Comparison between effect of desflurane/remifentanil and propofol/remifentanil anesthesia on somatosensory evoked potential monitoring during scoliosis surgery—A randomized controlled trial

M Shahnaz Hasan¹, Jin-Keat Tan¹, Chris Yin Wei Chan², Mun Keong Kwan², Fathil Syafiq Abdul Karim³ and Khean-Jin Goh³

Abstract

Background: Drugs used in anesthesia can affect somatosensory evoked potential (SSEP) monitoring, which is used routinely for intraoperative monitoring of spinal cord integrity during spinal surgery. Objective: The objective of this study was to determine whether combined total intravenous anesthesia (TIVA) technique with propofol/remifentanil is associated with less SSEP suppression when compared to combined volatile agent desflurane/remifentanil anesthesia during corrective scoliosis surgery at a comparable depth of anesthesia. Design: It is a randomized controlled trial. Setting: The study was conducted at the Single tertiary University Hospital during October 2014 to June 2015. Patients: Patients who required SSEP and had no neurological deficits, and were of American Society of Anesthesiologist I and II physical status, were included. Patients who had sensory or motor deficits preoperatively and significant cardiovascular and respiratory disease were excluded. A total of 72 patients were screened, and 67 patients were randomized and allocated to two groups: 34 in desflurane/remifentanil group and 33 in TIVA group. Four patients from desflurane/remifentanil group and three from TIVA group were withdrawn due to decrease in SSEP amplitude to <0.3 μV after induction of anesthesia. Thirty patients from each group were analyzed. Interventions: Sixty-seven patients were randomized to receive TIVA or desflurane/remifentanil anesthesia. Main outcome measures: The measurements taken were the amplitude and latency of SSEP monitoring at five different time points during surgery: before and after the induction of anesthesia, at skin incision, at pedicle screw insertion, and at rod insertion. Results: Both anesthesia techniques, TIVA and desflurane/remifentanil, resulted in decreased amplitude and increased latencies of both cervical and cortical peaks. The desflurane/remifentanil group had a significantly greater reduction in the amplitude (p = 0.004) and an increase in latency (p = 0.002) of P40 compared with the TIVA group. However, there were no differences in both amplitude (p = 0.214) and latency (p = 0.16) in cervical SSEP between the two groups. Conclusions: Compared with TIVA technique, desflurane/remifentanil anesthesia caused more suppression in cortical SSEP, but not in cervical SSEP, at a comparable depth of anesthesia.

Keywords

desflurane, propofol, remifentanil, scoliosis, somatosensory evoked potential, TIVA

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¹Department of Anesthesiology, University of Malaya, Kuala Lumpur, Malaysia
²Department of Orthopaedic Surgery, University of Malaya, Kuala Lumpur, Malaysia
³Division of Neurology, University of Malaya, Kuala Lumpur, Malaysia

Corresponding author:
Mohd Shahnaz Hasan, Department of Anesthesiology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia. Email: shahnaz@ummc.edu.my

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Introduction

Somatosensory evoked potentials (SSEPs) are routinely used to monitor spinal cord integrity during spinal surgery.\(^1\) Intraoperative changes of the SSEP may result from surgical injury or ischemia to the spinal cord. Studies have shown that intraoperative SSEP monitoring provides safer conditions for spinal manipulation, reduced neurological deficits, and combined with motor evoked potential (MEP) monitoring has superseded the Stagnara wake-up test.\(^2–5\) A large multicenter study of SSEP for spinal cord monitoring has reported that the sensitivity of SSEP was 92%, specificity 98.9%, positive predictive value 42%, and negative predictive value 99.93%.\(^6\)

However, SSEP signals can be affected by certain physiological variables such as blood pressure, Pa\(_{CO_2}\), Pa\(_{O_2}\), temperature, or hemoglobin concentration. Anesthesia also has a significant influence on SSEP monitoring. Increasing anesthesia concentrations suppress the evoked potential (EP) amplitude and prolong its latency. This effect is time and dose-dependent and is reversible. Inability to interpret SSEPs correctly might result in failure to identify spinal cord injury and hence delay in performing corrective measures. Conversely, it might lead to a false diagnosis of injury resulting in unwarranted treatment. Anesthetists, therefore, have an important role in their choice of anesthesia techniques and drugs in preserving the quality of SSEP to avoid misinterpretation. Most studies have shown that intravenous (IV) anesthesia is superior to inhalation anesthesia for SSEP monitoring in spinal surgery. Sevoflurane has been shown to decrease SSEP amplitude and increase its latency in a dose-dependent manner.\(^7\) With a comparable depth of anesthesia, Liu et al. found a significantly lower SSEP amplitude and prolonged SSEP latency with isoflurane.\(^8\) A study has also shown that propofol has a minimal effect on SSEP monitoring compared with sevoflurane.\(^9\)

