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Review Article

Effect of Low-dose dexmedetomidine on hemodynamics and postoperative outcome in patients undergoing anesthesia during off-pump coronary bypass surgery

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Abstract: To investigate the effect of dexmedetomidine (Dex) combined with sevoflurane on hemodynamic and postoperative outcome in patients undergoing Off-pump Coronary Artery Bypass (OPCAB) surgery. In this study, 70 patients who were initially treated with OPABS surgery were divided into the control group (CG) and the experimental group (EG). Before the operation, remifentanil combined with sevoflurane and Dex combined with sevoflurane were given respectively to induce anaesthesia. The changes of heart rate (HR), mean artery pressure (MAP), central venous pressure (CVP), cardiac displacement (CO), cardiac index (CI), mean pulmonary artery pressure (MPAP), and systemic vascular resistance (SVR) were monitored. The bi-spectral-index (BIS) and arterial lactic acid values, the duration of anaesthesia during surgery, the duration of surgery, the duration of wakefulness and extubation, and the volume of infusion and urine during surgery were monitored. Pain, nausea, vomiting, cognitive dysfunction, and other anaesthesia complications were observed within 7 days after surgery. The results showed that the time to awaken and extubation time in the EG were much shorter than that in the CG ($P<0.05$). Furosemide dose was less than that of the CG ($P<0.05$). Anaesthesia depth and arterial lactic acid value were lower than the CG ($P<0.05$). At the time of incision, descending before operation, leaving the room, and entering the ICU, as well as HR, MAP, CVP, MPAP, and SVR in the EG were greatly lowered than those in the CG ($P<0.05$), and CO and CI were higher than those in the CG ($P<0.05$). The probability that patients experienced agitation and nausea post-operation was greatly lower in the EG ($P<0.05$), indicating that Dex and sevoflurane anaesthesia induction was conducive to hemodynamic stability in patients undergoing OPABS surgery, can improve the patient's circulation perfusion, have a diuretic effect, and at the same time can also shorten the awaken time and extubation time of patients, and reduce risk of complications of postoperative irritability and nausea.

Keywords: OPABS surgery, Dex, remifentanil, hemodynamics, complications

Introduction

OPABS surgery has been widely used in clinical practice, which can greatly reduce the probability of perioperative nervous system injury caused by cardiopulmonary bypass, reduce the damage of myocardial function during operation, reduce perioperative bleeding and blood transfusion, as well as being good for postoperative pain relief, and reduces the probability of postoperative complications in respiratory, urinary and endocrine systems [1, 2]. Studies have shown that hemodynamic indicators can be greatly changed in patients with OPABS surgery due to cardiac movement, fixator, compression of the heart and intermittent interruption of coronary artery flow [3]. Therefore, how to improve the safety of OPABS surgery and improve the outcome of patients was the key issue of study. However, the commonly used hemodynamic indicators in OPABS surgery include heart rate, arterial pressure, central venous pressure, pulmonary artery pressure, stroke-volume (SV), cardiac output, right ventricular ejection fraction (RVEF), cardiac displacement, etc. [4, 5]. By monitoring the changes of hemodynamic indicators during surgery, doctors can clearly understand the status of patients, so that doctors can change the corresponding surgical instrument parameters according to the patient's changes, and ensure the safety of surgery.

Effective sedation and analgesia after surgery can provide comfort and safety for patients, and also can effectively reduce the incidence of postoperative anxiety and other complications. Patients with coronary heart disease need to follow a balance of myocardial oxygen supply and demand during pre-operative anaesthesia, and both anaesthesia and surgical mechanical stimulation will cause hemodynamic changes in patients, which is mainly caused by stress that promotes the production of catecholamine and other hormones [6, 7]. In patients with coronary heart disease during anaesthesia for non-stenting coronary artery bypass surgery, malignant stimulation will increase the probability of myocardial ischemia. Therefore, it is necessary to give patients beta-blockers, vasodilators, and local anaesthetic drugs before surgery to reduce the probability of myocardial ischemia during surgery. Previous studies have shown that Dex can protect patients' heart, nervous system and kidneys from ischemia and hypoxic injury during surgery [8]. In addition, the application of Dex in clinical anaesthesia can reduce the incidence of hypotension and other cardiovascular side effects. In addition, studies have shown that it can reduce the probability of postoperative delirium complications in patients [9]. Therefore, dexmedetomidine is often used in the anaesthesia of heart-related surgery and improves patients' systemic vascular resistance index, MAP, etc. [10]. However, there are few studies on the hemodynamic changes of patients with Dex after anaesthesia induction in OPABS surgery.

