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Original Article

Effects of total intravenous anesthesia and inhalation anesthesia on intraoperative cerebral oxygen saturation in children with obstructive sleep apnea syndrome

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Abstract: Objective: To compare the effects of total intravenous anesthesia (TIVA) and inhalation anesthesia (IA) on intraoperative cerebral oxygen saturation in children with obstructive sleep apnea syndrome (OSAS). Methods: Children with elective surgery (n=82) for OSAS were randomly divided into a TIVA group (group P) and an IA group (group S). Regional cerebral oxygen saturation (rSO2), heart rate (HR), blood pressure (BP), pulse oxygen saturation (SPO_2) and postoperative neuron-specific enolase (NSE) levels were measured and recorded before induction (T0), immediately after anesthesia (T1), 10 min (T2), 20 min (T3) and 30 min (T4) after anesthesia, immediately at the end of anesthesia (T5) and at recovery from anesthesia (T6). The operation time, recovery time and anesthesia-related complications were recorded. Results: There were no significant differences in mean arterial pressure (MAP) and SPO_2 between the two groups at each time point (P>0.05). The HR of patients in group S after T2 was significantly higher than that in group P (P<0.05). Compared with group P, the rSO2 value in group S was higher (P<0.05), while the NSE content was lower (P<0.05) at each time point after T2. There was no marked difference in operation time between the two groups (P>0.05). The recovery time in group S was longer, and the incidence of nausea and vomiting and agitation was significantly increased compared with group P (P<0.05). Conclusion: Compared with TIVA, IA can increase the value of cerebral oxygen saturation, decrease the content of NSE, and reduce the damage of nerve cells in children with OSAS during surgery, which has a certain brain protection effects.

Keywords: Cerebral oxygen saturation, total intravenous anesthesia, inhalation anesthesia, obstructive sleep apnea syndrome, brain protection

Introduction

The function of each organ system in children is gradually developed and matures with age, in which the development of the nervous system is particularly important. Compared with adults, the brain of children consumes more oxygen as their brain metabolism is more active, and once the brain's oxygen supply fails to maintain brain metabolism, it will damage brain cells, affecting the development of the nervous system [1, 2]. In general anesthesia, children are more prone to hypoxemia than adults due to the influence of anesthetic drugs and surgery, and once the body is hypoxic for too long, it will cause permanent damage to the nerves [3]. Therefore, it is of the essence to monitor the oxygen supply and demand of the brain in pediatric anesthesia. At present, the mainstream method for monitoring the balance of cerebral oxygen supply and demand is regional cerebral oxygen saturation (rSO2). Some studies have confirmed that the decrease of cerebral oxygen saturation occurs almost simultaneously with cerebral hypoxia, especially when cerebral oxygen saturation falls below 60% when the cerebral hypoxia is obvious, so the detection of cerebral oxygen saturation can determine whether the brain may be hypoxic [4, 5]. Currently, drugs for general anesthesia are mainly divided into intravenous anesthetics and inhalation anesthetics, both of which have pros and cons. Although numerous research has confirmed that both of them can be used in pediatric general anesthesia and play a good anesthetic effect [6, 7], little has been done to compare whether these

two drug delivery methods exert different effects on brain cells in children with obstructive sleep apnea syndrome (OSAS). Therefore, this paper mainly monitored rSO2 to explore the effects of total intravenous anesthesia (TIVA) and inhalation anesthesia (IA) on brain metabolism in children.

Materials and methods

General information

Patients who underwent tonsillectomy or adenoidectomy (n=82) in The First People's Hospital of Urumqi (Children's Hospital) from June 2018 to December 2019 were selected. Inclusion criteria: (1) patients aged 2-12 years with OSAS requiring tonsillectomy or adenoidectomy [8, 9]; (2) patients with ASA grade [10] I-II; (3) elective surgery patients who had not received surgery in the past year; (4) patients with a weight of 10-40 kg and a height of 80-130 cm; (5) patient who had not taken sedatives or analgesics within the last month. Exclusion criteria: (1) patients complicated with severe heart, liver, kidney or other organ dysfunction; (2) patients with mental illness; (3) patients who were allergic to anesthetic drugs. This study was conducted with the approval of the Ethics Committee of The First People's Hospital of Urumqi (Children's Hospital) and with the consent of the patient's family.

Research participants

Patients who underwent elective OSAS surgery (n=82) were enrolled and randomly divided into the TIVA group (group P) and IA group (group S) according to a computer random number method, with 41 patients in each group. The patients were then subjected to a single blind trial, i.e., the children and their patients did not know the mode of anesthesia to be performed.

