Original Article

Influence of different anesthesia methods on the cognitive ability and myocardial damage in cardiac surgery

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Abstract: Objective: Cardiac surgery is associated with some degree of cognitive dysfunction and myocardial injury. The aim of this study was to investigate the effect of two anesthesia methods on cognitive ability and myocardial damage in cardiac surgery patients. Methods: 90 patients undergoing cardiac surgery were collected in the study and were randomly divided into sevoflurane (S) and propofol (P) group. MMSE was performed to measure the cognitive function of patients. Heart rate (HR), mean arterial pressure (MAP), cardiac index (CI), and cardiac function index (CFI) were monitored and cardiac troponin I (cTnI), myoglobin, and creatinine kinase MB isoenzyme (CKMB) were determined using sandwich enzyme immunoassay method. Results: Compared to T0 time, the MMSE score was significantly decreased at T2 and T3 in both S and P groups, but no significant difference was found between the two groups. Moreover, there were no differences for any of the haemodynamic variables between the two groups, except CI at T4 time. And the concentration of cTnI, myoglobin, and CKMB increased significantly post-operatively with a peak at T2 time point in S and P groups. The level of cTnI and CKMB was lower in S group than in P group at T2. Conclusions: No significant difference was found on the influence of two anesthesia method on post-operative cognitive function. The implementation of sevoflurane anesthesia in cardiac surgery may exhibit a more favorable cardioprotective function and promote patients recovery.

Keywords: Sevoflurane, propofol, cardiac surgery, cognitive, myocardial damage

Introduction

Cognitive dysfunction and myocardial injury are common complications in patients undergoing cardiac surgery, which can result in organ failure, length hospital stay and harmful daily life [1, 2]. Several approaches have been performed to protect the myocardium from damage in cardiac surgery [3]. Inhaled anesthetic agents have a major protective effect in myocardial ischemia and reperfusion damage [4, 5]. Some specific anesthetic agents like isoflurane and sevoflurane can regulate this phenomenon. The mechanisms involved in the protective effect of volatile anesthetic regimens are opening of mitochondrial KATP channels, activation of p38 mitogen-activated protein kinase and an increase in mitochondrial reactive oxygen species [6-8].

Sevoflurane is one of the newest anesthetic drugs with fast induction of anesthesia and fast regression in comparison with other drugs. Previous studies on sevoflurane have shown that sevoflurane is effective in post ischemic repair and can cause a decrease in infarction size and threshold time for ischemic preconditioning (IPC) [9]. While propofol as an intravenous anesthetic agent can reduce myocardial dysfunction after ischemia, infarction size and tissue degeneration due to ischemia but in some other studies it has not shown any protection against ischemic and reperfusion damage could not have drug effect with stimulation of IPC [10].

Postoperative cognitive dysfunction is a common postoperative complications of many major surgery. The main performance for post-operative patients were memory, abstract thinking ability and directional force defects, often accompanied with decreased social activity ability. The cognitive dysfunction usually
result in prolonged hospital time, delayed recovery time, and increased mortality [11, 12]. The type of anesthesia has been assumed to be associated with the incidence of cognitive dysfunction and, and the anesthesia depth might influence the protection of brain function [13]. However, there is few studies to compare the effect of different anesthesia on postoperative cognitive and cardioprotective in patients undergoing cardiac surgery.

In this study, we investigate the value of sevoflurane and propofol in myocardial protection and effect on postoperative cognitive function.

**Materials and methods**

**Patients collection**

This study was approved by the Ethics Committee of Shanghai Jiaotong University Affiliated Shanghai Sixth People’s Hospital. The written informed consents were provided by the participants in advance.

In this study, we selected 90 patients who were scheduled for valve replacement operation which required at least 4 h of postoperative sedation. The exclusion criteria included patients with a Tu score >9, an ejection fraction of less than 30%, recent myocardial infarction (<4 weeks), uncontrolled hypertension, congestive cardiac failure, atrioventricular or left bundle-branch block, suffering from mental illness, any hepatic, renal, or pulmonary disease, any allergy to trial medications, or chronic opioid consumption. The patients were allocated randomly into one of two groups according to the drug used during anaesthesia: the control group (propofol, P, n=45) and the study group (sevoflurane, S, n=45).

