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Comparison of Remifentanil-Based Fast-Track and Fentanyl-Based Routine Cardiac Anesthesia for Intraoperative Device Closure of Atrial Septal Defect (ASD) in Pediatric Patients

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Data Collection B

Statistical Analysis C

Data Interpretation D

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Background: The aim of this study was to evaluate the effectiveness and safety of remifentanil-based fast-track anesthesia for intraoperative device closure of atrial septal defects (ASDs).

Material/Methods: The clinical data of 152 pediatric patients who received intraoperative device closure of ASD in our hospital from January 2015 to December 2017 were retrospectively analyzed. Patients were divided into 2 groups: group F (remifentanil-based fast-track anesthesia group, n=72) and group C (fentanyl-based routine anesthesia group, n=80). The relevant data from 2 groups were collected and analyzed.


Results: No significant differences were found in the preoperative data or intraoperative hemodynamic index between these 2 groups. Group C was significantly inferior to group F regarding the duration of mechanical ventilation, length of intensive care unit (ICU) stay, length of hospital stay, and hospitalization expenses ($P < 0.05$). In terms of postoperative complications, no death, third-degree atrioventricular block, occluder detachment, or residual leakage was reported in either group. The incidence of lung infections and bronchospasm was significantly higher in group C than in group F. There were no anesthetic-related complications.

Conclusions: The application of remifentanil-based fast-track anesthesia for intraoperative device closure of ASD is as effective and safe as fentanyl-based routine anesthesia. Moreover, remifentanil-based fast-track anesthesia has the advantages of shorter duration of mechanical ventilation, shorter length of hospital and ICU stay, fewer postoperative complications, and lower hospitalization expenses, and is therefore worthy of promotion in clinical practice.

MeSH Keywords: Anesthesia • Heart Defects, Congenital • Septal Occluder Device

Abbreviations: ASD – atrial septal defect; ICU – Intensive Care Unit; TTE – intraoperative echocardiography; ECG – electrocardiography; AVB – atrioventricular block

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Background

An atrial septal defect (ASD) is one of the most common congenital heart diseases, and is conventionally surgically repaired by cardiopulmonary bypass, which requires a relatively large incision [1,2]. In recent years, percutaneous closure of ASDs has become popular, but this technique requires radiation exposure [3,4]. Minimally invasive intraoperative device closure of ASD has the advantages of decreased trauma, rapid recovery, low cost and wide indications, and no need for X-ray equipment; this procedure has been widely used, especially in China [5–7]. Fast-track cardiac anesthesia refers to extubation immediately or within 6 h after surgery by selection of the appropriate anesthetic drugs and methods, while ensuring hemodynamic stability and depth of anesthesia. Subsequently, through fast-track cardiac anesthesia, the length of the intensive care unit (ICU) stay and hospital stay, as well as medical expenses, are reduced [8–10]. This study summarized and evaluated the effectiveness and safety of remifentanyl-based fast-track anesthesia for intraoperative device closure of ASDs.

Material and Methods

Clinical data

The present study adhered to the Declaration of Helsinki and it was approved by the Ethics Committee of Fujian Medical University (approval No. 2009024). In addition, all the patient's relatives signed the written informed consent. The clinical data of 152 pediatric patients who underwent minimally invasive intraoperative device closure of an ASD in our hospital were retrospectively analyzed from January 2015 to December 2017. The secundum ASD was diagnosed by transthoracic echocardiography (TTE) in all patients. Other preoperative examinations were performed, including 12-lead electrocardiogram, chest X-ray film, and routine blood and biochemical tests. In both groups, 25 patients had mild pulmonary hypertension (which was assessed by preoperative TTE and the result showed pulmonary artery systolic pressure was 20 to 30 mmHg); 22 patients were symptomatic, including recurrent pulmonary infection, shortness of breath, and growth retardation. The chest X-ray film showed pulmonary congestion, and TTE showed hemodynamic change with significant left-to-right shunts and/or heart chamber enlargement.

There were no therapeutic contraindications in any patients. Inclusion criteria were: secundum ASD with adequate surrounding rims, hemodynamically significant left-to-right shunt, significant heart chamber enlargement, with/without the presence of clinical symptoms. The exclusion criteria included severe pulmonary hypertension, association with other congenital heart disease, heart function failure, and inability to obtain informed consent [11,12].

According to the application of the different anesthetic methods, the patients were divided into 2 groups: group F (remifentanyl-based fast-track anesthesia group, n=72) and group C (fentanyl-based routine anesthesia group, n=80). The preoperative data, intraoperative hemodynamic index, postoperative length of mechanical ventilation, length of ICU stay, length of hospital stay, perioperative complications, and hospitalization expenses of the 2 groups were collected and analyzed.