Anesthesia methods

Preanesthetic drugs were not used before operation. As soon as the patient entered into the operating room, venous access and vital signs were established to monitor: rSO2 (the sensor of cerebral oximeter (FORE-SIGHT, Casmed Company, USA) was placed 2 cm above the left of the patient's forehead), blood pressure (BP), mean arterial pressure (MAP), heart rate (HR), pulse oxygen saturation (SPO_2) and bispect ral index (BIS). Mask oxygenation (oxygen flow rate: 5 L/min) was performed for 3 min, followed by nitrogen removal for anesthesia induction. Then, midazolam (0.2 mg/kg; Liyuexi, Jiangsu Nhwa Pharmaceutical Co., Ltd.), rocuronium (0.6 mg/kg: Xianlin, Zhejiang Xianju Pharmaceutical Co., Ltd.), sufentanil (0.5 μg/kg: Yichang Humanwell Pharmaceutical Co., Ltd.), propofol (2.0 mg/kg; Propofol 1% Fresenius, Limengxin, Xi'an Libang Pharmaceutical Co., Ltd.) were given sequentially, and endotracheal intubation mechanical ventilation was performed when the muscles were completely relaxed and the BIS value was below 60, with oxygen concentration of 80% and flow rate of 2 L/min. During the operation, group P was maintained with propofol pump (6-8 mg/kg/h) + remifentanil pump (0.25-1 μg/kg/min), while group S was maintained with sevoflurane (1%-3%). If the operation lasted for more than one hour, rocuronium (0.25 mg/kg) was added to maintain BIS value between 40-60. All anesthetics were stopped 5 min before the end of the operation. After the operation, the patient was sent to the anesthesia resuscitation room, and the tube was extubated after the child regained spontaneous breathing and consciousness. Only when the Steward resuscitation score [11] reached more than 4 points and the child was completely awake were they left the resuscitation room.

Outcome measures

Main outcome measures: Cerebral oxygen saturation and SPO_2 were measured and recorded immediately before induction, i.e. before oxygen and nitrogen removal (T0), immediately after anesthesia (T1), 10 min (T2), 20 min (T3) and 30 min (T4) after anesthesia, immediately at the end of anesthesia (T5) and at recovery from anesthesia (T6), and neuron specific enolase (neuron-specific enolase, NSE) in blood was measured after operation.

Secondary outcome measures: MAP and HR were measured and recorded before induction (T0), immediately after anesthesia (T1), 10 min (T2), 20 min (T3) and 30 min (T4) after anesthesia, immediately at the end of anesthesia (T5) and at recovery from anesthesia (T6). The operation time and anesthesia recovery time were recorded. Anesthesia-related complications

Table 1. Comparison of general information

Group	Group P	Group S	t	P/χ^2
Age (years)	7.54±4.12	8.03±3.51	-0.580	0.564
Gender (case)			0.198	0.656
Male	24	22		
Female	17	19		
Height (cm)	114.72±11.26	118.33±9.75	-1.552	0.125
Weight (kg)	31.82±6.59	29.77±7.43	1.322	0.190
ASA grading (case)			0.576	0.448
I	32	29		
II	9	12		

Note: ASA: American society of anesthesiologists. Group P: intravenous anesthesia group; group S: inhalation anesthesia group.

Table 2. Comparison of intraoperative conditions

Group	Group P	Group S	t	P
Operation time (min)	83.36±15.17	87.66±12.98	-1.379	0.172
Intraoperative blood loss (mL)	56.43±19.87	59.54±16.88	-0.764	0.447
Anesthesia recovery time (min)	31.56±10.17	40.38±13.42	-3.354	0.001
NSE content (ng/mL)	10.37±4.23	7.48±3.16	3.505	0.000

Note: NSE: neuron-specific enolase. Group P: intravenous anesthesia group; group S: inhalation anesthesia group.

were recorded at 24 hours postoperatively. Incidence of postoperative nausea, vomiting and restlessness (none; mild: restlessness occurs under strong stimulation such as sputum aspiration, which stops as soon as the stimulation stops; moderate: restlessness occurs without stimulation, but without stopping; severe: severe struggle, drug or physical methods are needed to stop it [12]) were observed, and only those with moderate to severe restlessness were recorded in this paper.