Other studies have found that the administration of opioids resulted in only clinically unimportant changes in SSEP amplitude and latency.\(^10–12\) Remifentanil is a very potent opioid with a very short context-sensitive halftime that is independent of the total dose used and the duration of the infusion. Therefore, the concurrent use of remifentanil would decrease the dose of propofol and volatile agent used, hence reducing the latter’s effect on SSEP during monitoring.\(^13,14\)

The aim of this study was to determine whether total intravenous anesthesia (TIVA) technique with propofol/remifentanil caused less SSEP suppression when compared to combined volatile agent desflurane/remifentanil anesthesia during corrective scoliosis surgery at a comparable depth of anesthesia as guided by bispectral index (BIS) measurements.

Materials and methods

After obtaining ethics committee approval from the Medical Ethics Committee, University Malaya Medical Center, Kuala Lumpur, Malaysia (Chairperson Professor Dr. Looi Lai Meng; Institutional Review Board reference no. 201410-639 dated October 29, 2014) and written informed consent, 67 patients who underwent elective posterior spinal fusion for adolescent idiopathic scoliosis surgery were recruited from October 2014 to June 2015. This study was registered with our National Medical Research Registry (NMRR) and has a reference ID, NMRR-14-1314-23176. Patients who required SSEP and had no neurological deficits, and were of American Society of Anesthesiologist I and II physical status, were included. Patients who had sensory or motor deficits preoperatively and significant cardiovascular and respiratory disease were excluded from the trial. Using a concealed allocation method, a computer-generated block randomization was used to allocate patients into two groups: desflurane/remifentanil group and TIVA group.

In the operating room, routine monitoring with pulse oximetry, electrocardiograph, and automated noninvasive blood pressure was performed before the induction of anesthesia. Patients were also additionally monitored for their BIS (Covidien, Mansfield, Massachusetts, USA) to assess the depth of anesthesia. For the desflurane group, patients were induced with IV propofol 2.5 mg/kg, IV target-controlled infusion (TCI), Minto model of remifentanil 5 ng/ml, and IV rocuronium 1 mg/kg to facilitate endotracheal intubation. Anesthesia was maintained with desflurane (end-tidal concentration of 4.6–4.8, minimum alveolar concentration (MAC) of 0.6–0.7) and TCI remifentanil 2–8 ng/ml, to maintain BIS value of 40–60 during surgery. For the TIVA group, anesthesia was induced with IV TCI propofol (Marsh model) 4 μg/ml, IV TCI remifentanil (Minto model) 5 ng/ml, and IV Rocuronium 1 mg/kg to facilitate tracheal intubation. Anesthesia was maintained with TCI propofol 2.5–4 μg/ml and TCI remifentanil 2–8 ng/ml to maintain a BIS value of 40–60 during surgery. End-tidal concentration of carbon dioxide was kept between 32 and 37 mmHg. IV tranexamic acid 20 mg/kg was administered to both groups. Boluses of muscle relaxant, IV rocuronium were given throughout the operation if needed.

An arterial line was placed after the induction of anesthesia for continuous monitoring of arterial blood pressure. Patient’s mean arterial pressure (MAP) was maintained above 60 mmHg. Patients were kept normothermic with core temperature of 36–37°C using forced air warming device (Bair Hugger™) and water bath coaxial fluid- and blood-warming device (HOTLINE®) throughout surgery.

