



Comparison of Effects of Sevoflurane and Propofol on Cerebral Oxygen Metabolism in Pediatric Anesthesia

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ABSTRACT

This paper aims to study the effect of sevoflurane and propofol on cerebral oxygen metabolism during the maintenance of paediatric anaesthesia. To this end, the children who had undergone surgical treatment in General Surgery Department were selected as study subjects, and they were divided into experimental group and control group. Patients in the control group received propofol to maintain anaesthesia, while patients in the experimental group maintained anaesthesia with sevoflurane. Then, the hemodynamic changes at different time points and the depth of anaesthesia were compared between the two groups of patients during anaesthesia maintenance. The results show that there was no significant difference in cerebral oxygen metabolism between these two groups; the content detected in the experimental group was significantly higher than that in the control group. Therefore, it is concluded that both the sevoflurane and propofol in the pediatric anaesthesia maintenance process has a good effect value, which can reduce cerebral oxygen metabolism in children and have a minor impact on hemodynamics, but the sevoflurane is significantly superior to propofol in reducing cerebral oxygen metabolism.

Key Words: Maintenance of Pediatric Anesthesia, Propofol, Sevoflurane, Cerebral Oxygen Metabolism

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Introduction

Pediatrics are a special group of people. Those from new-borns (within 1 month), infants (within 1 year of age), children (from 1 to 3 years of age) to children (from 3 to 12 years of age) may require surgery. However, due to the rapid and drastic changes in children's various physiological functions at various stages of development, they differ greatly from adults and have very distinct specificities. The development of the central nervous system in new-borns and infants is imperfect, so the heart rate changes easily occur in anaesthesia, and tolerance to respiratory depression drugs is poor (Guignard *et al.*, 2000). Besides, the Neonatal thermoregulatory function is poor, and it can easily cause the body temperature

to rise or fall, leading to the delayed wake-up after anaesthesia.

Phase III clinical trials for Sevoflurane was completed in 1986. Sevoflurane was first approved by the Japanese Drug Administration in 1990 for clinical use (Murray *et al.*, 2000). In recent years, it has been regarded as milestone drugs for inhalation anaesthesia by many famous anesthesiologists who believe that there are significant advantages in the induction and maintenance of general anaesthesia in children, besides, many organizations also reported their successful use of general anaesthesia in children. Sevoflurane is a colourless, transparent, aromatic, and non-irritant liquid; chemically unstable, it can produce five kinds of decomposition products

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when it is contacted with soda lime; when the oxygen mask is inhaled for about 2 minutes at 4% concentration, the consciousness of the patient can disappear; the deep anesthesia may induce generalized paralysis (Struys *et al.*, 2002). Compared with the conventional administration of small amounts of opioids and hypnotic sedatives under basic ketamine-based anesthesia, the advantages of sevoflurane anesthesia are that the child patient is calmer during the induction period, the hemodynamics are smoother, the amount of muscle relaxants is smaller, after surgery the child awakens more quickly and thoroughly. However, the incitement during the induction and recovery periods is one problem that needs to be overcome (Bhananker *et al.*, 2007). The discomfort felt immediately after awakening quickly is the important cause of postoperative agitation. Propofol is a short-acting intravenous anesthetic of alkyl acids. It is rapidly distributed throughout the body after intravenous injection and can produce a sleep state within 40 seconds in the rapidly and steadily way. T_{1/2α} is 1.8-8.3 minutes. It may be metabolized mainly in the liver with glucuronide, and metabolites are excreted from the urine for 34-60 minutes. The V_d was 2.83 L/kg and the plasma protein binding rate was 97% to 98% (Alkire *et al.*, 1995). If used in combination with fentanyl, the blood concentration of this product increases. The analgesic effect of this product is weak, which can reduce intracranial pressure, brain oxygen consumption and cerebral blood flow. It has inhibition effects on the respiratory system, possibly leading to temporary respiratory arrest; also inhibits the circulatory system, so that the blood pressure may occur. The anesthesia of this product recovers rapidly, about 8 minutes, and the nausea, vomiting and headache can occur during recovery (Satomoto, 2009). However, during the actual use, the induction of anesthesia may cause mild symptoms of euphoria in children. If young children suffer from heart disease, respiratory disease, liver and kidney disease or weakness, they should be used with caution.