In this research, patients who underwent OPABS surgery were divided into two groups. Before surgery, patients were given remifentanil (CG), or a small dose of Dex (EG) and anaesthesia induction with sevoflurane respectively. The differences of infusion volume, total urine volume, furosemide dose, operation time, anaesthesia time, postoperative recovery time and extubation time were compared. Monitoring instruments were used to monitor the changes and differences of hemodynamic parameters before anaesthesia induction, before branch descending surgery and after leaving the operating room. The arterial blood lactate concentration of patients in the two groups was compared at the time of admission, the time of anterior branch descending operation, the time of anestesia exit and the day after surgery. The differences in anaesthesia depth before incisional surgery, branch descending surgery, after exenteration and the incidence of postoperative complications such as irritability, nausea, vomiting, delirium and cognitive impairment were compared. The purpose of this research is to provide a theoretical basis for the application of Dex in anaesthesia induction of OPABS surgery in subsequent clinical coronary heart disease patients.

Materials and methods

Research subjects

From August 2017 to December 2018, patients from the Cardiac Surgery Department of The First Affiliated Hospital of Xiamen University who received their first OPABS surgery were selected. Inclusion criteria: patients diagnosed with IV by the American society of anaesthesiologists grade specified criteria [11]; people whose cardiac function was diagnosed at III level; people whose heart ejection fraction was greater than 50%. Exclusion criteria: patients with severely abnormal liver function; patients with severe renal dysfunction; patients with acute myocardial infarction and obstructive emphysema within the most recent 6 weeks; patients with moderate or severe valvular disease; those with a pacemaker. The procedures of this research have been approved by the Ethics Committee of The First Affiliated Hospital of Xiamen University and this study is in line with the Declaration of Helsinki. All patients included in this research have signed an informed consent.

Sample size calculation test group

According to the following equation, the sample content required by this study is calculated as follows.

$$n_1 = n_2 = 2 \cdot \left(\frac{\mu_\alpha + \mu_\beta}{\delta/\sigma}\right)^2 + \frac{\mu_\alpha^{\ 2}}{4} \qquad (1)$$

According to the principle of bilateral inspection level, α=0.05, β=0.1, then 1-β=0.90, assuming $\frac{\delta}{\sigma}$=0.80, it can be estimated that the sample content should be 34 cases per group. Therefore, there were 35 patients selected in each group, a total of 70 patients, who were initially treated with OPABS surgery as the study subjects. The patients were divided into two groups with a 1:1 ratio: the CG received remifentanil combined with sevoflurane anaesthesia induction, and the EG received Dex combined with sevoflurane anaesthesia induction.

Surgical anesthesia

All patients were given 0.1 mg/kg diazepam tablets orally one night before the operation and 1 h before the operation, 30 mg metoprolol tartrate tablets were also taken 1 h before the operation, and 0.2 mg/kg morphine hydrochloride and 0.3 mg scopolamine hydrobromide with intramuscular injection 30 min before the operation. After the patient entered the operating room, the left radial artery was punctured and catheterization was performed under the conditions of local anaesthesia, and then multifunctional anaesthesia monitoring was applied to monitor the patient's physiological indicators. The urine volume of patients was observed after coronary artery bypass surgery. Patients with urine volume less than 1 mL/kg/h were given furosemide. When induction of anaesthesia was conducted on patients, the order of intravenous drug use was 0.15 mg/kg midazolam, 0.2 mg/kg etomidate, 0.1 mg/kg vecuronium, 9 mg /kg fentanyl, and finally 1 Mg flumetasone. The mask was pressurized with oxygen, and the patient was intubated and connected to the ventilator after being unconscious with muscle relaxation. The initial parameters of the ventilator were set as follows: O_2 flow rate of 2 L/min, tidal volume of 10 mL/kg, a respiration rate of 12 times/min, CO_2 range of the end of expiratory breath of 35~45 mmHg. The patient was placed in a position with low head and high feet, followed by a single disinfection procedure, followed by a right internal neck vein puncture, and a double-lumen internal jugular vein catheter was inserted to detect the patient's central venous pressure. The arterial blood gas index of the patients was analyzed before the formal operation to adjust the parameters of the ventilator. Patients in the CG received intravenous infusion of 0.15 micron/kg/min of remifentanil and inhaled sevoflurane of 0.58~1.76 MAC to ensure that the patients were under anaesthesia.