Statistical analysis

The experimental data were analyzed using SPSS 19.0 and plotted by Graphpad Prism 5 software. The measurement data are expressed as mean ± standard deviation ($\bar{x}$ ± sd). The independent sample t-test or repeated measures ANOVA was employed for comparison between the two groups. The Bonferroni post-test was applied to compare the difference in measurement data between each two groups at each time point. The counting data are expressed as percentage, and the comparison between groups was conducted by χ^2 test. P<0.05 is considered to be statistically significant.

Results

Comparison of general information

There were no significant differences in age, gender, height, weight and ASA grading between the two groups (P>0.05, **Table 1**).

Comparison of intraoperative conditions

There were no significant differences in operation time and intraoperative blood loss between the two groups (P>0.05). The anesthesia recovery time in group S was significantly longer than that in group P (P<0.01). The postoperative blood NSE content in group P was significantly higher than that in group S (P<0.001). See **Table 2**.

Comparison of cerebral oxygen saturation

There was no significant difference in rSO2 value between the two groups at T0 and T1 (P>0.05), and the rSO2 at T1 was significantly lower than that at T0 (P<0.05). Compared with T0 and T1, the rSO2 value increased significantly at T2, T3, T4, T5 and T6 in both groups (P<0.05). The rSO2 in group S was significantly higher than that in group P at T2, T3, T4, T5 and T6, and the differences were statistically significant (P<0.001). See **Table 3**; **Figure 1**.

Comparison of general vital signs

There were no significant differences in MAP and SPO_2 between the two groups at T0, T1, T2, T3, T4, T5 and T6 (P>0.05). The HR of patients in group S was significantly higher than that in group P at T2 (P<0.05), but there was no difference with group P at T0, T1 and T6 (P>0.05). The MAP and HR at T1 were lower than those at T0 in both groups (P<0.05). See **Table 4**.

Table 3. Comparison of cerebral oxygen saturation

Time/Group	Group P	Group S	F	P
T0	73.87±3.40	74.68±3.25	-1.103	0.273
T1	69.39±4.13*	70.26±3.86*	0.985	0.327
T2	82.33±4.78**,ΔΔ	87.00±5.85***,ΔΔΔ	-3.958	<0.001
T3	83.90±3.71**,ΔΔ	87.80±4.97***,ΔΔΔ	-4.026	<0.001
T4	85.55±3.84**,ΔΔ	93.06±2.43***,ΔΔΔ	-10.594	<0.001
T5	85.18±4.91**,ΔΔ	92.26±2.69***,ΔΔΔ	-8.097	<0.001
T6	85.57±4.92**	92.84±3.39***	-7.791	<0.001

Note: Compared with T0, *P<0.05; compared with T0, **P<0.01; compared with T0, ***P<0.001; compared with T1, ΔΔP<0.01; compared with T1, ΔΔΔP<0.001. Group P: intravenous anesthesia group; group S: inhalation anesthesia group. T0: before induction; T1: immediately after anesthesia; T2: after anesthesia 10 min; T3: after anesthesia 20 min; T4: after anesthesia 30 min; T5: immediately at the end of anesthesia; T6: at recovery from anesthesia.

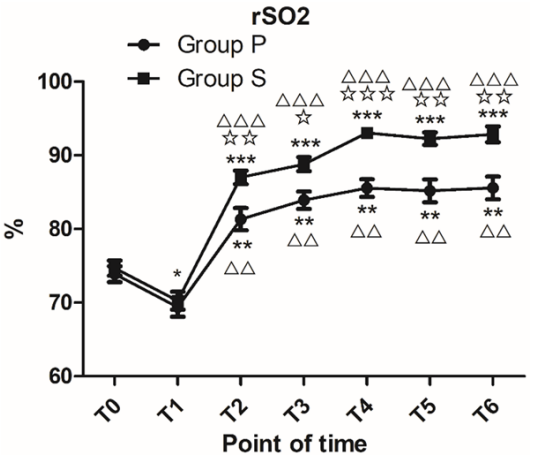

Figure 1. Comparison of cerebral oxygen saturation. Compared with T0, *P<0.05; compared with T0, **P<0.01; compared with T0, ***P<0.001; compared with T1, ΔΔP<0.01; compared with T1, ΔΔΔP<0.001; compared with group P, ☆P<0.05; compared with group P, ☆☆P<0.01; compared with group P, ☆☆☆P<0.001. Group P: intravenous anesthesia group; Group S: inhalation anesthesia group. T0: before induction; T1: immediately after anesthesia; T2: after anesthesia 10 min; T3: after anesthesia 20 min; T4: after anesthesia 30 min; T5: immediately at the end of anesthesia; T6: at recovery from anesthesia.

