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Effect of fast-track cardiac anesthesia on myocardial oxidative damage, inflammation and nerve related peptides of patients undergoing cardiac operation

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ABSTRACT

Objective: To study the effect of fast-track cardiac anesthesia on myocardial oxidative damage, inflammation and nerve related peptides of patients undergoing cardiac operation. **Methods:** Sixty patients with rheumatic heart disease undergoing heart valve surgery were randomly divided into the fast track group (n=30) and conventional group (n=30). Then myocardial injury indicators, mitochondrial oxidative stress indicators, inflammation indicators and nerve-related peptides of both groups were analyzed. **Results:** cTnI contents at T2-T4 points in time of both groups showed an increasing trend and the increasing trend of fast track group was weaker than that of conventional group; SOD contents as well as mitochondrial tristate respiratory function, respiratory control ratios and phosphorus oxygen ratios in myocardial tissue of fast track group were higher than those of conventional group, and MDA contents was lower than those of conventional group; plasma TNF-α, IL-6, IL-8, NSE, S100β and Aβ contents of fast track group were lower than those of conventional group. **Conclusions:** Fast-track cardiac anesthesia can protect myocardial cells, reduce mitochondrial oxidative stress, relieve inflammation and improve nerve function; it is an ideal anesthesia method for cardiac operation.

1. Introduction

Cardiac operation is a clinical common method of surgical treatment of congenital heart disease and rheumatic disease. Intraoperative ligaturing and reopening vessels will result in ischemia-reperfusion of myocardial cells, which will produce a large number of oxygen free radicals, cause oxidative stress damage and thereby affect the function of myocardial cells. During the operation, effective anesthesia method is needed to protect myocardial cells from oxidative stress damage without affecting the depth of anesthesia or causing neurological damage. Fast-track cardiac anesthesia is a new anesthesia concept developed in recent years, which uses sufentanil, sevoflurane and other anesthetics to improve the anesthetic effect and increase the controllability of anesthetic depth[1]. In the following research, the effect of fast-track cardiac anesthesia on myocardial oxidative damage, inflammation and nerve related peptides of patients who received cardiac operation was analyzed.

2. Materials and methods

2.1. Clinical information

Clinical case information. With approval of ethics committee, 60 patients with rheumatic heart disease undergoing heart valve surgery were selected for study. They were clearly diagnosed of rheumatic heart disease and conformed to surgical indication, with ASA grading of II grade or III grade. Those with autoimmune diseases

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or insufficiency of liver, kidney and lung function were excluded. According to anesthesia method, enrolled patients were randomly divided into fast track group (n=30) and conventional group (n=30).

Anestheisa methods: Fast track group received intramuscular injection of 0.3 mg scopolamine and 1 mg/kg pethidine 0.5 h before operation, received 1 μg/kg sufentanil, 0.1–0.2 mg/kg cisatracurium, 10–20 mg/kg disoprofol, 0.1–0.3 mg/kg etomidate and 0.1–0.2 mg/kg midazolam in anesthesia induction, received 2%–3% sevoflurane inhalation after nasotracheal intubation, received additional 1 μg/kg sufentanil before skin incision and thoracotomy respectively, and after thoracic cavity closure, sevoflurane concentration was adjusted to 1%. Conventional group received intramuscular injection of 0.3 mg scopolamine and 1 mg/kg pethidine 0.5 h before surgery, received 5–10 μg/kg fentanyl, 0.1–0.2 mg/kg cisatracurium and 10–20 mg/kg disoprofol in anesthesia induction and received sustained micro-pump implantation of 5 μg/(kg•min) fentanyl and 10 μg/(kg•min) disoprofol after endotracheal intubation.

2.2. Experimental methods

Plasma specimen collecting and index detecting methods: before arterial occlusion (T1), at 15 min (T2), 30 min (T3), 60 min (T4) and 180 min (T5) after arterial opening, heparin anticoagulation blood was collected and centrifuged to get plasma specimens, and Elisa was used to detect cTnI contents at T1-T5 points in time as well as TNF-α, IL-6, IL-8, NSE, S100β and Aβ contents at T5 point in time. Detecting methods of oxidative stress indicators in myocardial tissue: after extracorporal circulation ended, moderate amount of myocardial tissue of the left atrial appendage was collected, thiobarbituric acid assay kits were used to detect MDA contents, and xanthine oxidase assay kits were used to detect SOD activity.

Detecting methods of mitochondrial respiratory function: Clark oxygen electrode method was used to detect mitochondrial respiratory oxygen consumption, respiratory reaction media included 225 mmol/L mannitol, 75 mmol/L sucrose, 10 mmol/L KCl, 200 mmol/L Tris-HCl, 3 mmol/L sodium phosphate and 0.1 mmol/L EDTA, 1 mmol/L glutamic acid and 0.1 mmol/L malic acid were added to reaction system and then mitochondrial respiratory process was initiated, 200 nmol/L ADP was added and then tristate respiration was started, and when reaction curves showed obvious inflection point, four state respiration started; tristate respiratory rates, respiratory control ratios and phosphorus oxygen ratios (P/O) were calculated.