Remifentanil at 0.05 mg/kg/min was administered intravenously on the way to ICU after the operation. During the operation, patients in the EG were injected with Dex of 0.2 μ/kg/h intravenously, and sevoflurane of 0.58~1.76 mac was inhaled to ensure that the patients were under anaesthesia. After the surgery, the patient was transferred to the ICU unit and intravenous infusion of Dex was continued at 0.1 microns/kg/h.

In both groups, the inhalation concentration of sevoflurane was adjusted to maintain the BIS between 40 and 60, and intravenous injection of 0.05 mg/kg of vecuronium bromide every 30 min ensured that the pulse oxygen saturation was above 98%. If the MAP value is less than 60 mmHg during the operation, the infusion speed and the static injection speed of anaesthetic should be adjusted according to the actual situation to maintain the Hb value of the patient at about 10 g/L.

Indicators for further observation

A multifunctional monitor was used to monitor the changes in HR, MAP, CVP, CO, CI, MPAP, SVR, and BIS of patients before induction of anesthesia (T0), during skin resection (T1), during surgery (T2), after surgery (T3) and admission to ICU (T4). The mean lactate value of arterial blood gas was measured before, during, directly after and one day after the operation. It is necessary to monitor anaesthesia time, operation time, use of vasoactive drugs, time to awake and extubation time, infusion volume and urine volume during surgery. Pain, nausea, vomiting, cognitive dysfunction and other anaesthesia complications were observed within 7 days after surgery.

Statistical analysis

SPSS 19.0 software was used for statistical analysis in this research. Measurement data in line with normal distribution are expressed as $\bar{x}\pm s$. The independent sample t-test was used to compare the two sets of data. Analysis of variance was used to compare multiple sets of data. Enumeration data were expressed as per-

Table 1. Basic data comparison of the patients in two groups

Projects		Control group (n=35)	Test group (n=35)	Statistics (t value/χ^2 value)	P
Age		59.35±9.05	60.25±8.45	-1.423	0.267
Gender (case/percentage)	male	31 (88.57%)	28 (80.0%)	4.562	0.386
	female	4 (11.43%)	7 (20.00%)	3.226	
Weight (kg)		71.38±11.23	72.44±10.09	-2.528	0.339
High blood pressure (case/percentage)		26 (74.29%)	24 (68.57%)	3.058	0.208
Diabetes (case/percentage)		6 (17.14%)	7 (20.00%)	3.112	0.211
Myocardial infarction (case/percentage)		7 (20.00%)	8 (22.86%)	4.052	0.350
Cerebral infarction (case/percentage)		3 (8.57%)	4 (11.43%)	3.172	0.298
Ejection fraction		59.97±4.37	60.02±4.05	-1.338	0.452
Left ventricular size		52.29±5.17	53.44±6.04	-1.254	0.399
Mean arterial pressure		64.00±10.00	69.00±9.00	0.152	0.105
Heart rate		95.00±14.00	97.00±15.00	0.097	0.227

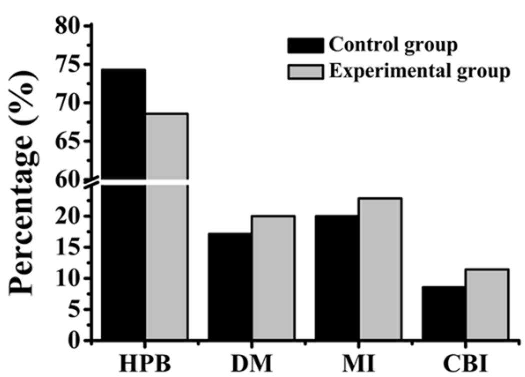

Figure 1. Comparison of disease probability.

centages (%), and the χ^2 test was used for comparison between groups. When P<0.05, the difference between groups was considered statistically significant.

