Clinical Neurology and Neurosurgery 180 (2019) 74–78

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Optimal stimulation intensity for Br(E)-MsEP waveform derivation at baseline in pediatric spinal surgery

Kazuyoshi Kobayashi, Kei Ando, Masaaki Machino, Kyotaro Ota, Masayoshi Morozumi, Satoshi Tanaka, Shunsuke Kanbara, Sadayuki Ito, Naoki Ishiguro, Shiro Imagama*

Department of Orthopaedic Surgery, Nagoya University Graduate School of Medicine, 65, Tsurumai-cho, Showa-ku, Nagoya, 466-8560, Japan

ARTICLE INFO

Keywords:
Br(E)-MsEP
Spine surgery
Pediatric
Optimal stimulation
Stimulation intensity

ABSTRACT

Objectives: Br(E)-MsEP monitoring is widely used in spinal surgery for detection of spinal cord injury. However, Br(E)-MsEP waveform derivation requires high-intensity stimulation, and this raises a concern of adverse effects due to the immature corticospinal tract in pediatric patients. The purpose of this study is to determine the optimal stimulation intensity required for derivation of Br(E)-MsEP waveforms at baseline in pediatric spinal surgery.

Patients and methods: The subjects were 85 pediatric patients (4–15 years old, mean age at surgery: 11.1 years old) who were treated with spinal surgery using a posterior only approach under Br(E)-MsEP monitoring. The main diagnoses were adolescent idiopathic scoliosis (n = 44), syndromic and neuromuscular scoliosis (n = 23), and congenital scoliosis (n = 12). A total of 1513 muscles in the lower extremities were chosen for monitoring.

Results: A baseline waveform was obtained in all 85 cases and baseline Br(E)-MsEP responses were obtained from 1437/1513 muscles (95%). The mean stimulation intensity for baseline waveform derivation was 156.4 mA (range: 100–200 mA), and the stimulation intensity was significantly correlated with age ($p < 0.05$). The mean stimulation intensities were 129 ± 12, 138 ± 20, and 167 ± 25 mA for children < 5, 6 to 10, and 11 to 15 years old, respectively.

Conclusion: There are no criteria for derivation of Br(E)-MsEP waveforms in pediatric patients undergoing spinal surgery. The stimulation intensity increased with age, and starting at a lower stimulation strength than that used in adults is appropriate for younger children.

1. Introduction

Intraoperative monitoring techniques have continued to evolve since their inception and are now part of standard care in surgical treatment of spinal disease. Among modalities such as somatosensory-evoked potentials (SSEPs), cord-evoked potentials after stimulation of the brain (D-wave), and free running electromyography (EMG), brain-evoked muscle-action potential (Br(E)-MsEP) monitoring has become widely used in spinal surgery for reduction of neurological deterioration and increased accuracy in detection of spinal cord injury [1–8]. Such monitoring has become a standard method due to its high sensitivity and importance in preserving motor function [9,10], and is similarly used in pediatric spinal surgery [4,29].

Br(E)-MsEP monitoring can be used to evaluate corticospinal tract function during surgery, and is mainly performed with high-intensity stimulation for stable high waveform detection. However, there are some potential adverse events of transcranial stimulation for Br(E)-MsEP monitoring, including tongue bite injury, endotracheal tube rupture, and mandibular fracture due to jaw muscle contractions during stimulation [11–15]. High-intensity stimulation has been suggested to be a cause of these events [11]. In children, immature corticospinal tracts may reduce the integrity of central motor pathways [16], and prevention of these adverse events may require reduced stimulation intensity. This makes it important to determine an optimal stimulation level for Br(E)-MsEP monitoring in pediatric spinal surgery.

There have been many reports of use of Br(E)-MsEP monitoring in pediatric spinal surgery, but with no specific method for stimulation as baseline. The purpose of this study is to analyze data obtained in pediatric spine surgery using Br(E)-MsEP monitoring to determine the optimal stimulation intensity for derivation of Br(E)-MsEP waveforms at baseline in this surgery.