2.3. Statistical analysis methods

SPSS21.0 software was used for statistical analysis. Comparison between two groups was by t test and comparison of different points in time within group was by repeated measure analysis of variance. Differences were considered to be statistically significant at a level of $P<0.05$.

3. Results

Plasma cTnI contents and variation trends of both groups were shown in Figure 1 and Table 1. At T1 point in time, cTnI contents of two groups had no differences; compared with T1 point in time, cTnI contents at T2-T4 points in time of both groups showed an increasing trend, and comparison of different points in time within group had differences ($P<0.05$); at T2-T4 points in time, compared with conventional group, plasma cTnI contents of fast track group significantly decreased, and comparison of same point in time between two groups had differences ($P<0.05$).

Mitochondrial oxidative stress injury indicators of both groups were shown in Figure 2 and Table 2. Figure 2 was for contents of oxidative stress related molecules in myocardial tissue of both groups: SOD contents in myocardial tissue of fast track group were higher than those of conventional group and MDA contents were lower than those of conventional group; Table 2 was for mitochondrial function indicators in myocardial tissue of both groups: mitochondrial tristate respiratory function, respiratory control ratios and phosphorus oxygen ratios in myocardial tissue of fast track group were higher than those of conventional group.

Contents of inflammation indicators and nerve related peptides of both groups were shown in Table 3. Inflammation indicators included tumor necrosis factor (TNF-α), interleukin-6 (IL-6) and interleukin-8 (IL-8); nerve related peptides included neuron specific enolase (NSE), S100β protein (S100β) and β-amyloid protein (Aβ). Detailed analysis results were as follows: plasma TNF-α, IL-6, IL-8, NSE, S100β and Aβ contents of fast track group were lower than those of conventional group.

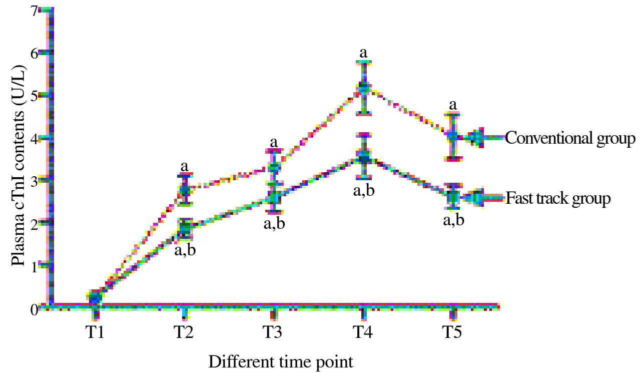

Figure 1. Variation trends of plasma cTnI contents of both groups.

Dotted line is for conventional group and solid line is for fast track group; plasma cTnI contents of both groups showed an increasing trend and the increasing trend of fast track group was weaker. [a]: compared with T1 point in time within same group, there are differences; [b]: compared with conventional group at same point in time, there are differences.

Table 1
Comparison of cTnI contents at different points in time between two groups.

Group	T1	T2	T3	T4	T5
Fast track group	0.24±0.03	1.84±0.22[ab]	2.59±0.33[ab]	3.54±0.51[ab]	2.60±0.27[ab]
Conventional group	0.22±0.02	2.76±0.33[a]	3.29±0.38[a]	5.18±0.60[a]	4.02±0.51[a]

[a]: compared with T1 point in time within same group, there are differences; [b]: compared with conventional group at same point in time, there are differences.

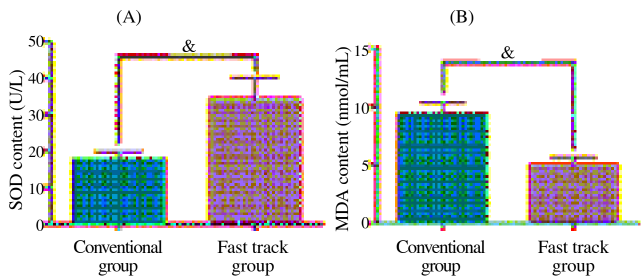

Figure 2. Contents of oxidative stress related molecules in myocardial tissue of both groups. Left figure is for SOD contents and right figure is for MDA contents.

4. Discussion

Fast-track anesthesia is a newly developed technology of anesthesia with advantages of strong controllability of intraoperative depth of anesthesia and fast postoperative recovery, and it is conducive to early extubation, reducing ICU staying time and promoting postoperative recovery[2]. In recent years, fast-track cardiac anesthesia is more and more used in cardiac operation and related studies of domestic and foreign scholars have also confirmed that it has positive value for stabilizing intraoperative vital signs and promoting postoperative recovery[3]. At present, most studies on fast-track cardiac anesthesia focus on intraoperative vital signs and other macroeconomic indicators as well as postoperative recovery speed and other subjective indicators, and the potential molecular targets about how the anesthesia method regulates body function are still to be elucidated.

