.

KEY WORDS: Hemoperfusion cartridge; Internal environment indicators; Blood glucose; Adsorption rate

World J Emerg Med 2013;4(4):290–293

DOI: 10.5847/wjem.j.issn.1920-8642.2013.04.009

INTRODUCTION

With the quick development of society and the increasing pressure from work, patients with acute poisoning have increased year by year. In the United States, there are about 4 millions poisoning patients every year and 300 000 of them need hospitalization. The death rate of the hospitalized patients varies from 0.2% to 0.8%. In recent years, poisoning and injury have become one of the top 5 main death causes in China. The rate of poisoning and injury in urban residents is 18/100 000, and in rural residents, 22/100 000. Of the total deaths, deaths due to poisoning account for 10.7%.^[1] At present, there is no effective antidote for most of the poisons. Hemoperfusion

(HP) can effectively remove fat-soluble macromolecules poisons with a high protein binding rate and has no significant effect on the internal environment, which has been widely used in patients with acute poisoning. However, few studies have been reported about whether HP cartridge may affect different indicators of internal environment such as blood pH, P_vCO_2 , P_vO_2 , lactate, potassium, sodium, free calcium, glucose and bicarbonate at different time points. This study was undertaken to determine the effect of HP cartridge on the indicators of internal environment in acute poisoning patients undergoing HP treatment at different time points.

METHODS

Subjects

Thirty patients with complete data were selected for analysis. At 30 minutes and 120 minutes, 1 mL of blood was collected respectively before and after HP cartridge (Absorba 300; Gambro, Hechingen, Germany) using a 2 mL 22 G arterial blood sampling machine (British BD). The levels of blood pH, P_vCO_2 , P_vCO_2 , lactate, potassium, sodium, free calcium, blood glucose and bicarbonate were automatically detected by a GEM Premier 3000 blood gas analyzer.

HP process

Femoral vein puncture was adopted by the placement of a Gam Cath (Model GDK-1115, GAMBRO Company) double lumen catheter. HP treatment was conducted through a disposable blood circuit of Ha Nahao dialysis artificial kidney, JF-800A HP machine of Jian Fan in Zhuhai and Sweden Gambro Adsorba 300C HP cartridge. The treatment lasted for 2–4 hours according to different poisoning of patients, poison concentration, and the flow rate of extracorporeal blood.

2 000 mL of 0.9% NaCl and 40 000 units of heparin calcium were used to wash the extracorporeal circulation piping and HP cartridge. During the HP treatment, 100–200 mL of 0.9% NaCl and 1 000–2 000 units of heparin calcium were used to wash the extracorporeal circulation piping and HP cartridge every one hour for the prevention of thrombosis. Arterial and venous terminal pressure of extracorporeal circulation was monitored and the blood flow rate was controlled at 100–180 mL/min. The heating device provided by HP machine was used to maintain the extracorporeal circulation piping blood temperature at 38–40 °C. At the end of the HP treatment, air back to the blood act was applied.

Statistical analysis

This retrospective study included 30 patients with complete data. The difference in each indicator before and

after HP cartridge at different time points was calculated by the formula $\delta = a - v$. Measurement data between the two groups were presented as mean $\pm$ SD and statistical analyses were performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were analyzed using paired *t*-test. *P* values < 0.05 were considered statistically significant. According to the formula, adsorption rate $\% = \frac{a-v}{a} \times 100$, the adsorption rate of each indicator was calculated respectively.

RESULTS

The levels of blood pH and P_vCO_2 , P_vCO_2 , blood lactate, potassium, sodium, free calcium, blood glucose, and bicarbonate after 30 minutes and 120 minutes before and after HP cartridge were detected respectively. The difference δ was calculated and then SPSS statistical software was used for analytical analysis (Table 1).

According to the formula,^[2] the adsorption rate of the indicators % is:

$$\delta = \frac{\text{Level of inlet blood} - \text{Level of outlet blood}}{\text{Level of inlet blood}} \times 100.$$

The adsorption rate of the indicators at different time points of HP was calculated (Figure 1).

Figure 1. Variances of the adsorption rate of the indicators by using HP ($n=30$).