SSEPs were recorded using either Natus Xltek System (Natus Medical Incorporated, San Carlos, California, USA) or Medelec Synergy system (Oxford Instruments Medical Limited, Old Woking, Surrey, UK). The cortical and cervical EPs were recorded using electrodes placed at 2 cm posterior to the central vertex, Cz (Cz’), and over the second cervical spinal process (Cv2), respectively, and reference to the frontal midline (Fz) according to the 10–20 system.
international system of electroencephalography electrode placement. Right and left posterior tibial nerves were alternately stimulated to get the SSEP measurements. SSEPs measured from stimulating the right tibial nerve were used for analyses in our study. Posterior tibial nerve stimulation was delivered at stimulus intensity of 2 mA of above threshold to elicit contraction of the foot muscles. This stimulus was kept constant during the surgery for each patient. Stimulus currents were set at 22–27 mA, lasting 200 μs, and were delivered at a rate of 3–5 Hz. The analysis time we used for each SSEP waveform was 100 ms, and 1000 sweeps were averaged. We used a 10 Hz to 10 kHz bandpass filter. The amplitude of P40 potential was determined by measuring the difference between the baseline and P40 peak. The latency of the SSEP was assessed by measuring the time from the stimulus onset to the P40 peak. The amplitude and latency of Cv2 were similarly measured from baseline to peak and stimulus onset to peak, respectively. Measurements were made by a neurophysiologist who was blinded to the group allocation of patients. Measurements of P40 amplitudes and latencies were obtained at five different time points—when the patients were awake, before and after the induction of anesthesia, at the start of skin incision, at the start of pedicle screw insertion, and at the start of rod insertion until correction of deformity. The primary outcome measures were the SSEP amplitude and latency after the induction of anesthesia, at the start of skin incision, at the start of pedicle screw insertion, and at the start of rod insertion. The patients were kept normotensive, normothermic, and normocapnic throughout the surgery. If at any point the SSEP amplitude decreased to <0.3 μV, patients were withdrawn from the trial because such low amplitude might be difficult to differentiate from mechanical injuries from the surgery and make the interpretation difficult.

IV morphine 0.1–0.15 mg/kg and fentanyl 1 μg/kg were given 1 h and 0.5 h, respectively, prior to the completion of surgery as postoperative analgesia. At the end of the surgery, IV atropine 0.02 mg/kg and neostigmine 0.05 mg/kg were given to reverse the neuromuscular blocking agent, and patients were extubated after fulfilling the safe extubation criteria.

We used GPower sample size calculation software version 3.0 to determine the sample size for this study. Based on the preliminary study done by Martin et al., which compared TIVA against volatile anesthetic desflurane, the mean (standard deviation (SD)) of the two groups were 27.6 (1.3) and 29.2 (2.3), respectively. With type 1 error of 0.05 and power of 0.8, the required sample size was 27 for each group. To add a 20% dropout rate, a total of 67 subjects were required.

Data were analyzed using SPSS software version 22. Independent *t*-tests were used to analyze quantitative data, and cross-tabulation was used to analyze qualitative data. Independent *t*-tests were used to compare the magnitude of change of amplitude and latency, from preinduction to after induction of anesthesia. Repeated measures analysis of variance test was used to assess the drug allocation effect over time during anesthesia. All relevant numerical data results were expressed as mean (SD). A *p* < 0.05 is considered statistically significant.

**Results**

A total of 72 patients were assessed for eligibility. Four were excluded as they did not meet inclusion criteria and one declined to participate. The remaining 67 patients were randomized and allocated to the two groups: 34 were allocated to desflurane/remifentanil group and 33 to TIVA group. Four patients from desflurane/remifentanil group and three from TIVA group were withdrawn from the trial due to decrease in SSEP amplitude to <0.3 μV after induction of anesthesia. Thirty patients from each group were analyzed (Figure 1). Demographic data such as age, gender, weight, height, and body mass index were similar in both groups (Table 1). The temperature and MAP between the two groups were not clinically significantly as shown in Table 1. The BIS value showed significant difference between the two groups (*p* = 0.008). However, all the BIS values were maintained within the anesthesia range from 40 to 60 for a comparable depth of anesthesia in both groups.

Both the cervical and cortical EP amplitudes and latencies were not significantly different before induction of anesthesia (time 1) between the two groups. The latency of P40 was significantly prolonged and its amplitude was significantly smaller in the desflurane/remifentanil group at the later time points from baseline compared with the TIVA group (Table 2). However, there were no significant differences in the amplitude and latency of the cervical EP between baseline and subsequent time points for the two groups.

Intraoperatively, none of the patients had any SSEP abnormalities, and there were no neurological deficit postoperatively. All patients were discharged well to the high dependency unit from the recovery room of the operating theatre.