Methods

Preoperative routine

Patients routinely fasted before surgery. Ketamine (5 mg/kg, intramuscular injection) was used for induction of basic anesthesia. The patient was monitored via electrocardiography (ECG) and pulse oximetry in the operating room. Glucose (5%) was continuously injected by the peripheral venous route. After successful tracheal intubation, mechanical ventilation was established using pressure-controlled mode. A catheter was placed into the radial artery following arterial puncture to monitor arterial blood pressure directly. A subclavian vein catheter was used to monitor central venous pressure. The temperature of the operating room was maintained at 25°C during the operation. The flow rate of intravenous (IV) fluids was maintained at an appropriate level (the fluids were warmed if necessary), and the patient's temperature was maintained at above 36.5°C. ECG results, blood oxygen saturation, body temperature, arterial pressure, central venous pressure, electrolytes levels, and blood gas analysis were monitored continuously. Any problems were addressed in a timely manner.

Fast-track anesthesia

Remifentanyl (1.5 µg/kg) and cisatracurium besilate (0.5 mg/kg) were administered intravenously for induction of anesthesia. Because the operation time was expected to be brief, anesthesia was maintained with remifentanyl (0.2–0.5 µg/kg/min, continuously injected by infusion pump) and 2% sevoflurane (intermittent inhalation depending on the heart rate and arterial pressure).

Routine anesthesia

Fentanyl (10 µg/kg) and cisatracurium besilate (0.5 mg/kg) were administered intravenously for induction of anesthesia. Anesthesia was maintained by using fentanyl (approximately 3–5 µg/kg/h, continuously injected by infusion pump) and 2% sevoflurane (intermittent inhalation depending on the heart rate and arterial pressure).

Table 1. Comparison of clinical data in both groups.

	Group F	Group C	p Value
Number of patients	72	80	
Male/Female	40/32	46/34	0.638
Age (years)	5.6±3.1	5.1±4.2	0.673
Body weight (kg)	18.9±4.1	19.3±3.8	0.863
ASD size (mm)	14.6±5.1	13.2±6.6	0.875
Pulmonary arterial pressure (mmHg)	31.2±4.5	29.3±5.7	0.855
Ejection fraction (%)	61.5±4.6	60.1±5.4	0.923

Surgical procedure

A small incision (2–3 cm) in the right anterior chest wall was used to access the thoracic cavity through the fourth intercostal space. The incision was at 2 cm anterior to the right phrenic nerve, and the pericardium was suspended. Heparin (1 mg/kg) was administered intravenously, and double-purse string sutures were applied to the right atrial wall. Under perioperative TTE guidance, the right atrial wall was incised inside the purse string. The delivery sheath loaded with an occluder was advanced into the right atrium, then entered the left atrium through the ASD. After the position of the sheath was determined, the left disc of the occluder was deployed. Then, the occluder was pulled back and positioned close and parallel to the atrial septum, and the right disc of the occluder was deployed and attached to the other side of the atrial septum. After the location of the occluder was checked by TTE, the delivery sheath was withdrawn. The purse string was tied to close the right atrial incision [5–7]. Extubation took place in the ICU in all patients. No additional sedative drugs were given in the ICU.

Statistical analysis

The continuous data were all normally distributed, and were statistically analyzed by the independent-samples *t* test. The chi-square test was used to compare the ejection fraction, the success rate of occlusion, and the number of postoperative complications between the 2 groups. According to the incidence of postoperative complications in the pre-survey, with $\alpha=0.05$ two-tailed and a power of 90%, the sample size of the 2 groups was estimated at 72 and 80, respectively, calculated by PASS 15. 0. A *P* value less than 0.05 was defined as statistically significant.

Results

The ASD closure was successfully accomplished in 150 patients and the instant close rate was 96.7%. The other 5 patients with a tiny residual fistula were kept under medical

close observation, and the closure rate was 100% in all patients at 1-year follow-up. One patient in group F and 1 patient in group C were converted to surgery due to occluder dislodgement. Transient perioperative arrhythmias occurred in 11 patients in both groups, which reflected automatic recovery without drug treatment. There were no blood transfusions, brain complications, embolizations, or new dysfunction of cardiac valves in any patients. There were no anesthesia-related complications.