Results

Comparison of the general data of patients

Among the 70 patients who underwent coronary artery bypass surgery, 59 were male and 11 were female, with an average age of 60.55±6.75 years. After dividing them into the CG and the EG, the differences in general information were compared. As shown in **Table 1**, there were no statistically significant differences (SSD) between the observation group and the CG in age, weight (kg), ejection fraction (EF), left ventricular size (LVS), MAP, and HR (P>0.05).

The rates of high blood pressure (HPB), diabetes mellitus (DM), myocardial infarction (MI), and cerebral infarction (CBI) were then compared. As shown in **Figure 1**, patients in the CG and the EG had a high probability of HPB, and the probabilities were 74.29% and 68.57%, respectively. Patients in the CG and EG had low rates of CBI, and the probabilities were 8.57% and 11.43%, respectively. After comparison, no SSD were found (P>0.05).

The general comparison of the patient's operation

The differences of infusion volume, total urine volume, operation time, anaesthesia time, recovery time and extubation time before and after surgery were compared, and the results were shown in **Figure 2**. According to **Figure 2**, the infusion volume of patients in the CG was 1124.00±294.00 mL, and the total urine volume was 580.09±140.36 mL. The infusion volume of the EG was 1144.00±163.00 mL, and the total urine volume was 632.17±110.39 mL. There were SSD between infusion volume and total urine volume (P>0.05).

According to **Figure 3**, the operation time of the patients in the CG was 270.14±28.07 min, the anaesthesia time was 316.10±29.74 min, the recovery time was 121.08±40.33 min, and the extubation time was 439.05±110.75 min. The operation time of the EG was 261.47±30.28 min, the anaesthesia time was 310.05±30.65 min, the recovery time was 86.74±38.27 min, and the extubation time was 240.55±73.85 min. After comparison, it showed that the waking time of the EG was much less than that of the CG (P<0.05), and the extubation time was much less than that of the CG (P<0.01).

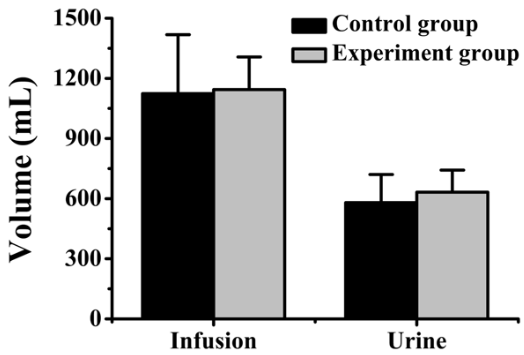

Figure 2. Comparison of infusion volume and urine volume between two groups.

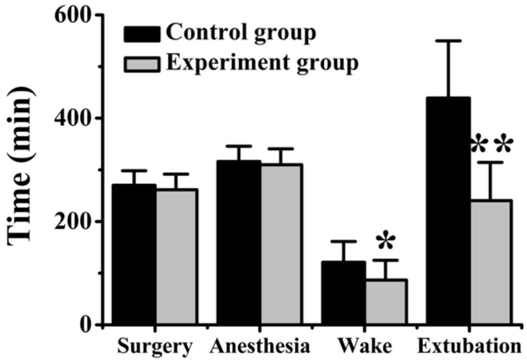

Figure 3. Comparison of operation time. Note: * indicated that there were SSD after comparison with the CG, P<0.05; ** indicated very SSD after comparison with the CG, P<0.01.