**Discussion**

Recently, SSEP monitoring has gained popularity and regarded as the standard of care for detecting spinal cord injury during spinal surgery, and it has superseded Stagnara wake-up test. It is reliable not only in idiopathic scoliosis but also in neuromuscular scoliosis spinal surgery and other spine instrumental surgeries. Most anesthetic agents have an effect on SSEP. Volatile agents produce a dose-dependent decrease in SSEP amplitude and an increase in SSEP latency although they have a better emergence from anesthesia compared with propofol, allowing earlier neurological function assessment postoperatively. However, propofol anesthesia is still superior to volatile agents.
in its effect on SSEP monitoring. Studies have shown that propofol anesthesia causes less suppression and better preservation of cortical SSEP and less variability compared with isoflurane8 and sevoflurane anesthesia.22 Opioids only cause minimal suppression of SSEP.10–12

In our study, we showed that both desflurane and propofol at comparable depths of anesthesia guided by BIS monitoring influenced SSEP signals. Desflurane caused a significant decrease in cortical EP amplitude and an increase in latency compared with propofol. However, there were no significant differences between desflurane and propofol anesthesia in both the cervical EP amplitude and latency. This reflects the greater effect of anesthetic drugs in the cortex compared with the spinal cord. Responses recorded from cortical polysynaptic pathways are more affected by anesthesia as it has a more pronounced effect on synaptic transmission than on axonal conduction. In animal studies, volatile anesthetics modulate both excitatory and inhibitory synaptic transmission of hippocampal pathway, whereas propofol produced more specific action on inhibitory synaptic events.23 Propofol produces inhibitory actions due to enhancement in the gamma-aminobutyric acid A (GABA A) receptors alone, while volatile anesthetics modulate synaptic transmission through GABA A, N-methyl-D-aspartate (NMDA), and non-NMDA receptors. This would explain the results in our study that desflurane has more influence in cortical SSEP than propofol.

Monitoring of SSEP via electrodes introduced into the epidural space has also been described and it is reliable in patients who underwent neuromuscular scoliosis surgery.24,25 It is less affected by volatile anesthetic agents compared with cortical EPs.26 This technique, also known as neurogenic mixed EP, has relatively low specificity because they correspond to the joined activation of both motor and sensory pathways.27 However, epidural recording electrodes can only be placed after the back has been surgically opened and may well be in the surgical field;

Figure 1. CONSORT flowchart.
hence, cortical EP recording is the preferred modality as it is less invasive with relative ease of application and less interference with surgery.28 Recording of cervical EPs besides cortical EPs in SSEP monitoring might be another option. It is relatively easy to apply, noninvasive, effective, reliable, and most importantly also less influenced by anesthesia. It can be used to monitor all spinal surgeries other than cervical spine surgery. Based on our study, desflurane and propofol had no significant differences in cervical SSEP. Hence, desflurane could be used to provide anesthesia for scoliosis surgery if cervical EP is the main parameter monitored during surgery. A recent preliminary study prospectively compared the effect of TIVA and desflurane on neurophysiological monitoring, which demonstrated that a volatile agent, desflurane regimen, is feasible during neurophysiological monitoring.15 The end-tidal concentration of desflurane in this study was 4.0–5.0 with a MAC value of 0.6–0.8, which is similar to the above study. Its low blood–gas partition coefficient allows more predictable and faster emergence from anesthesia compared with propofol and other volatile agents. Furthermore, if a rapid wake-up test is required during surgery, the use of desflurane would facilitate the process in less than 5 min.15 However, an older study suggested that volatile agents including desflurane when used in concentrations greater than 0.5 MAC may significantly affect neurophysiological monitoring.29 Another recent study by Sloan et al. indicates that 1/2 MAC (3%) of desflurane can be used in conjunction with SSEP and transcranial MEP monitoring for some adult patients undergoing spine surgery.30

Remifentanil is a very potent analgesia and could significantly reduce the MAC of volatile anesthetics when combined. It also acts synergistically with propofol in TIVA. Remifentanil is beneficial during this surgery because it reduces the concentration and dosage of both volatile and IV anesthetic agents. Hence, it can reduce the influence of the anesthetic agents on SSEP monitoring. Remifentanil has a very short context-sensitive halftime that is independent of the duration of infusion and the total dose used. Concurrent administration of remifentanil also allows faster recovery time to allow early neurological assessment postoperatively.13,14