Compared with adults, children's brain tissue has relatively poorer autoregulation function. In the process of surgical anesthesia for children, the imbalance of cerebral oxygen metabolism can easily cause damage to children's brain tissue (Figure 1). Hypoxia in children can cause serious brain damage in children. Therefore, during the anesthesia maintenance, close monitoring of cerebral oxygen metabolism is

of great significance. The commonly used anesthetic maintenance drugs in the clinic are sevoflurane and propofol. Studies have shown that both have the effect of reducing the metabolic rate of cerebral oxygen. In order to determine the effects of these two drugs on cerebral oxygen metabolism in children during pediatric anesthesia maintenance, this study randomly selected 119 patients who underwent surgical treatment in General Surgery Department from May 2014 to May 2015 as the study subjects. They were divided into two groups: the experimental group and the control group, and then the effects of cerebral oxygen metabolism were analysed for two groups in detail.

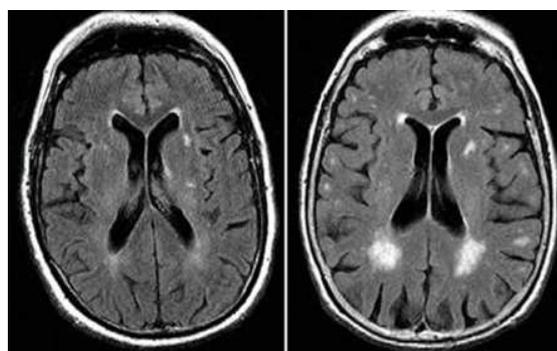


Figure 1. CT scan of a child with brain injury

Methods

General data

119 cases of children undergoing surgery in our general surgery department from May 2014 to May 2015 were selected as subjects of study. The selection was based on: 1). Children who need surgery in General Surgery Department; 2). Patients aged 4 to 14 years old; 3). Patients without liver, kidney and other congenital complications of children. The children were divided into experimental group and control group. The experimental group consisted of 60 children, 29 males and 31 females, aged 5 to 14 years with an average of (9.12±4.45) years; the control group included 59 children, 30 males, 29 females, aged 4 to 13 years old, average (9.58±4.29) years old. The basic indicators of the two groups of children were basically similar (P>0.05).

Method

After entering into the operating room, firstly, the intravenous access was established, and the infusion of electrolyte solution was made, when monitoring the vital signs such as blood pressure,

electrocardiogram, heart rate, and pulse oxygen saturation etc.; then, the patients received intravenous administration atropine 0.012m/kg and midazolam 0.15mg/kg. Intravenous injection of 0.6m/kg sufentanil, 30mg/kg propofol, and 0.15mg/kg vecuronium was made, followed by tracheal intubation for mechanical ventilation. In the control group, propofol was used for anesthesia maintenance, and sevoflurane was used for anesthesia maintenance in the experimental group. According to the patient's circulation and breathing state etc. the pump injection speed was adjusted.

For the hemodynamics of the two groups of children at different time points (t1: successful arteriovenous catheterization; t2: reduction of BIs to 50; t3: 15 min of surgery; t4: end of surgery) during anesthesia maintenance, its dynamic process and the depth of anesthesia were compared; the records and observation were made for indicators such as arteries in the radial artery, arterial oxygen saturation (sao2) in the internal jugular vein blood, jugular oxygen saturation (Sjvo2), cerebral oxygen uptake rate (CERO2), and the jugular vein blood oxygen content difference (Da-jvo2) etc. between two groups of children.

SPSS 22.0 statistical software was used for statistical analysis. The measurement data was expressed as the mean standard deviation. The t-test was used to count data using the xZ test. p<005 was considered statistically significant.

Results and analysis

The HR and MAP indicators at t2, t3, and t4 in the group were significantly lower than those at the time point t1 (P<0.05); the differences among the groups at various time points were not significant (P>0.05). See Table 1 for details.