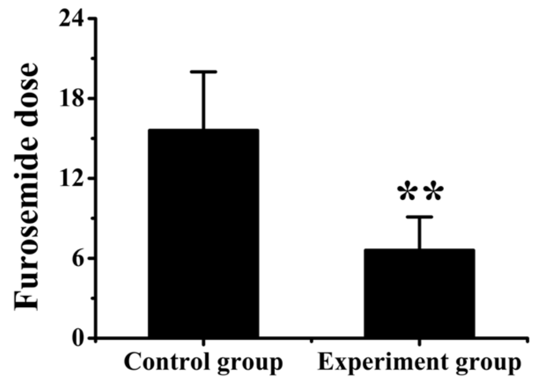

Figure 4. The dosage comparison of furosemide. Note: ** meant there were extremely SSD after comparison with the CG, P<0.01.

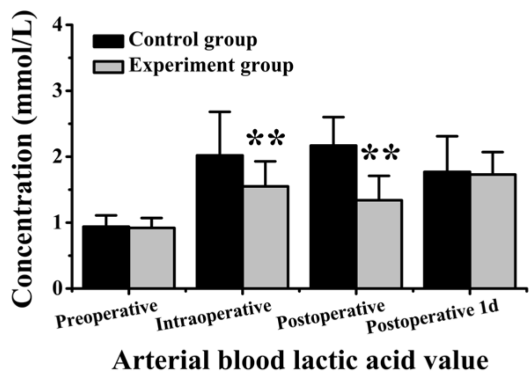

Figure 5. Comparison of arterial lactic acid concentration between two groups with different operative time. Note: ** meant there were extremely SSD after comparison with the CG, P<0.01.

The difference of furosemide dose during the operation was compared, and the results were shown in **Figure 4**. It showed that the furosemide dose of the CG was 15.60±4.40 mg, while the furosemide dose of the EG was 6.60±2.50 mg. After comparison, it showed that the furosemide dose in the EG was much lower than that in the CG (P<0.01).

Comparison of lactic acid concentration in patients with different operative times

The changes of mean lactate concentration in arterial blood gas were compared before, during, directly after and one day after surgery and the results were shown in **Figure 5**. It showed that the lactic acid concentration in the CG was 0.94±0.17 mmiol/L before surgery, while the acid concentration in the EG was 0.92±0.15 mmol/L, with no SSD (P>0.05). The lactic acid concentration of the CG was 1.77±0.54 mmol/L one day after the operation, while the acid concentration of the EG was 1.73±0.34 mmol/L (P>0.05). However, the lactate concentration in the CG was 2.02±0.66 mmol/L at the time of operation and 2.17±0.43 mmol/L after operation. The lactate concentration in the EG was 1.55±0.38 mmol/L and 1.34±0.37 mmol/L after surgery. The arterial lactic acid concentration in the EG was much lower than that in the CG (P<0.01).

Changes of hemodynamic parameters in patients with different operative time points

A multifunctional monitor was used to monitor the differences in HR, MAP, CVP, CO, CI, MPAP, and SVR before and after anesthesia and surgery, as shown in **Figure 6**. It was found that at the time of T0, there were SSD in hemodynamics (P>0.05). With the passage of time, there were SSD between the hemodynamic indexes at T0 and at time T1, T2, T3, and T4 (P<0.05). After comparing the hemodynamic indexes of the two groups, it was found that at time T1, T2,