In our study, there were no differences in both temperature and MAP between the TIVA and desflurane groups during anesthesia. Hypothermia and fluctuations in MAP have been shown to affect SSEP monitoring. Temperature was kept in the normal range using active patient-warming devices. Depth of anesthesia was kept constant, and any fluctuations in MAP were managed by administering vasoressor agents. In an animal study, every drop in 1°C has been shown to be associated with an increase in EP latency by 3% and a decrease in amplitude by 7%.31 Changes in SSEP may also be produced by other physiological factors such as hypoxia, hyperthermia, and large decreases in

| Table 1. Patient demographic data.a |
|------------------------------------|
|                                   |
| **Desflurane/remifentanil (n = 30)** | **TIVA (n = 30)** |
| Age (years) 15.5 (4.1) [11–32] | 16.5 (4.0) [11–29] | 0.38 |
| Gender (M/F; n) 5/25 | 8/22 | 0.35 |
| Weight (kg) 46.1 (8.8) [22.9–68.5] | 47.8 (8.6) [34.3–70.6] | 0.44 |
| Height (cm) 157.5 (7.3) [145.3–178.0] | 156.5 (7.7) [140.5–174.0] | 0.61 |
| BMI (kg/m²) 18.9 (2.9) [14.5–26.7] | 19.5 (2.9) [15.3–28.3] | 0.45 |
| BIS Time 1 96.2 (1.5) | 96.8 (1.5) | 0.008 |
| Time 2 50.3 (5.7) | 46.0 (4.6) |
| Time 3 49.3 (5.8) | 45.8 (4.9) |
| Time 4 48.8 (6.7) | 45.1 (5.1) |
| Time 5 50.1 (6.3) | 48.3 (4.5) |
| Temperature (°C) Time 1 36.6 (0.3) | 36.6 (0.3) | 0.909 |
| Time 2 36.2 (0.5) | 36.2 (0.4) |
| Time 3 36.2 (0.5) | 36.2 (0.4) |
| Time 4 36.2 (0.5) | 36.1 (0.5) |
| Time 5 36.2 (0.5) | 36.2 (0.5) |
| MAP (mmHg) Time 1 78.0 (8.6) | 81.4 (9.7) | 0.143 |
| Time 2 71.5 (8.7) | 74.1 (8.9) |
| Time 3 71.7 (9.9) | 73.3 (8.5) |
| Time 4 71.8 (8.4) | 74.1 (8.4) |
| Time 5 68.7 (5.7) | 71.8 (6.7) |

BIS: bispectral index; BMI: body mass index; MAP: mean arterial pressure; SD: standard deviation; Time 1: before induction of anesthesia; Time 2: after induction of anesthesia; Time 3: at the start of skin incision; Time 4: at the start of pedicle screw insertion; Time 5: at the start of rod insertion until correction of deformity; TIVA: total intravenous anesthesia.