The patients’ anesthesiologist and intensive care unit (ICU) physicians were blinded to group allocation in this investigation. All clinical data were recorded by a clinical research assistant not involved with the clinical care of the patient.

**Anesthesia treatment**

Anaesthetic induction was carried out with midazolam 0.1-0.3 mg kg⁻¹, etomidate 0.2-0.4 mg kg⁻¹, fentanyl 2-40 mg kg⁻¹ and cisatracurium 0.1 mg kg⁻¹. In group S, anaesthesia was maintained with sevoflurane, administered through the AnaConDa, using paediatric infusion pumps (model P7000, Alaris, Carefusion, Switzerland) with syringes preloaded with 50 ml of liquid sevoflurane. The infusion rate for maintaining anaesthesia was set to obtain an end-tidal sevoflurane concentration of 0.7-1.5%, adjusting the infusion rate to obtain a bispectral index (BIS) of 40-60 (with a quality signal index of >80%). In the postoperative period, the infusion rate was adjusted to obtain an end-tidal concentration of 0.5-1% in order to obtain target sedation with a target evaluated by BIS 55-65. In group P, propofol was administered using the same pumps with syringes preloaded with 50 ml of propofol 1%. During the intraoperative period, maintenance was achieved with an infusion of 4-10 mg kg⁻¹h⁻¹ in order to obtain a BIS of 40-60. In the postoperative period, the initial infusion rate was set at 1-4 kg⁻¹h⁻¹, which was then modified to achieve target sedation similar to that applied in group S.

**Monitoring cognitive function**

Simple intelligence state scale (MMSE) was performed to measure the cognitive function of patients with preoperative 12 h (T0), 12 h post-operation (T2), 24 h post-operation (T3) and 48 h post-operation (T4). We defined the time admission to ICU as T1. The cognitive assessment was carried at afternoon 3 o’clock, and MMSE score decreased ≥1 point than preoperative score was judged as postoperative cognitive dysfunction.

**Haemodynamic management and biomarker determination**

Heart rate (HR), mean arterial pressure (MAP), cardiac index (CI), and cardiac function index (CFI) were monitored using a radial arterial catheter and pulmonary artery catheter (Spacelabs Healthcare, Issaquah, WA). Data were collected at T0, T1, T2, T3 and T4.

Blood samples were collected at T0, T1, T2, T3 and T4. Concentrations of cardiac troponin I (cTnI), myoglobin, and creatinine kinase MB isoenzyme (CKMB) were determined in plasma using sandwich enzyme immunoassay method with the biochemical analyser Dimension (Siemens Healthcare Diagnostics, Deerfield, Illinois, USA).

**Statistical analysis**

Statistical analyses were performed using the SPSS 18.0 software and Graphpad Prism 5.
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software. The data were expressed as mean and standard deviation (SD). Categorical variables were compared using Chi-square test and continuous variables between groups were analyzed by unpaired t test. Data for the biochemical markers (cTnI, CKMB, myoglobin) were analyzed for normality with the Kolmogorov-Smirnov test. The differences were considered statistically significant when \( P \) values were less than 0.05.

Results

General information of the patients

90 patients were recruited and randomized into either sevoflurane (n=45), or propofol (n=45) group. There were no significant differences in patient characteristics in terms of demographics, medications and pre-existing medical conditions (all, \( P > 0.05 \), Table 1).

Comparison of cognitive function in the two groups of patients

MMSE was used to measure the cognitive function of patients, and the results showed that compared to T0 time, the MMSE score was significantly decreased at T2 and T3 time points in both S and P groups (\( P < 0.05 \), Table 2). However, no significant difference was found between the two groups at each time point (Table 2).

Haemodynamic stability and myocardial biomarkers in the two groups

There were no differences for any of the haemodynamic variables including HR, MAP, CI and CFI between the two groups (all, \( P > 0.05 \), Table 3). Moreover, compared to variables values at T0 only CI in S groups showed significant difference at T4 (\( P < 0.05 \), Table 3).