* Corresponding author at: Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine, 65 Tsurumai Showa-ward, Aichi, 466-8550, Japan.
E-mail address: imagama@med.nagoya-u.ac.jp (S. Imagama).

https://doi.org/10.1016/j.clineuro.2019.03.005
Received 15 October 2018; Received in revised form 24 February 2019; Accepted 3 March 2019
Available online 31 March 2019
0303-8467/

Table 1
Preoperative demographic data (n = 85).

Item	Value
Age (years) (mean ± SD)	11.1 ± 3.1
≤5 years / 6-10 years / 11-15 years (n)	7 / 22 / 56
Gender: female / male (n)	72 : 13
Disease (n)	
Adolescent idiopathic scoliosis	44
Syndromic and neuromuscular scoliosis	23
Congenital scoliosis	12
Os odontoideum	3
Arnold-Chiari malformation	3

2. Materials and methods

2.1. Patient population

A total of 105 surgeries for patients ≤15 years of age were performed at our hospital from January 2009 to December 2017. Eleven patients with preoperative motor deficits, eight with spinal cord tumor, and one with epilepsy were excluded, leaving 85 patients (13 males, 72 females) as the subjects of the study. All subjects were treated using a posterior only approach in a prone position under Br(E)-MsEP monitoring. The main diagnoses were adolescent idiopathic scoliosis (n = 44), syndromic and neuromuscular scoliosis (n = 23), and congenital scoliosis (n = 12) (Table 1). A total of 1656 muscles in the lower extremities were chosen for monitoring. The mean age at the time of surgery was 11.1 years old (range: 4–15 years old). This study was approved by the ethical committee of our university hospital.

2.2. Anesthetic management and general conditions during surgery

A minimal benzodiazepine dose was used as preanesthetic medication to avoid possible suppression of waveform latency and amplitude. Propofol (3–4 mg/kg), fentanyl (2 mg/kg), and vecuronium (0.12-0.16 mg/kg) were administered for induction, and anesthesia was maintained with propofol (50–100 μg/kg/min), fentanyl (1–2.5 μg/kg/h), and vecuronium (0.01-0.04 mg/kg/h). Concomitant hypotensive anesthesia was given as appropriate with continuous PGE1 and a short-acting β1 blocker (landiolol) to control systolic blood pressure at < 120 mmHg. Patients were maintained in a normothermic state and the temperature was raised in the event of possible intraoperative spinal damage. End-tidal CO_2 was maintained in the reference range throughout surgery. For intraoperative body temperature monitoring, a catheter with a vesical temperature sensor was used. Hemodynamic data were electronically recorded with invasive arterial BP monitoring, and systolic blood pressure variation was measured during surgery.

2.3. Stimulation and recording methods

We used a MS120B (Nihon Kohden, Tokyo, Japan) to perform transcranial stimulation. The stimulation parameters were a constant biphasic current of 5 stimuli in a row at 2-ms intervals, a 50–1000 Hz filter, and a 100-ms epoch time with ≤20 recorded signal responses. The stimulated point was 2 cm anterior and 6 cm lateral from the Cz location over the cerebral cortex motor area. Using the Neuromaster MEE-1232 ver. 05.10 (Nihon Kohden, Japan), which is expandable to 32 channels, muscle action potentials were recorded from the upper and lower extremities via a pair of needle electrodes 3 to 5 cm apart. In cervical surgery, the bilateral deltoid, abductor digit minimi, adductor longus, quadriceps femoris, hamstrings, tibialis anterior, gastrocnemius, abductor hallucis, and anal sphincter muscles were used as target muscles; and, in thoracic surgery, the bilateral trapezius, deltoid, biceps, triceps, abductor digit minimi, adductor longus, quadriceps femoris, hamstrings, tibialis anterior, gastrocnemius, abductor hallucis, and anal sphincter muscles were used as target muscles. The stimulation intensity was gradually increased from 100 mA in steps of 10 mA at the start of surgery, the baseline waveform was defined as the presence of an amplitude ≥5 μV in a left or right muscle, and an amplitude < 5 μV was defined as the absence of a waveform [17] (Fig. 1). Br(E)-MsEP data from the above muscles were used for analysis. These derivation definitions and protocols were determined prospectively and did not change over the study period.