Values are mean (SD) [range] or numbers.
any of our patients.32
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$\text{aValues are mean (SD).}$
$\text{TIVA: total intravenous anesthesia.}$
\begin{tabular}{lccc}
Time & Desflurane/ & TIVA & \\
      & remifentanil (n = 30) & (n = 30) & p \\
\hline
1 & 2.3 (1.2) & 2.7 (2.1) & 0.214 \\
2 & 1.1 (0.5) & 1.3 (0.7) & \\
3 & 1.3 (2.2) & 1.3 (0.7) & \\
4 & 0.9 (0.4) & 1.1 (0.6) & \\
5 & 0.9 (0.3) & 1.2 (0.6) & \\
\hline
\end{tabular}
\begin{tabular}{lccc}
Time & Cervical amplitude (µV) & \\
      & Time 1 & 2.3 (1.2) & 2.7 (2.1) 0.214 \\
      & Time 2 & 1.1 (0.5) & 1.3 (0.7) \\
      & Time 3 & 1.3 (2.2) & 1.3 (0.7) \\
      & Time 4 & 0.9 (0.4) & 1.1 (0.6) \\
      & Time 5 & 0.9 (0.3) & 1.2 (0.6) \\
\hline
\end{tabular}
\begin{tabular}{lccc}
Time & Cortical amplitude (µV) & \\
      & Time 1 & 3.4 (1.9) & 3.5 (1.9) 0.004 \\
      & Time 2 & 1.4 (0.7) & 2.0 (0.9) \\
      & Time 3 & 1.2 (0.8) & 2.0 (0.8) \\
      & Time 4 & 1.2 (0.8) & 2.0 (0.9) \\
      & Time 5 & 1.2 (0.8) & 2.1 (0.8) \\
\hline
\end{tabular}
\begin{tabular}{lccc}
Time & Cortical latency (ms) & \\
      & Time 1 & 27.2 (1.9) & 26.9 (2.0) 0.16 \\
      & Time 2 & 28.4 (1.5) & 28.0 (2.4) \\
      & Time 3 & 28.7 (1.6) & 27.9 (2.8) \\
      & Time 4 & 29.0 (1.5) & 28.1 (2.6) \\
      & Time 5 & 29.2 (1.7) & 28.0 (2.7) \\
\hline
\end{tabular}
\begin{tabular}{lccc}
Time & Cortical latency P40 (ms) & \\
      & Time 1 & 37.0 (1.8) & 36.2 (1.9) 0.002 \\
      & Time 2 & 38.5 (1.8) & 36.2 (1.8) \\
      & Time 3 & 38.8 (1.8) & 37.2 (1.8) \\
      & Time 4 & 38.9 (2.0) & 37.4 (2.0) \\
      & Time 5 & 39.0 (2.1) & 37.2 (2.0) \\
\hline
\end{tabular}
SD: standard deviation; SSEP: somatosensory evoked potential; Time 1: before induction of anesthesia; Time 2: after induction of anesthesia; Time 3: at the start of skin incision; Time 4: at the start of pedicle screw insertion; Time 5: at the start of rod insertion until correction of deformity; TIVA: total intravenous anesthesia.
$\text{6Values are mean (SD).}$
Our study has several limitations. BIS monitoring has been used as a guide to compare the depth of anesthesia between the two groups, desflurane and TIVA. However, equivalent value of BIS does not mean equivalent depth of anesthesia, especially when different drugs are being used. One should also take into consideration the variations that occur between individual patients. Ideally, the actual plasma concentration of propofol should be measured during surgery and comparison made with desflurane MAC values, but this was not possible in the study. Hence, it was not possible to deliver equipotent doses of desflurane and propofol.
In conclusion, compared with TIVA, desflurane/remifentanil anesthesia caused more suppression in cortical SSEP, but not in cervical SSEP, at a comparable depth of anesthesia guided by BIS monitoring.

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References
1. Nuwer MR and Packwood JW. Somatosensory evoked potential monitoring with scalp and cervical recording. Clin Neurophysiol 2008; 8: 180–189.
2. Nuwer MR, Dawson EG, Carlson LG, et al. Somatosensory evoked potential spinal cord monitoring reduces neurologic deficits after scoliosis surgery: results of a large multicentre survey. Electroencephalogr Clin Neurophysiol 1995; 96: 6–11.
3. Raw DA, Beattie JK and Hunter JM. Anaesthesia for spinal surgery in adults. Br J Anaesth 2003; 91(6): 886–904. PubMed PMID: 14633762. Epub 2003/11/25. eng.
4. Meyer PR Jr, Cotler HB and Gireesan GF. Operative neurological complications resulting from thoracic and lumbar spine internal fixation. Clin Orthop Relat Res 1988; (237): 125–131. PubMed PMID: 3191620. Epub 1988/12/01. eng.
5. Epstein NE, Danto J and Nardi D. Evaluation of intraoperative somatosensory-evoked potential monitoring during 100 cervical operations. Spine (Phila Pa 1976) 1993; 18(6): 737–747. PubMed PMID: 8516704. Epub 1993/05/01. eng.
6. Nuwer MR. Spinal cord monitoring with somatosensory techniques. J Clin Neurophysiol: Official Publication of the American Electroencephalographic Society 1998; 15(3): 183–193. PubMed PMID: 9681556. Epub 1998/07/29. eng.
7. Schindler E, Thiel A, Muller M, et al. Changes in somatosensory evoked potentials after sevoflurane and isoflurane. A randomized phase III study. Anaesthesist 1996; 45(suppl 1): S52–S56. PubMed PMID: 8775104. Epub 1996/07/29. eng.
8. Liu EH, Wong HK, Chia CP, et al. Effects of isoflurane and propofol on cortical somatosensory evoked potentials during comparable depth of anaesthesia as guided by bispectral index. Br J Anaesth 2005; 94(2): 193–197. PubMed PMID: 15516356. Epub 2004/11/02. eng.
9. Boisseau N, Madany M, Staccini P, et al. Comparison of the effects of sevoflurane and propofol on cortical somatosensory evoked potentials. Br J Anaesth 2002; 88(6): 785–789. PubMed PMID: 12173194. Epub 2002/08/14. eng.
10. Pathak KS, Brown RH, Cascorbi HF, et al. Effects of fentanyl and morphine on intraoperative somatosensory cortical-evoked potentials. Anesth Analg 1984; 63(9): 833–837. PubMed PMID: 6465579. Epub 1984/09/01. eng.
11. Schubert A, Drummond JC, Peterson DO, et al. The effect of high-dose fentanyl on human median nerve somatosensory-evoked responses. Can J Anaesth = Journal Canadien
21. Peterson DO, Drummond JC and Todd MM. Effects of halothane, enflurane, isoflurane, and nitrous oxide on somatosensory evoked potentials in humans. *Anesthesiology* 1986; 65(1): 35–40. PubMed PMID: 3014922. Epub 1986/07/01. eng.