Table 1. Effects of HP cartridge on different internal environment indicators at different time points ($n=30$, mean $\pm$ SD)

Variables	30 min	120 min	<i>t</i> value	<i>P</i> value
pH value	0.01 $\pm$ 0.01	0.01 $\pm$ 0.03	-0.614	0.542
P_vCO_2 (mmHg)	-0.09 $\pm$ 1.95	-1.33 $\pm$ 1.95	0.794	0.430
P_vO_2 (mmHg)	3.27 $\pm$ 5.31	2.20 $\pm$ 3.47	0.921	0.361
Blood sodium (mmol/L)	0.87 $\pm$ 1.70	-0.53 $\pm$ 1.33	-0.845	0.401
Blood potassium (mmol/L)	0.05 $\pm$ 0.17	0.03 $\pm$ 0.17	-1.835	0.072
Free calcium (mmol/L)	0.19 $\pm$ 0.04	0.06 $\pm$ 0.02	14.815	0.000
Blood glucose (mmol/L)	5.63 $\pm$ 2.28	1.19 $\pm$ 1.25	9.330	0.000
Blood lactate (mmol/L)	0.13 $\pm$ 0.28	-0.17 $\pm$ 0.27	4.156	0.000
Bicarbonate (mmol/L)	0.23 $\pm$ 1.28	0.35 $\pm$ 0.69	-0.477	0.635

DISCUSSION

Tsujimoto et al^[3] used polymyxin-B coated cellulose column direct HP to treat patients with septic shock. They found that HP could effectively decrease the number of CD 16+ CD 14+ monocytes and the presence of TLR-4, improve hemodynamics and oxygenation, and reduce the mortality rate.^[4] HP could effectively clear IL-6, IL-8, TGF- β , C-reactive protein and other inflammatory cytokines of septic patients.^[5,6] But it often causes the transient reduction of platelets, white blood cells, coagulation factors and bivalent cation.^[1] Few studies concentrated on whether HP has effect on the internal environment of patients. This study aimed to assess the influences of HP on the indicators of internal environment during the HP treatment of patients with acute poisoning at different time points.

Carbon kidney HP was used in the 1960s. The Gambro Adsorba 300C Carbon kidney HP cartridge used in this study has bigger specific surface area and more pore structure, whose main component is activated carbon. It can absorb fat-soluble, high-protein-binding poison efficiently and non-specifically. However, some studies reported that combined HP-hemodialysis for poisoning resulted from large doses of methotrexate or phenytoin, with a higher protein binding rate, can provide the better results of poison clearance.^[7-9]

Currently, the timing of the treatment depends on the clinical experience of doctors. HP treatment of patients with acute poisoning usually lasts 2 to 3 hours. Guenzet et al^[10] indicated that the optimal duration of treatment for HP was 90 minutes, and it was not related to the molecular weight of the cleared substance, which was shown by computer simulation analysis for HP treatment.

However, the saturated adsorption time of HP cartridge is not only related to the HP time but also to the extracorporeal blood flow rate and the levels of hematocrits and blood toxicants. For each HP treatment, total toxic removed by HP cartridge is not equal and clearance kinetics of HP cartridge for various poisons are not the same.^[2] Zhang et al^[11-13] found that for the clearance of paracetamol, sodium salicylate, digoxin, phenobarbital, etc by carbon renal HP, the clearance rate decreased with time. Mui et al^[14] reported that the adsorption capacity of activated carbon for drugs reached the maximum from the beginning to 20 minutes and the absorbing ability decreased with time. Shiratori et al^[15] found that the adsorption capacity of activated carbon for glucose reached the highest at the beginning with a fast adsorption rate and then went down slowly with time till equilibrium. Toxic removal by HP cartridge is neither

typical linear (first-order kinetics) elimination nor in line with the elimination of zero-order kinetics. Therefore, it is not reasonable to consider a simple time point as the end of HP treatment.

The balance of the adsorption capacity is the maximum value of adsorbed substance by material when the adsorption and desorption of substance on the carbon surface reach the dynamic equilibrium state. The clinical ideal state is to stop HP treatment only when HP cartridge reaches the equilibrium state of adsorption. This not only guarantees the maximum HP cartridge adsorption but also reduces the risk of complications. The level of difference (δ value) before and after HP cartridge reflects the clearance ability. Monitoring the difference at real-time can help to decide whether it is necessary to stop HP therapy. When the δ value is zero, it means that the absorbing ability of HP cartridge is saturated and it is the best time to stop HP treatment. In detecting blood poisons, however, the need of instruments and examiners doesn't match the requirements of patients with acute poisoning and bedside detection. Hence this study aimed to find alternative indicators for blood poisoning detection.

The indicators mentioned above at different time points could indirectly provide the specific time of HP treatment for patients with acute poisoning and motivate HP to the highest ability of poison clearance and minimize various complications in the treatment process. Figure 1 and Table 1 show that there was a significant difference ($P<0.05$) in the clearance rates of blood glucose, free calcium and lactate at different time points of HP treatment and obviously it has a significant effect on blood glucose. The difference in blood glucose levels before and after HP cartridge was smaller at 120 minutes than at 30 minutes (1.19 ± 1.25 mmol/L vs. 5.63 ± 2.28 mmol/L) and the clearance rate decreased dramatically from (72.28 ± 15.28)% to (14.87 ± 13.27)% ($P=0.000$). At the beginning of HP, the clearance rate of blood glucose was the highest and the scavenging ability decreased with time.