2.4. Statistical analysis

Analysis was performed using SPSS ver. 22 for Windows (IBM SPSS Inc., Chicago, IL). A Pearson correlation coefficient was calculated for the correlation between Br(E)-MsEP stimulation intensity and age. Correlations between stimulation intensity and other variables were analyzed using Spearman rank correlation coefficients. $P < 0.05$ was considered to be significant in all analyses.

3. Results

There were no intraoperative adverse events related to Br(E)-MsEP stimulation in all cases. A baseline waveform was obtained in 85/85 cases (100%) and acceptable baseline Br(E)-MsEP responses were obtained from 1437/1513 muscles (95%). The mean stimulation intensity for the baseline waveform derivation in all 85 cases was 156.4 mA (range: 100–200 mA) (Table 2). In all series, the brain was stimulated with the same intensity during the surgical procedures, and the waveform was not changed during surgery. The Br(E)-MsEP stimulation intensity was significantly correlated with age ($p < 0.05$) (Fig. 2, Table 3), but not with body mass index (BMI), blood pressure just before incision, and intraoperative body temperature (Table 3). The mean stimulation intensities were 129 ± 12, 138 ± 20, and 167 ± 25 mA for children aged < 5, 6 to 10, and 11 to 15 years old, respectively (< 5 vs. 6 to 10 years old, p = 0.07; 6 to 10 vs. 11 to 15 years old, $p < 0.01$; < 5 vs. 11 to 15 years old, $p < 0.01$) (Fig. 3). Two illustrative cases are described in the following paragraphs.

Case 1: The patient was a 10-year-old female with AIS (Fig. 4A). At the start of surgery, a stimulation intensity of 100 mA (Fig. 4B) gave a poorly derived waveform in the right hamstring. Waveform derivation was acceptable at 120 mA (Fig. 4B) and this was defined as baseline. Intraoperatively, reliable waveforms were obtained at 120 mA (Fig. 4B).

Case 2: The patient was a 8-year-old female with atlantoaxial subluxation due to os odontoideum (Fig. 5A). A stimulation intensity of 100 mA at baseline produced waveforms that were clear in all muscles at the start of surgery and intraoperatively (Fig. 5B).

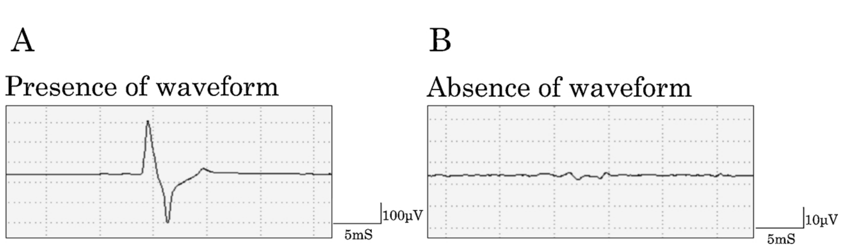

Fig. 1. Examples showing (A) the presence and (B) the absence of a waveform.

Table 2
Adverse events, waveform derivation rate, and stimulation intensity.

Item	Value
Adverse events (n)	0% (0)
Waveform derivation rate as baseline	
Per case (n = 85 cases)	100% (85 cases)
Per waveform (n = 1513 muscles)	95% (1437 muscles)
Stimulation intensity as baseline (mA)	156.4 ± 27.1

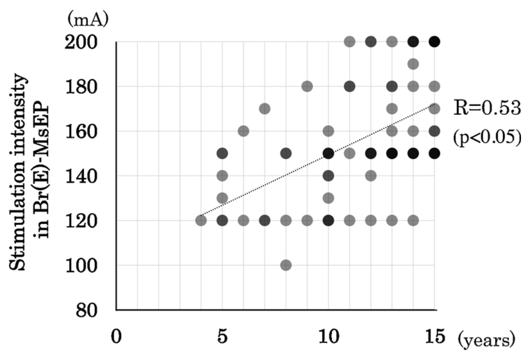

Fig. 2. Stimulation intensity and age had a significant positive correlation ($p < 0.05$).