Comparison of anesthesia complications

The rate of postoperative nausea, vomiting and restlessness in group S was significantly higher than that in group P (P<0.01). See **Figure 2**.

Discussion

Under normal physiological states, cerebral blood flow maintains a relative balance through the regulation of cerebral perfusion pressure and cerebral metabolism, and balanced and stable cerebral blood flow provides adequate oxygen supply and nutrition for brain nerve cells [13, 14]. However, when the cerebral blood flow can't keep pace with its oxygen consumption, it will cause cerebral hypoxia [15]. Since the brain metabolism of children is higher than that of adults, it is more difficult for children with OSAS to tolerate hypoxia. Especially when the HR decreases due to the influence of anesthetic drugs during anesthesia, while as the maintenance of cerebral blood supply in children mainly depends on the fast HR, the decreased HR may lead to reduced blood supply [16]. Although the SPO_2 can still be maintained due to sufficient oxygen intake before induction and controlled breathing during the operation, it is not known whether the brain is in a state of hypoxia. Prolonged hypoxia will significantly affect brain nerve cells [17], especially in children, which will affect their neurodevelopment [18]. Therefore, monitoring of brain oxygen saturation is crucial in pediatric surgery. Currently, cerebral oxygen saturation monitoring has been applied in surgical procedures, but mainly in cardiac surgery [19, 20]. Since cardiac surgery may involve operations such as clamping the aorta, which will have a greater impact on hemodynamics, monitoring rSO2 can more better monitor the cerebral hypoxia and can avoid nerve cell damage in real time. Actually, even in ordinary surgery, rSO2 also needs to be monitored, especially in long-term operations. Although SPO_2 is at normal levels during anesthesia, there is a possibility that there still may be cerebral hypoxia. The younger the age is, the greater the likelihood that hypoxia will cause nerve damage. Therefore, some studies have proposed that the monitoring of rSO2 should be universal in all kinds of surgery [5]. At present, general anesthesia maintenance drugs are mainly divided into intravenous anesthetics and inhalation anesthetics, both of which can achieve good anesthetic effect in maintaining anesthesia. However, the clinical application value of the two depends on which drug maintenance will better allow brain protection in pediatric anesthesia as they exert different effects on pediatric rSO2. In this paper, both two kinds of anesthesia maintenance drugs were investigated.

Table 4. Comparison of general vital signs

Index Group	MAP (mmHg)		HR (times/min)		SPO_2 (%)	
	Group P	Group S	Group P	Group S	Group P	Group S
T0	68.65±9.12	69.23±8.54	101.32±14.25	103.47±13.87	97.51±1.35	98.12±1.66
T1	62.43±7.58#	63.14±7.84#	92.58±15.61##	93.73±14.86##	99.32±0.82	99.24±0.71
T2	69.13±8.25	68.73±9.41	87.52±11.27**	98.32±15.48	99.54±0.61	99.63±0.64
T3	67.45±9.61	69.52±8.47	89.36±12.27**	98.67±14.56	99.56±0.65	99.75±0.52
T4	70.17±9.57	68.97±9.16	87.74±14.64***	101.26±13.93	99.72±0.41	99.67±0.78
T5	67.58±8.66	68.41±9.12	86.83±13.79**	97.58±15.19	99.83±0.64	99.91±0.24
T6	71.44±9.53	70.62±8.89	103.65±16.87	102.56±17.21	99.87±0.55	99.78±0.36

Note: Compared with T0, #P<0.05; compared with T0, ##P<0.01; compared with group S, **P<0.01; compared with group S, ***P<0.001. MAP: mean arterial pressure; HR: heart rate; SPO_2: pulse oxygen saturation. Group P: intravenous anesthesia group; group S: inhalation anesthesia group. T0: before induction; T1: immediately after anesthesia; T2: after anesthesia 10 min; T3: after anesthesia 20 min; T4: after anesthesia 30 min; T5: immediately at the end of anesthesia; T6: at recovery from anesthesia.