22. Fung NY, Hu Y, Irwin MG, et al. Comparison between sevoflurane/remifentanil and propofol/remifentanil anesthesia in providing conditions for somatosensory evoked potential monitoring during scoliosis corrective surgery. *Anaesthesia Intensive Care* 2008; 36(6): 779–785. PubMed PMID: 19115644. Epub 2009/01/01. eng.

23. Wakasugi M, Hirota K, Roth SH, et al. The effects of general anesthetics on excitatory and inhibitory synaptic transmission in the CA1 of the rat hippocampus in vitro. *Anesth Analg* 1999; 88(3): 576–80. PubMed PMID: 10072027. Epub 1999/03/11. eng.

24. Williamson JB and Galasko CS. Spinal cord monitoring during operative correction of neuromuscular scoliosis. *J Bone Joint Surg Br* 1992; 74(6): 870–872. PubMed PMID: 1447248. Epub 1992/11/01. eng.

25. Noordeen MH, Lee J, Gibbons CE, et al. Spinal cord monitoring in operations for neuromuscular scoliosis. *J Bone Joint Surg Br* 1997; 79(1): 53–57. PubMed PMID: 9024455. Epub 1997/01/01. eng.

26. Sebel PS, Erwin CW and Neville WK. Effects of halothane and enflurane on far and near field somatosensory evoked potentials. *Br J Anaesth* 1989; 65(2): 169–172. PubMed PMID: 1977431. Epub 1990/08/01. eng.

27. Pathak KS, Ammadio MD, Scoles PV, et al. Effects of halothane, enflurane, and isoflurane in nitrous oxide on multilevel somatosensory evoked potentials. *Anesthesiology* 1989; 70(2): 207–212. PubMed PMID: 2643892. Epub 1989/02/01. eng.

28. Lubicky JP, Spadaro JA, Yuan HA, et al. Variability of somatosensory cortical evoked potential monitoring during spinal surgery. *Spine* 1989; 14(8): 790–798. PubMed PMID: 2781392. Epub 1989/08/01. eng.

29. Sloan TB. Anesthetic effects on electrophysiologic recordings. *J Clin Neurophysiol* 1998; 15: 217–226. eng.

30. Sloan TB, Toleikis JR, Toleikis SC, et al. Intraoperative neurophysiologic monitoring in spine surgery. Developments and state of the art in France in 2011. *Orthop Traumatol Surg Res* 2013; 99(6 Suppl): S319–S327. eng.

31. Jou IM. Effects of core body temperature on changes in spinal somatosensory-evoked potential in acute spinal cord compression injury: an experimental study in the rat. *Spine* 2000; 25(15): 1878–1885. PubMed PMID: 10908929. Epub 2000/07/26. eng.

32. Kumar A, Bhattacharya A and Makhija N. Evoked potential monitoring in anesthesia and analgesia. *Anaesthesia* 2000; 55(3): 225–241. PubMed PMID: 10671840. Epub 2000/02/15. eng.