Table 3
Correlation coefficients for Br(E)-MsEP stimulation intensity with patient variables.

Variables	Correlation coefficient (r)	p
Age (years)	0.51	< 0.05
Body mass index (kg/m^2)	0.054	n.s
Blood pressure just before incision (mmHg)	0.031	n.s
Intraoperative body temperature (°C)	0.068	n.s

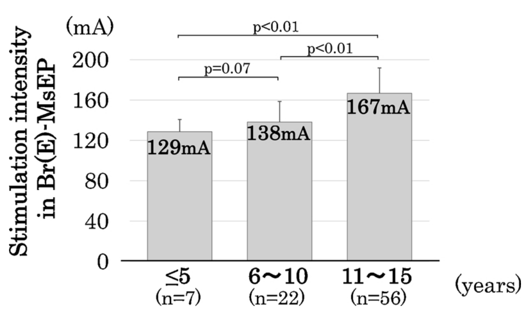

Fig. 3. Average stimulation intensity in each age subgroup (n = 85) (< 5 vs. 6 to 10 years old, p = 0.07; 6 to 10 vs. 11 to 15 years old, $p < 0.01$; < 5 vs. 11 to 15 years old, $p < 0.01$).

4. Discussion

Prevention of postoperative paraparesis is a high priority during spinal surgery. Intraoperative electrophysiologic monitoring using Br(E)-MsEPs is routinely performed during spinal surgery in an effort to identify a neurologic deficit in a timely fashion. This approach is applicable in pediatric cases, in which Br(E)-MsEP monitoring has been used to prevent nerve damage in treatment for conditions such as congenital spinal disease, spinal cord pathology, and spinal deformity.

The optimal stimulation intensity for Br(E)-MsEPs has not been examined previously in a study focused on pediatric surgery. Derivation of a Br(E)-MsEP waveform requires direct electrical stimulation of the masseter and temporalis muscles, leading to muscle contraction. Complications are rare, but there are several reports of adverse events of tongue lacerations, movement during surgery, and bleeding or burns at the sites of monitoring electrodes [11–15,18,19]. These events are a concern in children due to the immature spinal cord [16]. Spinal cord motor pathways undergo a prolonged period of maturation, and electrophysiologic maturity of the corticospinal tract is not complete until 13 years of age [16,20]. However, we believe that excessive stimulation in pediatric spine surgery is not appropriate from a safety perspective; therefore, determination of the optimal stimulation intensity is important.

Our data were collected before surgical incision, while an acceptable arterial blood pressure was maintained by the anesthesiologist. For reliable waveform derivation, anesthesia is also an important factor. Several studies have shown that younger children require larger doses of propofol for induction of anesthesia and more rapid infusion rates of this drug for maintenance of anesthesia, compared to older subjects [21,22]. Careful monitoring is mandatory in spine procedures and, especially for young patients, the anesthesia plan must be carefully considered because both inhalation and intravenous anesthetics can affect the Br(E)-MsEP response [23–27]. This plan should also take into account age, BMI, blood pressure, and bleeding volume, which are all also important for Br(E)-MsEP waveform derivation. In our series of 93 cases, the required stimulation intensity for acceptable waveform derivation increased with age. BMI, blood pressure, and intraoperative body temperature had no significant correlation with stimulation intensity. None of these cases had adverse events and all had reliable waveform derivation at the start of surgery.

