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SCIENTIFIC ARTICLE

Application of Narcotrend® Monitor for Evaluation of Depth of Anesthesia in Infants Undergoing Cardiac Surgery: a Prospective Control Study

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Abstract
Background and objectives: To investigate the clinic effectiveness, safety and feasibility of Narcotrend® monitor for evaluation of depth of anesthesia in congenital heart disease (CHD) infants undergoing cardiac surgery.
Methods: A total of 80 infants receiving general anesthesia in selective surgery were randomly selected. Infants were assigned into two groups (n = 40 per group). In the Narcotrend group, the depth of anesthesia was monitored with the Narcotrend monitor. In the standard group, the depth of anesthesia was controlled according to the experience. The mean arterial pressure (MAP) and heart rate (HR) were determined, as well as the dose of fentanyl, muscle relaxant, recovery time and extubation time were recorded.
Results: In both groups, vital signs were stable during the surgery. When compared with the standard group, the MAP and HR were more stable, the total dose of fentanyl and muscle relaxant were significantly reduced and the recovery time and extubation time were markedly shortened in the Narcotrend group.
Conclusion: The application of Narcotrend_monitor was beneficial to the control of the depth of anesthesia in CHD infants receiving total intravenous anesthesia, in which small amount of narcotics can achieve optimal anesthesia. Moreover, the recovery time and extubation time are reduced and the harmful consequence such as intraoperative awareness can be avoided.

Introduction

As the depth of anesthesia cannot be reliably judged by the cardiovascular measurements alone, especially during total intravenous anesthesia, a reliable method is needed to measure the hypnotic component of sedation and anesthesia [1]. There is currently much interest in the estimation of the depth of anesthesia by electroencephalography (EEG), as it may help to prevent underdosage and awareness, avoid overdosage as well as to allow rapid recovery [2]. Hypnotic effects are associated with a slowing of the EEG, and processed EEG variables such as the Bispectral Index (BIS) and spectral edge frequency have been developed to ease the EEG interpretation. However, this is time-consuming and requires special knowledge [3].

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The Narcotrend depth of anesthesia monitor (MonitorTechnik, Bad Bramstedt, Germany) is a computer-based EEG monitor designed to measure the depth of anesthesia [4]. It was developed by a research group at the Hannover University Medical School (Germany) and uses algorithms for automatic assessment of the raw EEG during the anesthesia and sedation. Two EEG channels are recorded and the signals from the two hemispheres of the brain are compared. The Narcotrend algorithm is based on a pattern recognition of the raw EEG and classifies the EEG epochs in different stages - from A (awake) to F (increasing burst suppression down to electrical silence). It differentiates a total of 14 different stages, displaying them on a computer along with raw signal EEG, median frequency, spectral edge frequency and a trend analysis.

Children can benefit from depth of anesthesia monitoring for several reasons. The incidence of awareness during anesthesia in children is 4~8 times higher than in adults [5]. Furthermore, the doses of anesthetics are remarkably different between children and adults, due in part to a higher clearance and volume of distribution in children [6]. EEG monitoring may help the anesthesiologists to better adjust the doses of anesthetics to individual needs [7]. The precise dosing of anesthetics leading to improved recovery and home readiness also yields cost savings.

Unlike other monitor devices, the age-related changes in the EEG are incorporated into the Narcotrend algorithm. Numerous studies have evaluated the role of Narcotrend monitor in adult anesthesia, yielding mixed results [8,9]. In children, there are only a few reports on the use of Narcotrend monitor in the inhalation anesthesia [10,11]. These studies suggest that, during sevoflurane or desflurane-based anesthesia, the EEG monitoring with Narcotrend monitor can differentiate awake children from those who are deeply anesthetized.

Numerous studies have demonstrated that intra-operative monitoring of depth of anesthesia is important to assure a successful surgery, maintain vital signs, preserve stable hemodynamics, reduce side effects, achieve the optimal anesthesia, realize favorable analgesic and muscle relaxing, avoid the intra-operative awareness and facilitate rapid recovery [12]. In this study, we performed intra-operative anesthesia monitored with the Narcotrend monitor in infants with congenital heart disease (CHD) who were admitted to the Institute of Heart Diseases, and evaluated the effectiveness, safety and feasibility of Narcotrend for evaluating depth of anesthesia.