Table 1. Comparison of hemodynamic parameters between two groups at different time points

Index	Group	T1	T2	T3	T4
HR	Test group	78.26 ±1.90	72.48 ±1.52	72.46 ±0.83	72.14 ±1.34
	Control group	77.51 ±1.38	71.93 ±1.33	71.63 ±0.64	71.67 ±0.55
MAP	Test group	81.53 ±1.32	75.64 ±0.43	74.55 ±0.84	74.26 ±0.95
	Control group	82.07 ±0.91	75.13 ±0.62	74.18 ±0.56	73.51 ±1.21

Table 2 shows the changes of the heart rate during anesthesia maintenance surgery in the control group and the observation group. There is little difference for each indicator between two groups (P>0.05).

Table 2. Changes in heart rate during anesthesia maintenance surgery

Group	n	A1	A2	A3	A4
Test group	60	78.4±2.0	73.6±1.4	72.5±0.9	72.0±1.0
Control group	59	78.3±21.8	73.2±1.4	71.4±0.8	71.7±0.8
P	-	>0.05	>0.05	<0.05	>0.05

Table 3. Differences in oxygen content and cerebral oxygen metabolism in cerebral arteriovenous blood

Group	A1	A2	A3	A4
Control group	48.0±5	42.0±9	42.3±9	47.5±10
Test group	48.1±5	37.3±9	37.3±9	48.0±10
P	>0.05	<0.05	<0.05	>0.05

Table 4. Brain oxygen uptake rate and cerebral oxygen metabolism

Group	A1	A2	A3	A4
Control group	36.2±5	33.1±5	38.6±6	35.9±5
Test group	36.3±5	31.1±5	33.1±5	33.5±9
P	>0.05	<0.05	<0.05	>0.05

Table 5. Oxygen saturation and cerebral oxygen metabolism in the jugular vein

Group	A1	A2	A3	A4
Control group	60.2±6	64.9±8	62.7±4	60.0±5
Test group	60.1±6	68.0±9	65.1±5	60.6±5
P	>0.05	<0.05	<0.05	>0.05

To compare the cerebral oxygen metabolism under the indicators in these two groups, Table 3, 4, and 5 list the cerebral oxygen metabolism in the control group and the observer group. In the tables, it can be seen that in the A1 phase, there were no significant differences in the three indicators such as oxygen content in cerebral arteriovenous blood, brain oxygen uptake rate, and oxygen saturation rate in the jugular vein in the control group and the observation group; in A2 and A3 phase, the difference between the two groups in the three observational parameters was statistically significant (P<0.05); in the A4 phase, there was a statistically significant difference in the cerebral oxygen uptake rate between the two groups (P<0.05).

Conclusions

Cerebral blood flow (CBF) refers to the flow of blood through the cerebral blood vessel cross section per unit time, that is, the product of the linear velocity of the blood flow and the cross-sectional area of the blood vessel. Due to the volatility of brain activity, CBF changes along with it. Its regulation mechanism includes: (1) Flow-metabolism matching, i.e., CBF is regulated by the need of local brain metabolism, and the changes in brain metabolism will cause corresponding changes in CBF; (2) Perfusion pressure-flow auto-regulation. Assuming that the cerebral oxygen metabolic rate is unchanged and the mean arterial



pressure fluctuates in the range of 50-150 mmHg, the CBF remains basically unchanged; when the perfusion-flow regulation mechanism is impaired, CBF changes significantly with the change of MAP. Below or above the automatic adjustment range, CBF is only regulated by cerebral perfusion pressure. Too low CBF can cause ischemia, while too high shall result in local tissue edema and even hemorrhage. CMRO₂ refers to the amount of oxygen consumed by brain tissue per unit of time. CBF increases with the increase of CMRO₂ during fever, while CBF decreases with the decrease of CMRO₂ when using low-temperature barbiturates. The automatic adjustment range for human preterm infants, term new-borns, infants, and older children has not been determined.

The oxygenation of brain tissue depends primarily on whether the oxygenation of arterial blood is good or not, and also whether cerebral blood flow matches brain oxygen consumption. Under normal circumstances, there exists the coupling relationship between cerebral blood flow and actual brain metabolic needs; when the local brain metabolism increases, then the corresponding regional cerebral blood flow shall increase. Oxygen supply and oxygen consumption in the brain tissue are considered to be important indicators reflecting whether the aerobic metabolism of the brain is normal; monitoring the supply and demand balance of cerebral oxygen in surgical anesthesia is helpful for brain protection. Cerebral oxygen metabolism in children during perioperative period is getting more and more attention, and the brain is in the peak period of growth and development in childhood, because of the faster metabolism than adults, high oxygen consumption, poor tolerance to hypoxia, besides, for brain tissue cells during surgical anesthesia, if hypoxia occurs, it will cause serious damage to the brain of the child. Therefore, in the process of anesthesia maintenance, close monitoring of cerebral oxygen metabolism is of great significance.