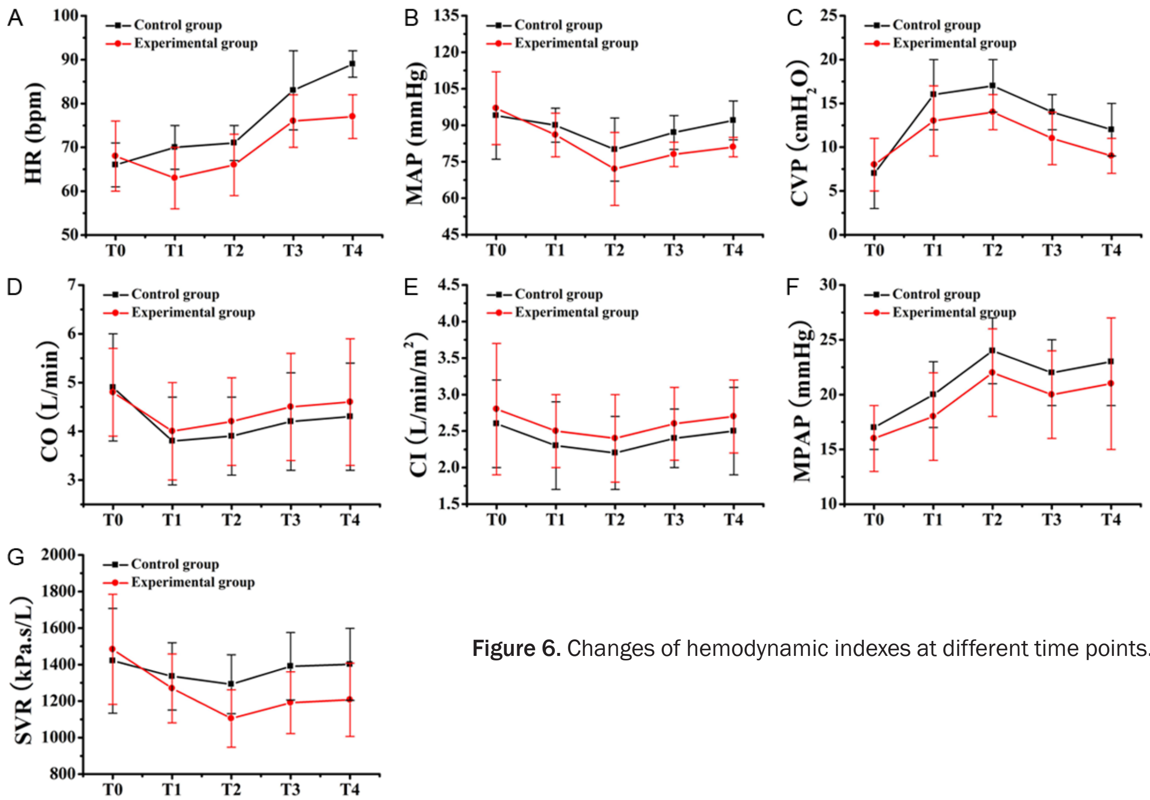

Figure 6. Changes of hemodynamic indexes at different time points.

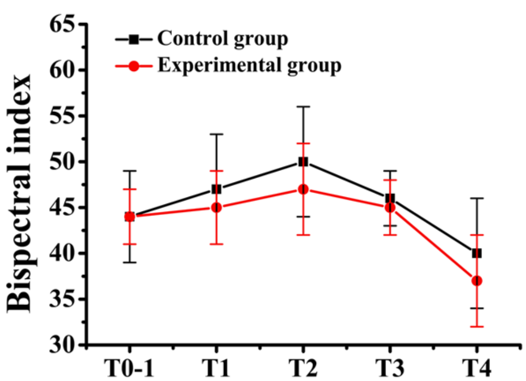

Figure 7. Comparison of the changes of anesthesia depth at different operation time points.

T3, and T4, the HR, MAP, CVP, MPAP, and SVR of the EG were lower than those of the CG ($P<0.05$), while the CO and CI were higher than those of the CG ($P<0.05$).

The depth change of anesthesia at different time points in the operation

Changes in the depth of BIS at different time points were monitored and the differences were compared. The results are shown in **Figure 7**. At T0-T1, there were SSD in BIS ($P>0.05$). At T1 and T2, BIS in both groups was higher than T0-T1 ($P<0.05$). At T2, BIS was higher than T1 in both groups ($P<0.05$). At the time of T4, BIS in both groups was lower than that at the time of T0-T1 ($P<0.05$). After comparing the differences, it was found that BIS at T1 and T2 in the EG was higher than that in the CG ($P<0.05$).

Analysis of postoperative complication probability

The incidence of postoperative complications in patients treated with different anaesthesia was compared, and the results were shown in **Table 2**. It showed that the probability of postoperative vomiting, delirium and cognitive impairment in both groups was less than 10%, and there were SSD ($P>0.05$). However, the incidence of irritability and nausea in the CG and EG was 20.00% and 14.29% respectively. The probability of irritability and nausea in the EG and CG was only 2.86% and 0.00% respectively. Moreover, the probability of irritability and nausea in the CG was higher than that in the EG ($P<0.05$).