Methods

Patients and grouping

A total of 80 infants aged 5 to 10 months and diagnosed with CHD were recruited from January 2010 to October 2011 and randomly allocated into two groups. In the Narcotrend group, depth of anesthesia was monitored intra-operatively (n = 40). In the standard group, the depth of anesthesia was monitored according to the clinical experience (n = 40). The heart function was classified as grade II-III. The CHD included atrial septal defect (ASD; n = 20), ASD + ventricular septal defect (VSD) (n = 20), patent ductus arteriosis + ASD + VSD (n = 20), descending aortic coarctation (n = 10), VSD + Mitral or tricuspid regurgitation (n = 10). Infants with a history of central nervous system diseases or cerebrovascular diseases were excluded from this study.

Total intravenous anesthesia

In both groups, infants received total intravenous anesthesia. After intravenous access, we determined anesthesia induction, tracheal intubation, skin incising, thoracotomy, establishment of cardiopulmonary bypass, aortic cross-clamping, cooling, intracardiac deformity correction, aortic opening, rewarming, discontinuation of cardiopulmonary bypass, extubation and wound closure, the mean arterial pressure (MAP), heart rate (HR), body temperature, arterial oxygen saturation (SaO_2), NT stage (NTS), NT index (NTI), total dose of sedative, total dose of analgesic, total dose of muscle relaxant, recovery time and extubation time. Before surgery, patients had fasted for 4-6 hours and oral midazolam (0.5 $mg.kg^{-1}$) was administered at 30 minutes before surgery. Three electrodes were placed on the forehead and then connected to the anesthesia monitor. The skin resistance was < 6.0 kilohm and the difference between two electrodes was < 2.5 kilohm. When the data were stabilized for 3 minutes, the parameters were monitored as the baseline level.

Processing and records

After recording baseline data, we performed intravenous injection of fentanyl (5-10 $\mu g.kg^{-1}$), vecuronium bromide (0.1-0.15 $mg.kg^{-1}$) and midazolam (0.02 $mg.kg^{-1}$) to induce anesthesia. When the patient had no awareness and their muscle relaxed, we carried out intranasal intubation. The tide volume and respiratory rate were maintained at 10 $ml.kg^{-1}$ and 32-34 $breaths.min^{-1}$, respectively. Ventilation was done with air and oxygen in pressure control mode for anesthesia maintenance. In the Narcotrend group, the narcotic was administered according to the findings during anesthesia monitoring. In the standard group, the narcotic was administered according to the clinical experience. In both groups, anesthesia maintenance was carried out with fentanyl, vecuronium bromide and midazolam. After surgery, patients were transferred to the intensive care unit (ICU). When the disease condition was stable, extubation was done. Indications for extubation included the recovery of spontaneous breathing, consciousness, stable cardiac and pulmonary functions, urine volume of > 3-4 $ml.kg.^{-1}min^{-1}$, acceptable blood gas analysis results, small amount of drainage fluid and stable electrolytes. At 3 minutes after stable data, immediately after anesthesia induction, we determined tracheal intubation, skin incising, thoracotomy, cardiopulmonary bypass establishment, aortic cross-clamping, cooling, intracardiac deformity correction, aortic opening, rewarming, discontinuation of cardiopulmonary bypass, extubation and wound closure. The MAP, HR, body temperature, arterial oxygen saturation (SaO_2), NT stage (A = consciousness; B = light sleep and relaxation; C = deep sleep; D = upper limit of anesthesia; E = lower limit of anesthesia; F = fulminant suppression), NT index, total dose of sedative, total dose of analgesic, total dose of muscle relaxant, time to recovery and extubation time were recorded. We used time to recovery, extubation time and intra-operative awareness for statistical analysis.

Statistical analysis

We employed SPSS version 12.0 for Windows for statistical analysis. Quantitative data were expressed as mean ± standard deviation (SD). Comparisons between two groups were done with *t* test and a value of $P < 0.05$ was considered statistically significant. Qualitative data were expressed as percentage and compared with chi square test (Table 1).