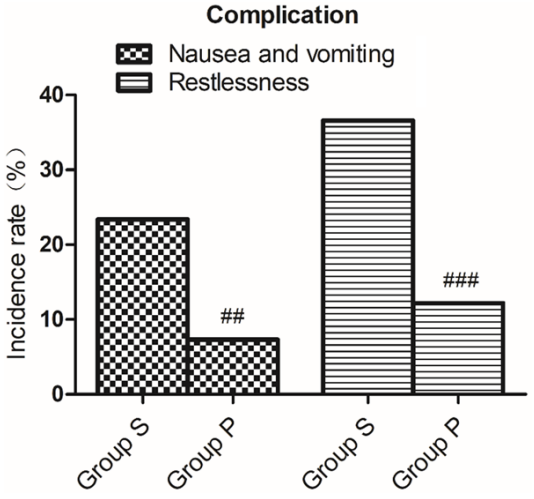

Figure 2. Comparison of anesthesia complications. Compared with group S, ##P<0.01; compared with group P, ###P<0.001. Group P: intravenous anesthesia group; group S: inhalation anesthesia group.

In this study, both groups of patients showed a decrease in rSO2 after induction compared with that before induction. At this time, there was no further oxygen inhalation during intubation, and the cerebral oxygen saturation began to decline, while SPO_2 was still normal, indicating that SPO_2 could not reflect cerebral metabolism and hypoxia. In addition, the rSO2 in children maintained by IA was found to be significantly higher than that of TIVA group at each time point after anesthesia intubation, and the postoperative NSE index of IA group was significantly lower than that of TIVA group. NSE is one of the markers of brain injury. When brain injury occurs, the metabolism of neurons changes. NSE can enter the blood from nerve cells through the blood-brain barrier, so the content of NSE in the blood will increase. In this paper, the NSE content in TIVA group was higher than that in IA group, which suggesting that maintenance with IA can better maintain the cerebral oxygen supply and reduce the injury of nerve cells. While it was observed that the MAP and SPO_2 did not differ significantly between the two groups before induction or after anesthesia. We speculate that although the intraoperative HR in the inhalation group was significantly higher than that in the intravenous anesthesia group, the BP was not affected and the hemodynamics was relatively stable. What's more, the recovery time of patients in group S was significantly longer than that in group P, while the rSO2 of the patients in group S was still higher than that in group P, indicating that the recovery time did not affect rSO2. Moreover, the incidence of postoperative nausea, vomiting and restlessness in group S was significantly higher than that in group P, but there were no more serious consequences, nor were there any obvious adverse reactions after treatment. Though the cause of postoperative restlessness of sevoflurane has not been clearly studied, the brain injury in group P was found to be more serious while the incidence of postoperative restlessness was lower, so it can be speculated that there is no significant relationship between cerebral hypoxia and the incidence of restlessness. Therefore, compared with maintaining anesthesia by TIVA, IA can improve cerebral oxygen saturation and maintain cerebral oxygen supply better, but its mechanism needs further research. The reason behind it may be that sevoflurane can reduce oxygen metabo-

lism in the brain [21], which in turn reduces oxygen consumption, thereby reducing the incidence of cerebral hypoxia. However, IA also increases the incidence of postoperative nausea, vomiting and restlessness increases, so that it should be used with caution in emergency patients with full stomach. There are still many shortcomings in this study. For example, as the surgery selected is short-to-medium-term surgery, whether a long-term surgery of more than 3 hours will come to the same conclusion needs to be further demonstrated. In addition, the rSO2 detected in this paper can only represent the local cerebral oxygen saturation to indicate the possibility of hypoxia or ischemia in the brain locally, but whether it applies to the whole brain remains to be studied.

In summary, IA results in prolonged recovery time over TIVA, while as the recovery time has no obvious effect on cerebral oxygen saturation. IA maintenance is still worthy of clinical promotion in that it can improve the value of intraoperative cerebral oxygen saturation in OSAS children, with better cerebral protection effect. In addition, close attention should be paid to the occurrence of anesthesia complications in patients, and IA may not be suitable for patients with a full stomach.

Disclosure of conflict of interest

None.

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References

[1] McCann ME and Soriano SG. Does general anesthesia affect neurodevelopment in infants and children? BMJ 2019; 367: l6459.

[2] Duan C, Hare MM, Staring M and Deligiannidis KM. Examining the relationship between perinatal depression and neurodevelopment in infants and children through structural and functional neuroimaging research. Int Rev Psychiatry 2019; 31: 264-279.

[3] Sun LS. Introduction to "anesthesia and neurodevelopment in children": a supplement from the sixth pediatric anesthesia neurodevelopmental assessment (PANDA) symposium. J Neurosurg Anesthesiol 2019; 31: 101-102.

[4] He Y, Yao P, Xie Y and Cao Y. Comment on: "usefulness of cerebral rSO2 monitoring during CPR to predict the probability of return of spontaneous circulation". Resuscitation 2019; 142: 193-194.