Table 2. The probability analysis of postoperative complications

Complication	CG (n=35)	EG (n=35)	χ^2 value	P
Restless	7 (20.00%)	1 (2.86%)	6.667	0.015
Nausea	5 (14.29%)	0 (0.00%)	6.326	0.023
Emesis	0 (0.00%)	0 (0.00%)	2.289	0.214
Delirium	3 (8.57%)	2 (5.71%)	3.062	0.093
Cognitive disorder	2 (5.71%)	1 (2.86%)	3.113	0.124

Discussion

Dex is a highly selective α2 receptor agonist that reduces sympathetic activity in the body by acting on α2 adrenergic receptors before and after prominence in the central nervous system, ultimately causing peripheral blood vessels to dilate and lower blood pressure [12]. The effects of Dex and remifentanil were analyzed on different indicators of patients undergoing OPABS surgery. The results showed that there were SSD between the infusion volume and the total urine volume between the two patients. The furosemide dose in the remifentanil group was higher than that in the Dex group, indicating that Dex had the effect of promoting urination, which was consistent with the research results of Horvt et al. (1996) [13]. However, the concentration of lactic acid in arterial blood in the remifentanil group increased greatly, indicating that Dex can improve microcirculation perfusion in the body. Moreover, it can reduce the content of catecholamines in patients' plasma and thus reduce systemic circulation resistance [14]. Due to the sedative effect of Dex, Dex has a small inhibitory effect on respiration, and studies have shown that Dex can improve the safety of tracheal extubation and reduce the extubation time [15]. This is consistent with the findings of this study that the postoperative recovery time and extubation time of patients in Dex group were lower than those in remifentanil group, suggesting that Dex can effectively inhibit the effect of the sympathetic nervous system in patients, and it has the characteristics of short action time and fast recovery, and has a higher safety than remifentanil [16, 17].

A large number of studies have shown that the use of left anterior descending bypass surgery can cause an increase of heart rate, central venous pressure and average pulmonary artery pressure, as well as the decrease of mean artery pressure in patients [18, 19]. Other studies have shown that in addition to the above indexes, the indexes of cardiac displacement, cardiac index and systemic vascular resistance can also be reduced when left descending branch or right coronary anastomosis is used [20], which is consistent with the change rule of hemodynamic indexes found in patients under anaesthesia with Dex in this study. However, there were SSD from before anaesthesia induction, which may be because the effect of Dex is longer than remifentanil, and it can effectively stimulate the central nervous system of patients, thus causing the sedative effect in the body and reducing the high nerve activity [21]. The hemodynamic index changes of the two groups were detected at different time points, and the results showed that the heart rate and blood pressure fluctuation of Dex anesthesia group were smaller, suggesting that Dex combined anesthesia can reduce the patient's heart rate, systemic circulatory resistance, decrease myocardial work, and prolong diastolic perfusion [22]. In this research, it was concluded that after the use of Dex, the probability of postoperative irritability and nausea in patients was greatly reduced, which suggested that the use of Dex for anaesthesia induction in patients with off-pump coronary artery bypass surgery could reduce the probability of postoperative complications in patients, and improve and promote the postoperative rehabilitation effect of patients [23]. In this research, patients undergoing OPABS surgery were studied, Dex and remifentanil combined with sevoflurane were used to induce anaesthesia in patients before surgery, to monitor hemodynamic changes, arterial lactic acid value and anaesthesia depth index of patients at different time points, and to analyze the incidence of postoperative complications. The results showed that Dex combined with sevoflurane was beneficial to the hemodynamic stability of patients undergoing unstopped coronary artery bypass surgery. It can also improve the patient's circulation perfusion, and has a diuretic effect, but also can shorten the patient's recovery time and extubation time, reduce the probability of postoperative complications of irritability and nausea. However, we only studied the occurrence probability of a small number of postoperative complications in this research, and further samples are needed to study the effect of Dex on the postoperative nervous system of patients. In conclusion, the results can lay a theoretical foundation for the anaesthesia induction method of Dex combined with sevoflurane in OPABS surgery.

Disclosure of conflict of interest

None.

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