Results

Surgery time was 120-180 minutes; the aorta was clamped for 45-95 minutes, and the cardiopulmonary bypassing was performed for 58-110 minutes. There were no marked differences in age, gender, height, body weight, disease distribution and type of surgery between the two groups.

Case presentation

A 6-month-old male infant weighing 7 kg was classified as ASA III and diagnosed with VSD+MI+TI. During the surgery, we monitored depth of anesthesia with Narcotrend monitor. The NTS and NTI were A-B_0 and 90-95, respectively. Sedation was succesful and we used intravenous fentanyl (5 μg) and vecuronium (0.75 mg) for anesthesia induction followed by tracheal intubation. When the NTS was D_1, the NTI was 47, heart rate was 135 beats.min^{-1}, and blood pressure was 90-95/45-65 mmHg, suggesting stable anesthesia induction. We did cardio-pulmonary bypass (CPB) and administered fentanyl (5 μg) and vecuronium (0.75 mg) again. The NTS was D_2, NTI was 40-42, and body temperature was 27-30℃. The NTS of E_0, NTI of 30-28 and body temperature of 25℃ suggested favorable anesthesia. When the NTS was E_1 and NTI was 19-21, anesthesia was a little bit deep and we administered the above drugs additionally. After surgery, we rewarmed the patient to 30℃. When the NTS was D_2 and NTI was 40-45, fentanyl (5 μg.kg^{-1}) and vecuronium (0.5 mg) were administered. When the body temperature reached 36.5℃, NTS was D2-C2, and NTI was 65, in which the aorta clamping was done for 75 min and cardiopulmonary bypass was performed for 95 min. When the patient was discharged from the surgery room, the NTS was C_0,-B_1 and NTI was 75-81. At 2.5 h after surgery, extubation was done and mechanical ventilation discontinued. The patient had conscious awareness and normal movement in all limbs. No complications were observed and he got discharged 8 days after surgery.

Table 1 Vital signs in two groups at different time points.

Time point	MAP (mm Hg)		HR (beats.min^{-1})		Body temperature (°C)		SaO_2 (%)	
	Narcotrend	Standard	Narcotrend	Standard	Narcotrend	Standard	Narcotrend	Standard
Baseline	62±11.2	70.5±10.5	141±10.9	143±20.6	37.5±1.1	37.8±1.2	98.0±1.0	97.2±1.8
After induction	65±10.1	60.5±5.5	125±9.5	150±12.8	37.4±1.2	37.6±1.3	99.5±1.8	98.6±1.6
Tracheal intubation	58.5±9.5^a	64.5±11.5	135±8.5^a	148±10.8	37.2±1.1	37.4±1.2	99.4±0.4	99.1±0.5
Skin incising	61.4±10.5^a	70.5±14.5	140±10.0^a	165±12.6	37.2±1.1	37.3±1.3	99.6±0.3	99.4±0.5
Thoracotomy	59.2±10.2^a	63.5±10.5	136±12.5^a	148±13.6	36.8±1.0	36.9±1.1	99.7±0.3	99.6±0.4
Establishment of Cardiopulmonary bypass	49.5±6.4^a	61.5±10.3	122±10.4^a	135±12.6	34.5±0.8	34.9±0.9	99.8±0.7	99.1±0.8
Aortic cross-clamping	42.5±6.5^a	50.5±9.5	10±12.6^a	70±10.6	30.5±2.0	30.4±3.0	99.4±0.2	99.0±0.6
Cooling	48.5±5.5^a	55.1±9.8	60±10.5^a	100±10.4	28±2.2	28±2.3	99.4±0.3	99.0±0.8
Intracardiac deformity correction	46.5±4.5^a	59.5±8.5	0	0	26±1.2	26±1.0	99.8±0.2	99.6±0.8
Aortic opening	50.1±5.5^a	55.5±7.5	50±15.5^a	65±12.6	33±1.2	33±1.1	99.7±0.1	99.3±0.3
Rewarming	55.1±6.5^{ab}	57.4±8.2	120±10.6^{ab}	156±10.6^c	37±1.0	37.2±1.0	99.8±0.2	99.4±0.4
Discontinuation of cardiopulmonary bypass	60.5±10.2^{ab}	65.5±9.5^c	140±12.4^{ab}	170±10.2^c	37.2±1.1	37.5±1.0	99.7±0.3	99.2±0.8
Extubation	70.5±10.5^{ab}	73.5±10.9^c	145±10.4^{ab}	165±10.4^c	36.9±0.5	37.1±0.4	99.8±0.2	99.4±0.7
Wound closure	72.5±14.5^{ab}	82.5±15.2^c	142±5.6^{ab}	162±10.6^c	36.8±0.4	36.9±0.6	99.8±0.4	99.4±0.6

