



Research Article

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Concentration change and clinical significance of plasma S100 protein in cardiopulmonary bypass perioperative period

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ABSTRACT

To seek for evaluation indicators of cerebral injury in cardiopulmonary bypass (CPB) perioperative period and discuss the change and clinical significance of S100 protein in CPB perioperative period. 40 patients of congenital heart disease or heart valve disease were subject to open-heart surgery under CPB. The occurrence of neurological complications in perioperative period was observed. The concentration of plasma S100 protein was measured at different time points in CPB perioperative period. 3 cases of neurological complications occurred after surgery, including 2 cases of mental symptom and 1 case of cerebral infarction. The start of CPB caused great increase of S100 protein plasma concentration which recovered to the preoperative level 24 to 48 hours after surgery. Patients with neurological complications had a significantly higher S100 protein concentration than those without neurological complications and their S100 protein concentration still maintained a high level 24 hours after surgery. CPB can cause significant increase of plasma S100 protein level and has important clinical significance for the evaluation of cerebral injury after surgery.

Key words: S100 protein; CPB; cerebral injury

INTRODUCTION

Though CPB and surgery technology have been further improved, cerebral injury is still one of the major complications after cardiac surgery. Seeking for a specific plasma biochemical indicator that can reflect cerebral injury has important clinical significance. In 2002, we preliminarily observed the change of brain specific protein S100 after CPB and the evaluation of cerebral injury.

EXPERIMENTAL SECTION

Clinical data

There were 40 cases in this group, including 28 males and 12 females at 18-68, and 13 cases with congenital ventricular septal defect repair, 2 cases with atrial septal defect repair, 23 cases with heart valve replacement surgery and 2 cases with heart valve replacement plus coronary artery bypass grafting. Through preoperative supersonic inspection, all patients had no carotid artery stenosis, hypertension, diabetes or history of neuropathy and psychosis and had normal renal function.

Method

Anesthesia induction: we gave 0.5 mg/kg midazolam, 0.5 mg/kg ketamine, 0.1~0.12 $\mu\text{g}/\text{kg}$ vecuronium bromide and 10 $\mu\text{g}/\text{kg}$ fentanyl. Maintenance of anesthesia: gave 40 $\mu\text{g}/\text{kg}$ fentanyl through intravenous drip till CPB started; inhaled 0.5%~1% isoflurane; added vecuronium bromide and midazolam at an interval of 1~1.5 hours; added diazepam, droperidol and morphine according to the situation in CPB; used moderate blood dilution; the packed cell volume after dilution was about 0.25~0.30; maintained anus temperature at 28~34 $^{\circ}\text{C}$ (perfusion flux was 2.2~2.4 $\text{L}\cdot\text{min}^{-1}/\text{m}^2$ at normal temperature; blood temperature was controlled at 50~80 mmHg (1 kPa=7.5 mmHg); used α steady state in CPB; arterial partial pressure of oxygen (PaO_2) was 250 mmHg; rewarmed to anus temperature 36 $^{\circ}\text{C}$ after the completion of intracardiac operation and stopped CPB after the circulation became steady.

We established regular CPB and conducted heart valve replacement or heart malformations diorthosis of congenital heart disease with front median incision. Mitral valve replacement was subject to right atrium interatrial septum admission passage; aortic valve replacement was subject to aorta ascendens root incision surgery; patients with ventricular septal defect repair were subject to right atrium parallel interatrial groove incision surgery.

Monitoring indicators and method

We conducted systematic neural examination 1 day before surgery and one day and seven days after surgery, mainly including standard clinical neurological function examination, and conducted CT, MRI and electroencephalogram (EEG) examination if necessary; used plasma S100 protein ELISA kit produced by American Biokey Company, collected 4ml venous blood through jugular vein before CPB, at 20 minutes after CPB started, at the end of CPB and at 2h, 4h, 8h, 24h and 48h after CPB and measured plasma S100 protein concentration.

Statistical treatment

Data in the result were expressed as mean \pm standard deviation ($\bar{x} \pm s$). Statistical method used one-way analysis of variance and SPSS 10.0 software was used for statistical analysis.

RESULTS AND DISCUSSION

Clinical result : All patients had a smooth surgery process. The average CPB time was 88.0 \pm 29.1 minutes and aortic cross clamp time was 55.7 \pm 23.8 minutes. Three cases (7.5%) of neurological complications occurred after surgery with CPB time respectively as 105 minutes, 120 minutes and 146 minutes, including 1 case of double valve replacement and 1 case of mitral valve replacement plus coronary artery bypass grafting. Mental symptom occurred after surgery in these cases which recovered to the normal level 7 days after surgery. There was one case of patient with mitral valve replacement plus coronary artery bypass grafting who suffered from large-area cerebral infarction at the right after surgery which was proved by CT examination.