Young children have an immature corticospinal tract that could reduce the integrity of the central motor pathway [16]. The immature spinal cord in children has also been suggested to require a higher Br(E)-MsEP threshold in intraoperative monitoring, compared with that in adults [20,28]. The discrepancy between these findings and our results may have occurred for several reasons. First, in our series, there was no case with motor deficit preoperatively, and therefore, there was no disorder of spinal cord function, which might have made it relatively easy to detect a waveform. Second, a baseline waveform was defined as the presence of an amplitude ≥5 μV; however, with this definition even a relatively weak waveform could be regarded as baseline, and as a result, a waveform with comparatively low amplitude was included as detectable. Third, in adult surgery, 200 mA is routinely used as baseline stimulation. However, we think that it is desirable to respond more flexibly by changing settings based on spinal cord function (presence or absence of motor paralysis) for each disease and preoperative motor status. Given our results, further investigation of the stimulation intensity for reliable waveform derivation in pediatric spine surgery is required.

There are several limitations in this study. First, the number of cases is small and included various diseases. Second, stimulation with a high current might cause injury to a developing spinal cord; however, this risk is unknown and could not be confirmed in our series. Third, since the study was retrospective, we could not control for all physiologic variables that might affect the Br(E)-MsEP response, and in particular, we did not perform a detailed investigation of the depth of anesthesia and disappearance of vecuronium. The baseline waveform in our series was detected over 60 min after administration of vecuronium in all cases, which makes it difficult to define the pharmacological effect of vecuronium on the results. In addition concomitant hypotensive anesthesia was performed to maintain intraoperative systolic blood pressure at < 120 mmHg, and this might have influenced the results. A final limitation is that we did not evaluate the patients using modalities other than Br(E)-MsEP, such as D-wave monitoring. However, the strengths of the study include multi-channel detection of lower limb muscle waveforms, and acquisition of baseline Br(E)-MsEP responses before skin incision and blood loss; thus, the effect of surgical invasion on the evaluated waveform was minimal and showed no association with the baseline response. Furthermore, there are no universally accepted criteria for derivation of Br(E)-MsEP waveforms in pediatric patients, and

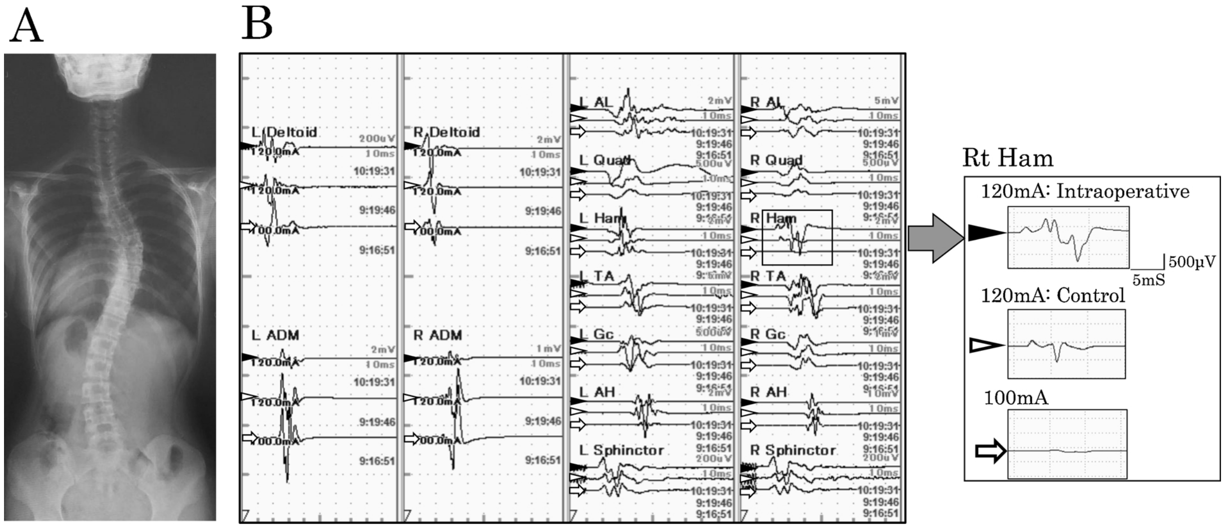

Fig. 4. (A) Preoperative PA radiograph of a 10-year-old female with AIS. (B) At the start of surgery, when the stimulation intensity was 100 mA (open arrow), the waveform was poorly derived in the right hamstring. At 120 mA, all derivations were acceptable (open arrowhead), and this was defined as baseline. In this case, intraoperatively, reliable waveforms were obtained with stimulation of 120 mA (arrowhead).