The commonly-used anaesthetic maintenance drugs in clinic are sevoflurane and propofol. Sevoflurane has clinical features such as rapid onset, rapid recovery, low blood gas distribution coefficient, and easy control; to a certain extent, only slight respiratory and circulatory effects exist. Propofol can increase cerebral blood flow perfusion and decrease cerebral oxygen uptake. During the operation of the patient, Propofol drug can increase blood oxygen content, brain oxygen uptake rate, and

SjvO₂, but has no significant impact on other clinical indicators, also, after the surgery, rapid recovery can be achieved. Thus, both drugs have the effect of lowering the cerebral oxygen metabolism rate and protecting the brain function, and also have a smaller impact on hemodynamics (Denman *et al.*, 2000). Relevant experts stated that the increase of SjvO₂ level can reflect the increase of cerebral oxygen intake in children, resulting in the occurrence of cerebral oxygen supply greater than oxygen consumption; cerebral oxygen uptake rate (CERO₂) can reflect the brain's oxygen uptake as a more sensitive indicator of hypoxia. The increase in the difference of arterial-internal jugular veins oxygen content (Da-jvO₂) indicates the increased oxygen utilization.

The results of this study showed that the HR and MAP indicators at t₂, t₃, and t₄ in both groups were significantly lower than those at t₁, and there was no significant difference in cerebral oxygen metabolism at t₁ and t₄. The content of SjvO₂ detected in experiment group at the time points t₂ and t₃ was obviously higher than that in control group, but the detection levels of CERO₂ and Da-vo₂ were low, which fully demonstrated the superiority of sevoflurane in reducing cerebral oxygen metabolism.

References

- Alkire MT, Haier RJ, Barker SJ, Shah NK, Wu JC, Kao YJ. Cerebral metabolism during propofol anesthesia in humans studied with positron emission tomography. *Anesthesiology* 1995; 82(2): 393-403.
- Bhananker SM, Ramamoorthy C, Geiduschek JM, Posner KL, Domino KB. Anesthesia-related cardiac arrest in children: update from the Pediatric Perioperative Cardiac Arrest Registry. *Anesthesia & Analgesia* 2007; 105(2): 344-50.
- Denman WT, Swanson EL, Rosow D, Ezbicki K, Connors PD. Pediatric evaluation of the bispectral index (BIS) monitor and correlation of BIS with end-tidal sevoflurane concentration in infants and children. *Anesthesia & Analgesia* 2000; 90(4): 872-77.
- Guignard B, Menigaux C, Dupont X, Fletcher D, Chauvin M. The effect of remifentanyl on the bispectral index change and hemodynamic responses after orotracheal intubation. *Anesthesia & Analgesia* 2000; 90(1): 161-67.
- Kaisti KK, Långsjö JW, Aalto S, Oikonen V, Sipilä H. Effects of sevoflurane, propofol, and adjunct nitrous oxide on regional cerebral blood flow, oxygen consumption, and blood volume in humans. *Anesthesiology* 2003; 99(3): 603-13.
- Murray JP, Geiduschek JM, Ramamoorthy C, Haberkern CM, Hackel A. Anesthesia-related cardiac arrest in children: initial findings of the Pediatric Perioperative Cardiac Arrest (POCA) Registry. *Anesthesiology* 2000; 93(1): 6-14.
- Satomoto M. Neonatal exposure to sevoflurane induces abnormal social behaviors and deficits in fear



conditioning in mice. *Anesthesiology* 2009; 110(3): 628-37.

Struys MM, Jensen EW, Smith W, Smith NT, Rampil I. Performance of the ARX-derived auditory evoked

potential index as an indicator of anesthetic depth: a comparison with bispectral index and hemodynamic meas. *Anesthesiology* 2002; 96(4): 803-16.