^{a}P < 0.05 vs standard group; ^{b}P > 0.05 and ^{c}P < 0.05 vs Baseline and After induction.

Table 2 Anesthesia procedures.

	Narcotrend stage	Narcotrend index
Awake	A	95-100
	B_0	90-94
Sedated	B_1	85-89
	B_2	80-84
Light anesthesia	C_0	75-79
	C_1	70-74
	C_2	65-69
General anesthesia	D_1	57-64
	D_2	47-56
	D_3	37-46
General anesthesia with deep hypnosis	E_0	27-36
	E_1	20-26
	E_2	13-19
General anesthesia with increasing burst suppression	F_0	5-12
	F_1	1-4

Narcotrend stage and index (version 4.0) [14]

NT anesthesia

Under Narcotrend monitoring, the vital signs were stable during the surgery, during anesthesia induction, maintenance and recovery. Maintenance was easy to achieve. The Narcotrend monitor can reflect the depth of anesthesia and sedation through detecting brain waves, which may be used to regulate narcotics/sedatives dosage. In the anesthesia control in the Narcotrend Group, NTS was maintained at D0-2 before CPB and NTI was 40-52. Following CPB, anesthesia was maintained at D or E0-2 with reduction of body temperature, NTI was 35-5, and NTS at F0-1 should be avoided. The NTI of 20-14 can reduce the dose of narcotics or increase the interval between two administrations. When the body temperature returned to 28-30℃, additional narcotics were required. After CPB discontinuation, anesthesia was then maintained at D-B and NTI was above 58-60 (Table 2).

Comparisons

In both groups, the vital signs were stable during surgery. When compared with the standard group, the MAP and HR were more stable ($P < 0.05$), and the total dose of sedative, analgesic and muscle relaxant was significantly reduced in the Narcotrend group (Table 3). In the Narcotrend group, the time to recovery and extubation time were 2.5 ± 1.0 h and 3.0 ± 1.0 h, respectively, and intra-operative awareness and breathing were absent. In the standard group, the time to recovery and extubation time were 5.5 ± 1.0 h and 10.0 ± 1.0 h, respectively, and intra-operative awareness and breathing were present in two infants. Significant differences between two groups ($P < 0.05$) were noted in recovery time, extubation time and intra-operative awareness and breathing.

Discussion

Our results revealed that, with the help of anesthesia depth monitoring with the Narcotrend monitor, a low dose of anesthetics is required to achieve optimal anesthesia, the time to recovery from the anesthesia shortened, intra-operative awareness is avoided and the hemodynamics are maintained stable.

General anesthesia does not promote effective strategies for monitoring its depth. Currently, observation of clinical signs remains instrumental in monitoring depth of anesthesia during surgery. Clinical signs are difficult to measure, aside from blood pressure and heart rate. Moreover, the interaction between surgery and anesthesia complicates clinical signs, which adds further difficulty to the monitoring of anesthesia depth[13-14]. Clinical signs vary among patients because they present different responses to surgery and anesthesia, which may result in deep or light anesthesia.