As a result, the values of myocardial biomarkers including cTnI, myoglobin, and CKMB were not normal at any of the studied time points (T1-T4). The concentration of cTnI, myoglobin, and CKMB increased significantly post-operatively with a peak at T2 time point (Figures 1-3). What’s more, the value of cTnI, and CKMB was significantly different in S group compared to P group (\( P < 0.05 \), Figures 1, 2).

Discussion

With the development of science and technology, the medical level of cardiac surgery, anesthesia and cardiopulmonary bypass have constantly improved. The mortality rate in cardiac surgery and some serious complications like infection, blood loss and stroke have significantly reduced [14, 15]. However, the cognitive dysfunction after cardiac surgery is still a big trouble for surgeons and anesthesiologists. Therefore, how to prevent and reduce the incidence of postoperative cognitive dysfunction in patients after heart surgery especially valvular surgery perioperative clinical research related personnel is a key point. In this study, we assessed the effect of two anesthetic drugs on postoperative cognitive dysfunction in cardiac surgery patients. The results showed that compared to the time preoperative 12 h, the MMSE score in both sevoflurane and propofol groups were significantly decreased at 12 h post-operation and 24 h post-operation. But no significant difference was found between the two groups at any time point.

Table 1. General information of patients with cardiac surgery

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>S group (n=45)</th>
<th>P group (n=45)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (year)</strong></td>
<td>53.7±4.3</td>
<td>54.2±3.7</td>
<td>0.657</td>
</tr>
<tr>
<td><strong>Gender (male/female)</strong></td>
<td>29/16</td>
<td>30/15</td>
<td>0.824</td>
</tr>
<tr>
<td><strong>Height (cm)</strong></td>
<td>168.2±7.6</td>
<td>165.7±7.8</td>
<td>0.710</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>75.9±11.8</td>
<td>76.2±12.7</td>
<td>0.155</td>
</tr>
<tr>
<td><strong>BMI (kg/m(^2))</strong></td>
<td>25.3±3.1</td>
<td>26.4±3.5</td>
<td>0.137</td>
</tr>
<tr>
<td><strong>ASA grade (II/III)</strong></td>
<td>24/21</td>
<td>22/23</td>
<td>0.673</td>
</tr>
<tr>
<td><strong>Surgery time (min)</strong></td>
<td>208.4±51.2</td>
<td>211.6±49.9</td>
<td>0.886</td>
</tr>
<tr>
<td><strong>CPB time (min)</strong></td>
<td>105.7±22.4</td>
<td>107.3±21.6</td>
<td>0.176</td>
</tr>
<tr>
<td><strong>Anesthesia time (min)</strong></td>
<td>278.4±19.5</td>
<td>276.9±46.3</td>
<td>0.391</td>
</tr>
<tr>
<td><strong>Preoperative haemoglobin (mg/dL)</strong></td>
<td>13.8±1.6</td>
<td>13.7±1.5</td>
<td>0.467</td>
</tr>
<tr>
<td><strong>Mean Euroscore II</strong></td>
<td>6.5±3.7</td>
<td>6.2±3.9</td>
<td>0.408</td>
</tr>
</tbody>
</table>

Table 2. Comparison of MMSE score at different time points in the two groups

<table>
<thead>
<tr>
<th>Time</th>
<th>S group</th>
<th>P group</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>29.15±0.76</td>
<td>29.03±0.81</td>
</tr>
<tr>
<td>T1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>T2</td>
<td>22.01±0.71*</td>
<td>22.51±0.64*</td>
</tr>
<tr>
<td>T3</td>
<td>23.74±0.56*</td>
<td>24.11±0.78*</td>
</tr>
<tr>
<td>T4</td>
<td>25.24±0.61</td>
<td>25.83±0.84</td>
</tr>
</tbody>
</table>