In the process of implementing fast-track cardiac anesthesia, sufentanil was used instead of fentanyl. Its affinity for μ opioid receptor is more than 10 times of that of fentanyl, and it more easily penetrates the blood-brain barrier and the cell membrane, has stronger narcotic analgesic effect and weaker inhibition of respiration, and can meet the myocardial oxygen supply[4]. Besides, sufentanil has the effect of both dilating vascular smooth muscle and reducing vascular resistance, and is favorable for the stability of intraoperative vital signs[5]. The drug selected for intraoperative anesthetic maintenance was sevoflurane. Its narcotic effect is exact and faster to be cleared, and it can improve the controllability of anesthetic depth and thereby avoid cardiac injury and nerve function injury caused by excessive anesthesia[6].

Occlusion and opening of blood vessels during cardiac operation can cause myocardial ischemia and reperfusion, and thereby cause myocardial cell damage through oxidative stress injury, inflammation injury and other ways. Myocardial cells are rich in enzymes and structural proteins, and in the case of cell damage and destruction, a variety of molecules in cytoplasm will be released into plasma. cTnI is a subtype of troponin specifically existing in myocardial cells, and plasma cTnI level can accurately reflect the degree of myocardial cell injury. Analysis of serum cTnI contents at different points in time showed that cTnI contents of both groups showed an increasing trend after opening of aorta and the increasing trend of cTnI contents of fast track group was weaker than that of conventional group, which indicated that myocardium protective effect of fast-track cardiac anesthesia was superior to that of conventional anesthesia.

Myocardial ischemia-reperfusion will generate large amounts of oxygen free radicals in local part and damage myocardial cells through oxidative stress injury[7]. Myocardial mitochondria is an

Table 2
Mitochondrial respiratory function indexes in myocardial tissue of both groups.

Group	Sample No.	Tristate respiratory function [nmol/(min·mg protein)]	Respiratory control ratio (RCR)	Phosphorus oxygen ratio (P/O)
Fast track group	30	305.62±34.23	10.14±1.32	4.68±0.55
Conventional group	30	214.55±22.49	7.64±0.89	3.62±0.43
t		6.283	6.968	5.293
P		<0.05	<0.05	<0.05

Table 3
Comparison of inflammation indicators and nerve related peptides of both groups.

Group	Nerve related peptides			Inflammation indicators		
	NES (ng/mL)	S100β (ng/L)	Aβ (ng/L)	TNF-α (ng/L)	IL-6 (ng/L)	IL-8 (ng/L)
Fast track group	6.73±0.84	522.32±65.53	245.24±30.45	23.49±3.43	41.23±5.69	67.59±9.34
Conventional group	11.38±1.34	847.80±90.34	409.28±40.50	50.14±6.29	79.14±9.49	109.45±12.58
t	8.823	7.928	8.283	11.384	8.856	9.109
P	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

important target of oxygen free radical injury, and oxygen free radicals can directly damage proteins and lipids in mitochondrial membrane structure, interfere with mitochondrial respiratory function and cause disorder of ATP generation and insufficient energy supply of myocardial cells[8]. In the process of myocardial mitochondrial oxidative stress, large amounts of reducing substances SOD in the cytoplasm are consumed, and large amounts of lipid peroxidation products MDA are generated[9], accompanied by mitochondrial respiratory function disorder at the same time[10–11]. Contents of oxidative stress related molecules and mitochondrial respiratory function were evaluated respectively, and results showed that SOD contents as well as mitochondrial tristate respiratory function, respiratory control ratios and phosphorus oxygen ratios in myocardial tissue of fast track group were higher and MDA contents was lower, which could reflect the reducing effect of fast-track cardiac anesthesia on oxidative stress response as well as the protective effect on mitochondrial respiratory function.

Ideal anesthesia method during operation not only helps to protect myocardial cells, but can also effectively control the depth of anesthesia, avoid nerve function injury caused by deep anesthesia level and improve postoperative cognitive function. Inflammation is considered as one of the important ways to cause neuronal damage, and study has shown that release of inflammatory mediators in gliacytes as well as inflammation around the hypothalamus are closely related to neurological damage[12]. TNF-α is an important initiator of inflammation; IL-6 and IL-8 are pro-inflammatory factors that promote differentiation and activation of a variety of inflammatory cells in the early inflammatory response[13]. Enhanced inflammation will cause mass release of NSE and S100β in neurons and gliacytes and mass accumulation of Aβ, and thereby lead to neurological damage and increase the risk of postoperative cognitive dysfunction[14,15]. Analysis of postoperative serum inflammation indicators and nerve related peptides showed that serum TNF-α, IL-6, IL-8, NSE, S100β and Aβ contents of fast track group were lower than those of conventional group.

Based on above discussions and analysis, it is concluded that fast-track cardiac anesthesia is an ideal anesthesia method for cardiac operation because it can more effectively protect myocardial cells, reduce mitochondrial oxidative stress, relieve inflammation and improve nerve function.

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