In children's anesthesia, especially infants, brain development is not yet mature and the synapses may continue to form for up to 5 years. Thus, children's brain electrical activity is different from that of adults. Physiological studies showed that brain electrical activity-based anesthesia depth monitoring can be used to monitor drug-induced arousal. To date, bispectral index (BIS) and auditory evoked potential (AEP) have been used in the monitoring of depth of anesthesia. However, the electrodes should be placed at designated sites, which may also cause pain. In addition, under hypothermia during the intravenous anesthesia and cardiopulmonary bypass, there is evidence that the BIS is inconsistent with anesthesia depth. Additionally, BIS calculation is usually delayed and, thus, BIS is not suitable for real time monitoring and may be interrupted by electrical coagulation. Moreover, BIS is not a reliable variable for the

Table 3 Surgery time, time of aorta clamping and time of CPB in children with different CHDs.

Type of surgery	n	Surgery time (min)	Time of aorta clamping (min)	Time of CPB (min)
ASD	20	120	50-70	60-75
ASD+VSD	20	122	70-85	75-85
ASD+PDA	20	130	60-70	75-90
COA	10	160	80-90	85-100
VSD+MI+TI	10	180	75-95	80-110

prediction of analgesic and immobilization. Thus, BIS has significant limitation in clinical anesthesia guidance. In AEP detection, sound stimulation is required and, thus, cannot be used in deaf patients. AEP can be used to monitor deep anesthesia when auditory feedback is absent and excessive anesthesia is difficult to identify. The index is nearly zero and detection is susceptible to be interrupted by the alternating current and noise. Detection of anesthesia depth with Narcotrend monitor is a new strategy for monitoring depth of anesthesia, in which the EEG can be detected to reflect brain status. This detection is based on raw EEG and uses Kugler Multi-parameter statistics and computer processing. In the detection, the EEG signals are classified into 6 levels that include 14 stages: A0-2, B0-2, C0-2, D0-2, E0-2 and F0-1. In addition, the changes in the power spectrum of α, ß, γ and δ are also presented. Level A represents consciousness, level B sedation, level C light anesthesia, level D general anesthesia, level E deep anesthesia and level F absence of EEG.[15] In addition, 100 points are used to reflect the EEG index (100 = conciousness, 0 = deepest anesthesia), describing the whole process from consciousness to deep anesthesia, which allows application to be more precise. The quantification of anesthesia has the characteristics of individualization. Thus, monitoring of depth of anesthesia with Narcotrend monitor is superior to that with BIS and AEP [16].

Heart surgery anesthesia is different from that in other surgeries. Besides routine management, hypothermia and CPB are required for surgery. Thus, the anesthetic dosage and depth are difficult to control. Light anesthesia is not potent enough to inhibit movement, stretch and pain reflexes. Stress increased heart rate and blood pressure may elevate oxygen consumption, which may aggravate the myocardial ischemia and / or hypoxia, resulting in an increased risk for surgical complications. Conversely, deep anesthesia may suppress respiration and circulation and prolong the course of diseases, which may worsen damage to circulation and respiration or even cause death. Following treatment with awakening extension drugs may cause cardiovascular side effects. For patients treated with cardiovascular drugs (such as digitalis, ß-blocker), acetylcholinesterase inhibitors to treat cardiovascular side effects may cause bradycardia and arrhythmia. When the depth of anesthesia is monitored using the Narcotrend monitor, anesthesia may be guided according to the anesthesia index, which makes the dose of anesthetics more precise.

In the standard group (a 6-month-old patient weighing 7 kg), anesthetics were administered 2-3 times from anesthesia induction to tracheal intubation, in which 3-5 µg of fentanyl and 0.75 mg of vecuronium were administered (0.35 mg of midazolam was given once). During the CPB (1 h), anesthetics were administered 2-3 times. In addition, the anesthetics were administered twice from the CPB discontinuation to wound closure (50 min). In the present study, the anesthetics were administered 7-8 times during the entire surgery. The total dose of fentanyl was 35-40 µg and that of vecuronium was 5~5.6 mg. In the Narcotrend group, anesthetics were administered 1-2 times from anesthesia induction to tracheal intubation. During the CPB (1 h), anesthetics were administered 1-2 times. In addition, the anesthetics were administered once from the CPB discontinuation to wound closure (50 min). In the present study, the anesthetics were administered 4-5 times during the entire surgery. The total dose of fentanyl was 20-25 µg and of vecuronium was 3-3.75 mg. Statistical analysis showed the total dose of anesthetics was markedly higher in the standard group than in the Narcotrend group.