*, in the same group compared to T0, \( P < 0.05 \); -indicated no data.
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It is reported that cardiac surgery constitutes a suitable but still suboptimal model for the study of potential cardioprotective effects of anesthesia agents [16]. Previous studies have also shown that the use of anesthesia agents decrease the use of vasopressors [17, 18]. Volatile anaesthetics improve recovery of contractile function of the stunned myocardium. Sevoflurane increased blood flow in the brain, liver and heart after implantation of an left ventricular assist device in healthy minipigs [19]. The cardioprotective effect was independent of changes in coronary blood flow or a reduction in cardiac work. In addition to its preconditioning effects, sevoflurane also appears to exhibit cardioprotective effects against reperfusion injury. This effect has been attributed to its radical scavenging properties and the reduction of post-ischaemic adhesion of neutrophils [20]. Moreover, It has been suggested that sevoflurane may preserve myocardial function better than propofol in patients under-going coronary artery bypass surgery. Troponin I concentration was significantly lower in the sevoflurane group than in the propofol group [21, 22]. Compared with propofol, anaesthesia with either sevoflurane or desflurane resulted in a shorter duration of stay in the ICU in adults after coronary artery surgery [23, 24].

In our study, the demographic characteristics of patients were equal and with no significant difference. There were no differences for any of the haemodynamic variables including HR, MAP, CI and CFI between the two groups. In addition, the concentration of cTnI, myoglobin, and CKMB increased significantly post-operatively with a peak at 12 h after cardiac surgery. The level of cTnI is a sensitive and specific marker of myocardial injury. A sevoflurane induced reduction in cTnI levels is associated with a lower incidence of late adverse cardiac events [25]. The current study showed that use of sevoflurane led to a relative decreased cTnI and CKMB level compared with the propofol group.

There are several shortages of the research: first the sample size is relatively insufficient and statistics results might have bias; second, the time is short, within the postoperative 48 h after surgery making most of biochemical indicators observed only in the early postoperative;

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group</th>
<th>T0</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>S</td>
<td>75±14</td>
<td>68±11</td>
<td>85±20</td>
<td>83±9</td>
<td>76±12</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>79±12</td>
<td>70±16</td>
<td>83±23</td>
<td>86±11</td>
<td>81±13</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>S</td>
<td>84±14</td>
<td>67±15</td>
<td>85±18</td>
<td>88±17</td>
<td>80±11</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>86±16</td>
<td>71±18</td>
<td>83±17</td>
<td>90±18</td>
<td>82±13</td>
</tr>
<tr>
<td>CI (L/min/m²)</td>
<td>S</td>
<td>1.9±0.1</td>
<td>2.6±0.8</td>
<td>3.0±0.6</td>
<td>3.1±0.5</td>
<td>3.2±0.4*</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>1.8±0.2</td>
<td>2.7±0.6</td>
<td>3.2±0.6</td>
<td>3.2±0.6</td>
<td>3.6±0.8</td>
</tr>
<tr>
<td>CFI (min⁻¹)</td>
<td>S</td>
<td>3.6±1.1</td>
<td>5.1±1.4</td>
<td>4.7±1.2</td>
<td>4.5±1.1</td>
<td>4.4±1.1</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>3.8±1.0</td>
<td>4.9±1.2</td>
<td>4.6±0.9</td>
<td>4.5±1.3</td>
<td>4.3±1.0</td>
</tr>
</tbody>
</table>

HR, heart rate; MAP, mean arterial pressure; CI, cardiac index; CFI, cardiac function index. *, compared to T0, P<0.05.
third, lack of long-term follow-up data. Despite the lacking significance of our data, promising trends are reported, which might translate in reduced postoperative adverse events and reduced treatment cost. This emphasizes the importance of collecting clinical outcome data on this important topic in the future. Larger randomized trials are highly likely to reveal an improved clinical outcome by exposure to volatile anesthetics.

In summary, our results showed that postoperative cognitive dysfunction was observed in cardiac surgery patients. The MMSE score before and after surgery in sevoflurane group was less than in the propofol group but with no statistically difference. Additionally, sevoflurane anesthesia has a better cardioprotective effect on patients undergoing cardiac surgery according to several indicators than propofol anesthesia.

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Disclosure of conflict of interest

None.

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