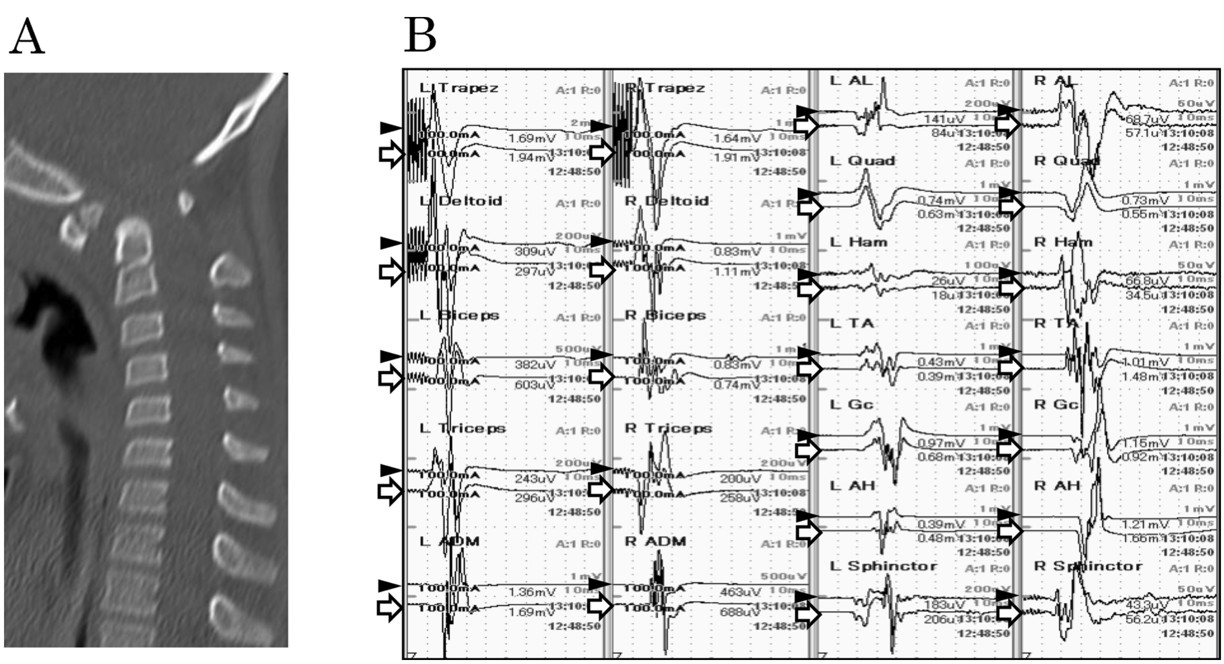

Fig. 5. (A) Preoperative radiograph of an 8-year-old female with atlantoaxial subluxation due to os odontoideum. (B) Stimulation intensity was set at 100 mA as baseline at the start of surgery. Waveform derivation was recognized clearly in all muscles at baseline (open arrow) and intraoperatively (arrowhead).

the results of this study provide a starting point for standardization of a baseline stimulation protocol.

In conclusion, we examined the stimulation intensity for derivation of Br(E)-MsEP waveforms at baseline in pediatric spinal surgery. The stimulation intensity increased with age and there were no intraoperative or postoperative adverse events related to stimulation and recording of Br(E)-MsEPs. These results suggest that starting at a lower stimulation strength is appropriate for younger children. There is a need for further investigation of the stimulation intensity required for reliable waveform derivation intraoperatively.

Conflicts of interest and source of funding

None of the authors have a conflict of interest. Funding was from institutional sources only.

References

[1] Y.L. Lo, Y.F. Dan, A. Teo, et al., The value of bilateral ipsilateral and contralateral motor evoked potential monitoring in scoliosis surgery, Eur. Spine J. 17 (2008) S236–8.