Table 1 shows that the preoperative parameters were not significantly different between the 2 groups ($P>0.05$). Table 2 shows that the intraoperative hemodynamic parameters were stable in these 2 groups, and no significant difference was observed between these 2 groups ($P>0.05$). Table 3 shows that no significant difference was observed in the procedural time between the 2 groups. The duration of mechanical ventilation, length of ICU stay, length of hospital stay, and hospitalization cost in group F were significantly less than those in group C ($P<0.05$). Table 4 shows that no deaths, third-degree atrioventricular blocks (AVB), occluder detachments, residual shunts, hepatic insufficiencies, heart failures, or renal insufficiencies were reported after this procedure in either group. Significantly fewer patients exhibited postoperative pulmonary infection and bronchospasm in group F than in group C ($P<0.05$).

There were no patients lost to follow-up. The duration of follow-up was 1–2 years. No late-onset occluder embolizations or surgical interventions occurred. No patients had newly developed complete heart block or aortic or mitral valve regurgitation. There were no deaths, thromboembolic events, occluder erosions, or other fatal complications, and there were no anesthesia-related complications in the follow-up. The clinical efficacy of all patients was satisfactory.

Discussion

ASD is a common congenital heart disease; traditional treatment methods include surgical repair under cardiopulmonary

Table 2. Comparison of interoperative hemodynamic data in both groups during the procedure.

	Group F	Group C	p Value
After intubation			
CVP (mmH ₂ O)	6.2±1.3	5.7±2.3	0.743
MAP (mmHg)	97.6±9.3	97.2±6.7	0.830
HR (beats/min)	107.1±19.4	106.8±17.8	0.891
Skin incision			
CVP (mmH ₂ O)	6.4±2.2	6.2±2.7	0.757
MAP (mmHg)	110.6±10.8	108.3±11.8	0.856
HR (beats/min)	121.3±22.5	117.5±25.8	0.879
Occluder release			
CVP (mmH ₂ O)	6.4±1.5	6.2±1.9	0.857
MAP (mmHg)	104.6±8.2	101.8±9.9	0.882
HR (beats/min)	112.7±18.7	108.5±21.2	0.942
After procedure			
CVP (mmH ₂ O)	6.7±1.8	6.5±2.1	0.814
MAP (mmHg)	111.5±11.1	114.7±12.8	0.786
HR (beats/min)	116.5±18.3	115.9±17.9	0.905

CVP – central venous pressure; MAP – mean arterial pressure; HR – heart rate.

Table 3. Comparison of interoperative and postoperative clinical data in both groups.

	Group F	Group C	p Value
Operative time(minutes)	38.0±11.2	41.2±12.5	0.892
Mechanical ventilation time (h)	1.1±0.8	3.4±1.9	0.041
Intensive care time (h)	5.6±2.0	11.5±4.4	0.037
Hospital stay (days)	1.8±0.6	3.2±1.4	0.044
Successful occlusion rate	97.2%	97.5%	0.915
Medical cost (Ten thousand RMB)	2.7±0.8	3.8±1.3	0.045

bypass and percutaneous device closure [1–4]. However, these 2 techniques have advantages and disadvantages. The former method is associated with systemic inflammatory responses, multiple organ dysfunction, and various disfiguring scars [13]. The latter one features no scarring or pain, but doctors and patients are exposed to X-rays, which may lead to radioactive damage [3,4]. In recent years, minimally invasive intraoperative device closure has been widely used in China and has achieved satisfactory clinical outcomes [5–7]. The technical advantages include no need for cardiopulmonary bypass, no X-ray radiation exposure, a greater scope of application, and a small incision in the right anterior chest. Most importantly, if device closure fails, the procedure can be converted to surgical repair immediately in the operating room. Moreover, this

technique does not require large equipment and has a short learning curve and lower hospitalization expenses. Therefore, it can be used in a greater variety of conditions.

The use of opioids in cardiac anesthesia has become the dominant method due to their minimal impact on hemodynamics and their effective analgesia. However, large doses of opioids can significantly increase the incidence of postoperative respiratory dysfunction and the length of mechanical ventilation and the ICU stay. These not only increase hospitalization expenses, but also increase the likelihood of nosocomial infections [14,15]. The concept of fast-track cardiac anesthesia has been proposed and advocated in the field of cardiac anesthesia in recent years. The purpose of fast-track cardiac anesthesia

Table 4. Comparison of clinical data of postoperative complication in both groups.

	Group F	Group C	p Value
Death	0	0	
Complete atrioventricular block	0	0	
Occluder dislodgement	0	0	
Signifant residual fistula	0	0	
Cardiac failure	0	0	
Hypohepatia	0	0	
Renal impairment	0	0	
Palmonary infection	3	11	0.041
Bronchospasm	0	5	0.033

is to maintain the patient's perioperative hemodynamic stability and reduce the use of mechanical ventilation after surgery, which leads to early extubation [16–18]. The key features of fast-track cardiac anesthesia are the replacement of long-acting opioids with short-acting opioids or the reduction of the dose of long-acting opioids and the combined use of inhaled anesthetics and other short-acting intravenous anesthetics, which can result in early extubation after cardiac surgery. This study aimed to summarize the clinical experience of fast-track cardiac anesthesia for minimally invasive intraoperative device closure of ASDs.