There were some similarities between the clearance ability of blood glucose and that of drugs for HP cartridge.^[11,14] Indirectly it provided the specific time of HP treatment for patients with acute poisoning by detecting the difference. Future studies can focus on indirect judgement of toxic clearance by detecting the difference of the blood glucose levels before and after HP cartridge. We try to find simpler, faster, and more inexpensive indicators of emergency bedside detection as alternatives of complex, time-consuming and expensive poison traditional detection method, while maximizing the benefits of patients during HP treatment.

ACKNOWLEDGEMENTS

We are grateful to Dr. Zhan-wei Du, College of Computer Science and Technology, Jilin University, for his support in data processing and literature review.

Funding: None.

Ethical approval: The study was approved by the Ethical Committee of Tianjin Medical University General Hospital, Tianjin, China.

Conflicts of interest: The authors declare that there is no conflict of interest.

Contributors: Wang LJ proposed the study, analyzed the data and wrote the first draft. All authors contributed to the design and interpretation of the study and to further drafts.

REFERENCES

- 1 Wang DB. Internal Medicine. Beijing: Peking University Medical Press 2012: 1019–1026.
- 2 Kang MS, Gil HW, Yang JO, Lee EY, Hong SY. Comparison between Kidney and Hemoperfusion for Paraquat Elimination. *J Korean Med Sci* 2009; 24: S156–160.
- 3 Tsujimoto H, Ono S, Hiraki S, Majima T, Kawarabayashi N, Sugawara H, et al. Hemoperfusion with polymyxin B-immobilized fibers reduced the number of CD16+CD14 + monocytes in patients with septic shock. *J Endotoxin Res* 2004; 10: 229–237.
- 4 Mitaka C, Tomita M. Polymyxin B-immobilized fiber column hemoperfusion therapy for septic shock. *Shock* 2011; 36: 332–338.
- 5 Yamamoto S, Kutsukake K. FljA-mediated posttranscriptional control of phase 1 flagellin expression in flagellar phase variation of *Salmonella enterica* serovar Typhimurium. *J Bacteriol* 2006; 188: 958–967.
- 6 Sato N, Kojima K, Horio Y, Goto E, Masunaga A, Ichiyasu H, et al. Successful treatment of severe amiodarone pulmonary toxicity with polymyxin B-immobilized fiber column direct hemoperfusion. *Chest* 2013; 143: 1146–1150.
- 7 Utrup TR, Mueller EW, Healy DP, Callcut RA, Peterson JD, Hurford WE. High-dose ciprofloxacin for serious gram-negative infection in an obese, critically ill patient receiving continuous venovenous hemodiafiltration. *Ann Pharmacother* 2010; 44: 1660–1664.
- 8 Eyer F, Felgenhauer N, Pfab R, Thürmel K, Zilker T. Treatment of severe intravenous phenytoin overdose with hemodialysis and hemoperfusion. *Med Sci Monit* 2008; 14: CS145–148.
- 9 Liu LY, Zhu YJ, Li XL, Liang YF, Liang ZP, Xia YH. Blood hemoperfusion with resin adsorption combined continuous veno-venous hemofiltration for patients with multiple organ dysfunction syndrome. *World J Emerg Med* 2012; 3: 44–48.
- 10 Guenzet J, Bourin M, Laurent D, Aminou T. Theoretical study of haemoperfusion: drugs obeying a one-compartment pharmacokinetics model. *Methods Find Exp Clin Pharmacol* 1985; 7: 259–268.
- 11 Zhang ZJ, Peng LB, Luo YJ, Zhou CY. Prospective experimental studies on the renal protective effect of ulinastatin after paraquat poisoning. *World J Emerg Med* 2012; 3: 299–304.
- 12 Chu JX, Shen JH, Jiang WH. Dynamic determination of the medicine concentration of poisoned blood of acephate. *Fa Yi Xue Za Zhi* 2006; 22: 217–219.
- 13 Lai DP, Ren XH, Yao JP, Liu ML, Xu G, Chen ZJ, et al. Study On the effect using hemoperfusion to treat tylenol poisoned patients. *Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi* 2012; 30: 310–312.
- 14 Mui EL, Cheung WH, Valix M, McKay G. Dye adsorption onto char from bamboo. *J Hazard Mater* 2010; 177: 1001–1005. Epub 2010 Jan 11.
- 15 Shiratori N, Lee KJ, Miyawaki J, Hong SH, Mochida I, An B, et al. Pore structure analysis of activated carbon fiber by microdomain-based model. *Langmuir* 2009; 25: 7631–7637.

Received April 21, 2013

Accepted after revision August 28, 2013