[5] Takegawa R, Shiozaki T, Ogawa Y, Hirose T, Mori N, Ohnishi M, Ishihara T, Shintani A and Shimazu T. Usefulness of cerebral rSO2 monitoring during CPR to predict the probability of return of spontaneous circulation. Resuscitation 2019; 139: 201-207.

[6] Tesoro S, Marchesini L and De Robertis E. Pediatric anesthesia. Transl Med UniSa 2019; 20: 1-3.

[7] Rehfuss A, Bogaert G and Kogan BA, Spinal anesthesia in children: most pediatric urologists are not on board. J Pediatr Urol 2019; 15: 263.e1-263.e5.

[8] Paduano S, Paduano FP, Aiello D, Barbara L, Zampogna S, Pujia R, Malara C, Cantile T and Ferrazzano GF. OSAS in developing age: screening of a Southern Italy population. Eur J Paediatr Dent 2019; 20: 302-305.

[9] Dachuri S, Sachidananda R, Montevecchi F, Rashwan M, Vicini C, Gandla S, Pugazhendi SK and Vasista SR. Barbed reposition pharyngoplasty in Indian population: a new palatal surgery for OSAS. Indian J Otolaryngol Head Neck Surg 2019; 71: 249-253.

[10] Blaeser S and Struck CJ. A history of ASA standards. J Acoust Soc Am 2019; 145: 77.

[11] Croughan P and Gee RE. How should physicians steward limited resources while ensuring that patients can access needed medicines? AMA J Ethics 2019; 21: E630-635.

[12] Kim JA and Ahn HJ. Intraoperative use of dexmedetomidine for the prevention of emergence agitation and postoperative delirium in thoracic surgery: a randomized-controlled trial. Can J Anaesth 2019; 66: 371-379.

[13] Brandi G, Stocchetti N, Pagnamenta A, Stretti F, Steiger P and Klinzing S. Cerebral metabolism is not affected by moderate hyperventilation in patients with traumatic brain injury. Crit Care 2019; 23: 45.

[14] Zhou M and Huang Z. Effect of comprehensive cerebral protection program on cerebral oxygen metabolism and vascular endothelial function in elderly patients with acute cerebral infarction. Iran J Public Health 2019; 48: 299-304.

[15] Mitra S, Bale G, Highton D, Gunny R, Uria-Avellanal C, Bainbridge A, Sokolska M, Price D, Huertas-Ceballos A, Kendall GS, Meek J, Tachtsidis I and Robertson NJ. Pressure passivity of cerebral mitochondrial metabolism is associated with poor outcome following peri-

natal hypoxic ischemic brain injury. J Cereb Blood Flow Metab 2019; 39: 118-130.
[16] Wong K, Kiringoda R, Kanumuri VV, Barber SR, Franck K, Sahani N, Brown MC, Herrmann BS and Lee DJ. Effect of anesthesia on evoked auditory responses in pediatric auditory brainstem implant surgery. Laryngoscope 2020; 130: 507-513.
[17] Nosrati R, Lin S, Mohindra R, Ramadeen A, Toronov V and Dorian P. Study of the effects of epinephrine on cerebral oxygenation and metabolism during cardiac arrest and resuscitation by hyperspectral near-infrared spectroscopy. Crit Care Med 2019; 47: e349-e357.
[18] Albrecht E, Vorobeichik L, Jacot-Guillarmod A, Fournier N and Abdallah FW. Dexamethasone is superior to dexmedetomidine as a perineural adjunct for supraclavicular brachial plexus block: systematic review and indirect meta-analysis. Anesth Analg 2019; 128: 543-554.
[19] Konishi A and Kikuchi K. Cerebral oxygen saturation (rSO2) during open heart surgery and postoperative brain dysfunction. Masui 1995; 44: 1322-1326.
[20] Konishi A and Kikuchi K. Association of postoperative brain dysfunction and atherosclerosis, intraoperative rSO2 and CO_2 reaction in open heart surgery. Masui 1996; 45: 287-292.
[21] Laaksonen L, Kallioinen M, Langsjo J, Laitio T, Scheinin A, Scheinin J, Kaisti K, Maksimow A, Kallionpaa RE, Rajala V, Johansson J, Kantonen O, Nyman M, Siren S, Valli K, Revonsuo A, Solin O, Vahlberg T, Alkire M and Scheinin H. Comparative effects of dexmedetomidine, propofol, sevoflurane, and S-ketamine on regional cerebral glucose metabolism in humans: a positron emission tomography study. Br J Anaesth 2018; 121: 281-290.