In fast-track anesthesia, a sufficient depth of anesthesia should be maintained to minimize the various stress responses during the procedure and to ensure that patients resume spontaneous breathing after the operation. Therefore, the rational application of short-acting analgesics, inhaled anesthetic drugs, and short-acting muscle relaxants is crucial for this type of anesthesia. Remifentanyl is a narcotic analgesic that is frequently-used clinically [19–21]. Its clinical characteristics include stable hemodynamics, rapid pain relief, and strong analgesic effects. Its elimination mainly occurs due to the rapid clearance of the drug rather than redistribution, and this process is mostly independent of the duration of continuous infusion. Therefore, the dose and rate of administration can be quickly and accurately adjusted according to the depth of anesthesia and the requirements of the operation. Rapid recovery and reduced hypnotic effects after anesthesia are 2 main advantages of remifentanyl. Sevoflurane is a novel inhalational anesthetic with many advantages, including rapid induction, easy maintenance of stable anesthesia, no obvious adverse effects, an odor that is easily accepted by children, a minor impact on hemodynamics, and myocardial protection [22,23].

Our Cardiovascular Department has rich experience in intraoperative device closure of ASDs, and the operative time is obviously controllable for this procedure. In such procedure,

access to the left atrium can easily be established from the right atrium via the ASD to deliver the occluder. Therefore, the operative time is generally within 20–30 min. Compared to percutaneous device closure, the delivered path of minimally invasive intraoperative device closure of ASD is shorter and the techniques are more maneuverable and easier to master. Once the occluder is dislodged, it can be easily found, and the procedure can be quickly converted to traditional surgical repair. The whole procedure is guided by continuous color Doppler TTE alone, without X-ray exposure, which makes the entire operation easier and safer. The rapid recovery after this procedure is also very important. We used intermittent inhalation of sevoflurane and continuous infusion pump of remifentanyl to maintain anesthesia, and the depth of perioperative anesthesia was easy to manipulate. The hemodynamics were maintained stability during the procedure. The postoperative analgesic effect was also satisfactory. Additionally, fast-track cardiac anesthesia can provide sufficient analgesic and sedative effects to eliminate sympathetic reactions, inhibit stress, and reduce oxygen consumption. Compared to conventional anesthesia, the postoperative duration of mechanical ventilation and the postoperative length of ICU and hospital stays were significantly shorter, and the corresponding hospitalization expenses were significantly reduced with fast-track anesthesia. Fast-track anesthesia has obvious advantages; however, patient selection should be performed cautiously according to strict indications. Preoperative and intraoperative TTE evaluations are important when selecting patients. In addition, the skills of the surgeon and sonographer should also be considered. For patients with inadequate rims of ASDs, a possible need for cardiopulmonary bypass surgery during the operation, and a relatively long operative time, conventional anesthesia is recommended.

Studies have shown that the occurrence of pulmonary infections is closely related to the duration of intubation and mechanical ventilation [24–28]. Pulmonary infections can result

in a longer hospital stay, increased hospitalization expenses, and increased mortality. Early extubation and discontinuation of positive-pressure mechanical ventilation can reduce the risk of respiratory complications and injury of the airway and lungs, reduce stress and discomfort associated with endotracheal intubation and sputum suction, improve overall heart function, especially diastolic compliance, and promote early recovery and stability of heart and lung function. Furthermore, early extubation can significantly reduce the cost of treatment and the workload of medical personnel. In this study, the incidence of postoperative pulmonary complications in group F was significantly higher than in group C. This suggests that fast-track cardiac anesthesia has advantages in terms of postoperative recovery.

There are some limitations to this study. It was a single-center, retrospective study with a small sample. We plan to perform prospective, multicenter, randomized controlled studies in the future to more objectively research the clinical outcome of fast-track cardiac anesthesia. In addition, other hospitals

using alternative anesthesia techniques may have different clinical results.

Conclusions

The application of remifentanyl-based fast-track cardiac anesthesia for minimally invasive intraoperative device closure of ASD is as effective and safe as conventional anesthesia. In addition, fast-track cardiac anesthesia has several advantages, including a short duration of mechanical ventilation, decreased length of hospital and ICU stay, fewer postoperative complications, and lower hospitalization expenses, and is therefore worthy of promotion in clinical practice.

Conflict of interests

None.

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