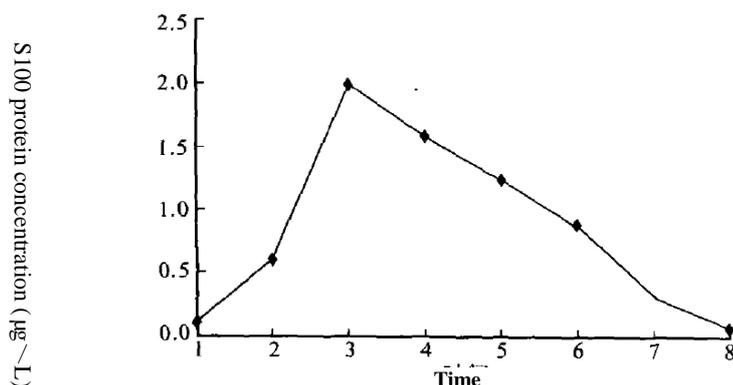


Fig-1 Change of S100 protein concentration in CPB perioperative period

Notes: 1: before CPB; 2: at 20min after CPB started; 3: at the end of CPB; 4: 2h after CPB; 5: 4h after CPB; 6: 8h after CPB; 7: 24h after CPB; 8: 48h after CPB

Change of plasma S100 protein concentration. After CPB started, S100 protein concentration in plasma of patients increased rapidly, which was 0.62 \pm 0.15 $\mu\text{g}/\text{L}$ at 20 minutes after CPB and reached the peak value (1.98 \pm 0.89 $\mu\text{g}/\text{L}$) at the end of CPB. The highest concentration was 2.31 $\mu\text{g}/\text{L}$. Plasma S100 protein concentration decreased steadily after the end of CPB and maintained a high level within 8 hours after CPB. See figure 1. Three patients with neurological complications after surgery had a significantly higher S100 protein concentration at the end of CPB

than other patients and their S100 protein concentration still maintained a high level 24 hours after surgery, respectively 0.52 $\mu\text{g} / \text{L}$, 0.8 $\mu\text{g} / \text{L}$ and 1.35 $\mu\text{g} / \text{L}$. For the patient with large-area cerebral infarction at the right, the plasma S100 protein concentration increased secondarily after surgery, which was 1.35 $\mu\text{g} / \text{L}$ at 24h and 2.41 $\mu\text{g} / \text{L}$ at 48.

CONCLUSION

3%~6% patients had obvious brain disorder after cardiac surgery^[1]. Neurologic and psychiatric examination found that the occurrence rate of cerebral injury was up to 60%~70%^[2-3]. Currently, the evaluation of cerebral injury can only be obtained through clinical neurologic and psychiatric examination, EEG, CT and MRI. Patients are in narcotism in early period of postoperation and require the support of breathing machine or their recirculating state is unstable. They are not suitable for or cannot coordinate with clinical examination. Therefore, specific biochemical indicators have very important clinical significance for the evaluation of cerebral injury. S100 is considered as the specific protein of brain. The concentration of S100 protein in plasma and cerebrospinal fluid has specificity for the evaluation of cerebral injury. It is not influenced by hemolysis, CPB, low temperature, heparin and diprivan etc^[4]. For patients with cerebral embolism, the concentration of S100 protein in plasma increases significantly. The higher the concentration, the larger the lesion area^[5].

Plasma S100 protein concentration higher than 0.5 $\mu\text{g} / \text{L}$ is considered as pathological level^[6]. Our observation found that all patients' plasma S100 protein concentration was lower than 0.5 $\mu\text{g} / \text{L}$ before CPB, rapidly increased after CPB started, reached the peak value at the end of CPB, gradually decreased within 8 hours hereafter and recovered to the preoperative level at 24~48h after surgery. These patients had a smooth postoperative recovery and no obvious neurologic and psychiatric symptom and sign were found. However, subclinical cerebral injury might exist. Three patients with neurological complications after surgery had a significantly higher S100 protein concentration at the end of CPB than other patients. For the patient with large-area cerebral infarction, the plasma S100 protein concentration increased again at 48h after surgery. S100 protein is a protein of large molecular weight and cannot pass blood brain barrier in normal situation. Cerebrospinal fluid and plasma have obvious concentration difference. The increase of its concentration in plasma was caused by brain tissue injury and the significant increase of permeability of blood brain barrier^[7]. Patients with neurological complications had a high level of plasma S100 protein concentration at the end of CPB, which still maintained a high level at 24~48h after CPB or increased again after decrease. It has been reported^[8] that plasma S100 protein concentration can reflect the degree of cerebral injury. The half-life period of plasma S100 protein was 3.5h^[9] on average after CPB and still maintained a high level at 6~8h after surgery, indicating that S100 protein is continuously released to blood. For patients in this group, plasma S100 protein level still maintained a high level at 8h after the end of CPB. For the patient with large-area cerebral infarction, S100 protein concentration increased secondarily after surgery, indicating that the concentration of S100 protein in plasma at the end of CPB might have certain clinical significance for the evaluation of the degree of cerebral injury, which will not necessarily have obvious clinical symptoms. The S100 protein level of patients with neurological complications mostly maintained a high level at 24~48h after surgery.

Our research shows that CPB can cause the increase of S100 protein level in plasma and it can evaluate the degree of cerebral injury after CPB. Continuous postoperative monitoring has important value for the diagnosis of brain function defect and judgment of prognosis.

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