In the standard group, time to recovery was 5-6 h and extubation time was 7-10 h. In the Narcotrend group, the time to recovery was shorter than 2-3 h and extubation time was 2.5-3.5 h. In the standard group, the patients recovered slowly, the recovery was incomplete and patients presented agitation and excitation. In several patients, non-invasive mechanical ventilation was required. In the Narcotrend group, recovery from anesthesia was smooth and the consequence of muscle relaxation, sedation and analgesic was absent. Agitation and excitation were not observed and mechanical ventilation was not required following extubation. In the standard group, 2 patients developed movement reflex, limb movement and eyelash reflex during the surgery, suggesting intra-operative awareness. Thus, evaluation of anesthesia depth with heart rate, blood pressure and SpO_2 is unreasonable and experience shows it is not reliable due to absence of quantitative variables. During the routine monitoring of anesthesia depth, administration of anesthetics at pre-designed time points is not feasible, which may lead to instable anesthesia (deep or light anesthesia). Our results demonstrated that the Narcotrend monitor could be used to monitor the depth of anesthesia precisely, which is superior to other strategies and can be used to guide anesthesia (Tables 4-5).

Table 4 Total dose of sedative, analgesic and muscle relaxant in two groups.

Group	Midazolam (mg)	Fentanyl (µg)	Vecuronium bromide (mg)
Narcotrend	0.5±0.1[a]	10±1.2[a]	3.2±0.4[a]
Standard	0.6±0.2	20±1.4	4.5±1.0

[a]P < 0.05 vs. standard group; mean ± SD.

Table 5 Time to recovery and extubation time.

Group	Time to recovery	Extubation time
Narcotrend	2.5 ± 1.5	3.0± 1.0
Standard	5.5 ± 1.2	10.0 ± 1.3

P < 0.05 vs. standard group; time (h), n = 40, mean ± SD.

Detection with continuous electrodes may assure high-quality EEG signals. The Narcotrend monitor has some advantages. It has two channels: one is used for EEG monitoring during general anesthesia, and the other to compare the statuses of two hemispheres [17-20]. Anesthesia depth monitoring with the Narcotrend monitor has no influence on the heart surgery in the presence of CPB, but BIS may affect the CPB. Thus, pulsatile perfusion may significantly affect the brain electrical activity and consciousness, and low or high PaO_2 and low $PaCO_2$ may reduce the blood flow and also inhibit brain electrical activity. Hypothermia can also compromise brain electrical activity. Thus, although the changes in BIS are closely related to CPB, determination of anesthesia depth cannot completely depend on BIS during the CPB and hypothermia.

There were still limitations in this study. 1) During the CPB, rapid body temperature reduction leads to the display of F in the monitor, suggesting deep anesthesia. This is not consistent with the actual condition thus, requiring further studies; 2) The NT electrode for infants is a little bit large, and its fixation requires the aid of tape. However, this does not influence monitoring. It is imperative to manufacture the electrode in a small size. In future studies, additional indicators (such as blood pressure and body movement), together with that displayed in Narcotrend can be used to evaluate the depth of anesthesia. In addition, the monitoring of, respiration and arterial oxygen saturation may also be integrated into the Narcotrend monitor, benefitting intra-operative monitoring of anesthesia. In addition, a warning device can be integrated into this monitor to detect general anesthesia and burst suppression.

In sum, the Narcotrend monitor can be used to individually and quantitatively monitor the depth of anesthesia for infants receiving heart surgery, in which the vital signs and hemodynamics are stable and the depth of anesthesia is intuitive and definite. This is a multi-faceted, multi-parameter, continuous and real-time method for the monitoring of anesthesia depth with promise in future clinical practice.

Conflict of interest

All authors declare no conflict of interest.

References

1. Tang ZH, Liu SH, Cheng ZG, Li QC, Wang YJ, Guo QL - Narcotrend for monitoring the anesthetic depth during endotracheal intubation in sevoflurane anaesthesia. Nan Fang Yi Ke Da Xue Xue Bao. 2010;30(7):1654-1657, 1662.
2. Gan TJ, Glass PS, Windsor A, Payne F, Rosow C, Sebel P, Manberg P - Bispectral index monitoring allows faster emergence and improved recovery from propofol, alfentanil, and nitrous oxide anaesthesia. Anesthesiology. 1997;87:808-815.
3. Schultz B, Grouven U, Schultz A - Automatic classification algorithms of the EEG monitor Narcotrend for routinely recorded EEG data from general anaesthesia: a validation study. Biomed Technik. 2002;47:9-13.
4. Lai RC, Lu YL, Huang W, et al. - Application of a narcotrend-assisted anaesthesia in-depth monitor in the microwave coagulation for liver cancer during total intravenous anaesthesia with propofol and fentanyl. Chin J Cancer. 2010;29(1):117-120.
5. Davidson AJ, Huang GH, Czarnecki C, et al. - Awareness during anaesthesia in children: a prospective cohort study. Anesth Analg. 2005;100:653-661.
6. Mazoit JX - Pharmacokinetic / pharmacodynamic modeling of anesthetics in children: therapeutic implications. Paediatr Drugs. 2006;8:139-150.
7. Powers KS, Nazarian EB, Tapyrik SA, et al. - Bispectral index as a guide for titration of propofol during procedural sedation among children. Pediatrics. 2005;115:1666-1674.
8. Schneider G, Kochs EF, Horn B, Kreuzer M, Ningler M - Narcotrend® does not adequately detect the transition between awareness and unconsciousness in surgical patients. Anesthesiology. 2004;101:1105-1111.
9. Kreuer S, Bruhn J, Larsen R, Bialas P, Wilhelm W - Comparability of Narcotrend™ index and bispectral index during propofol anaesthesia. Br J Anaesth. 2004; 93:235-240.
10. Weber F, Gruber M, Taeger K - The correlation of the Narcotrend® Index and classical electroencephalographic parameters with endtidal desflurane concentrations and hemodynamic parameters in different age groups. Paediatr Anaesth. 2005;15:378-384.
11. Weber F, Hollnberger H, Gruber M, Frank B, Taeger K - The correlation of the Narcotrend Index with endtidal sevoflurane concentrations and hemodynamic parameters in children. Pediatr Anesth. 2005;15:727-732.
12. Kent CD, Domino KB - Depth of anaesthesia. Curr Opin Anaesthesiol. 2009;22(6):782-787.
13. Kreuer S, Biedler A, Larsen R, Altmann S, Wilhelm W - Narcotrend monitoring allows faster emergence and a reduction of drug consumption in propofol–remifentanil anaesthesia. Anesthesiology. 2003;99:34-41.
14. Kreuer S, Wilhelm W - The Narcotrend monitor. Best Pract Res Clin Anaesthesiol. 2006;20(1):11111-9.
15. Panousis P, Heller AR, Burghardt M, Bleyl JU, Koch T - The effects of electromyographic activity on the accuracy of the Narcotrend monitor compared with the Bispectral Index during combined anaesthesia. Anaesthesia. 2007;62(9):868-874.
16. Sinha PK, Koshy T - Monitoring Devices forMeasuring the Depth of Anaesthesia – An overview. Indian Journal of Anaesthesia. 2007; 51(5): 365-381.
17. Sandin RH, Enlund G, Samuelsson P, Lennmarken C. Awareness during anaesthesia: a prospective case study. Lancet. 2000; 355(9205):707-711.
18. Palanca BJ, Mashour GA, Avidan MS - Processed electroencephalogram in depth of anaesthesia monitoring. Curr Opin Anaesthesiol. 2009;22(5):553-559.
19. Kreuer S,Wilhelm W.–The Narcotrend monitor. Best Pract Res Clin Anaestheisol. 2006;20:111-119.
20. Honan D, Doherty D, Feizelle H - A comparison of the effects on bispectral index of mild vs. moderate hypothermia during cardiopulmonary bypass. Eur J Anaesthesiol. 2006;23(5):385-390.