[2] K. Kobayashi, K. Ando, H. Yagi, et al., Prevention and prediction of postoperative bowel bladder disorder using an anal plug electrode with Tc-MsEP monitoring during spine surgery, Nagoya J. Med. Sci. 79 (2017) 459–466.

[3] K. Kobayashi, S. Imagama, Z. Ito, et al., Prevention of spinal cord injury using brain-evoked muscle-action potential (Br(E)-MsEP) monitoring in cervical spinal screw fixation, Eur. Spine J. 26 (2017) 1154–1161.

[4] K. Kobayashi, S. Imagama, Z. Ito, et al., Transcranial motor evoked potential waveform changes in corrective fusion for adolescent idiopathic scoliosis, J. Neurosurg. Pediatr. 19 (2017) 108–115.

[5] M.G. Fehlings, D.S. Brodke, et al., The evidence for intraoperative neurophysiological monitoring in spine surgery: does it make a difference? Spine 35 (2010) S37–46.

[6] A.A. Gonzalez, D. Jeyanandarajan, C. Hansen, et al., Intraoperative neurophysiological monitoring during spine surgery: a review, Neurosurg. Focus 27 (2009) E6.

[7] K. Kobayashi, K. Ando, R. Shinjo, et al., Evaluation of a combination of waveform

amplitude and latency in intraoperative spinal cord monitoring, Spine (2018) [in press].
[8] K. Kobayashi, K. Ando, H. Yagi, et al., Efficacy of an anal needle electrode for intraoperative spinal cord monitoring with Tc-MsEP, Asian Spine J. (2018) [in press].
[9] K. Kobayashi, K. Ando, R. Shinjo, et al., A new criterion for the alarm point using a combination of waveform amplitude and onset latency in Br(E)-MsEP monitoring in spine surgery, J. Neurosurg. Spine (2018) [in press].
[10] K.D. Luk, Y. Hu, Y.W. Wong, et al., Evaluation of various evoked potential techniques for spinal cord monitoring during scoliosis surgery, Spine 26 (2001) 1772–1777.
[11] D.B. MacDonald, Safety of intraoperative transcranial electrical stimulation motor evoked potential monitoring, J. Clin. Neurophysiol. 19 (2002) 416–429.
[12] A. Williams, G. Singh, Tongue bite injury after use of transcranial electric stimulation motor-evoked potential monitoring, J. Anaesthesiol. Clin. Pharmacol. 30 (2014) 439–440.
[13] A. Tamkus, K. Rice, The incidence of bite injuries associated with transcranial motor-evoked potential monitoring, Anesth. Analg. 115 (2012) 663–667.
[14] Y.J. Chae, J.Y. Kim, J.Y. Yoo, Y.H. Choi, K.S. Park, Tongue bite in a patient with tracheostomy after prone position: a case report, Korean J. Anesthesiol. 60 (2011) 365–368.
[15] M. Mahmoud, J. Spaeth, S. Sadhasivam, Protection of tongue from injuries during transcranial motor-evoked potential monitoring, Paediatr. Anaesth. 18 (2008) 902–903.
[16] T.H. Koh, J.A. Eyre, Maturation of corticospinal tracts assessed by electromagnetic stimulation of the motor cortex, Arch. Dis. Child. 63 (1988) 1347–1352.
[17] A. Muramoto, S. Imagama, Z. Ito, et al., The cutoff amplitude of transcranial motor-evoked potentials for predicting postoperative motor deficits in thoracic spine surgery, Spine 38 (2013) E21–7.
[18] S.R. Hays, D.A. Schwengel, Transient hypotension as a complication of monitoring transcervical motor evoked potentials, Anesthesiology 90 (1999) 314–317.
[19] S.N. Parikh, C.T. Mehlman, R.W. Keith, A third-degree burn caused by a neurogenic motor-evoked potential monitoring electrode during spinal surgery: a case report, Spine 28 (2003) E21–4.
[20] A. Nezu, S. Kimura, S. Uehara, et al., Magnetic stimulation of motor cortex in children: maturity of corticospinal pathway and problem of clinical application, Brain Dev. 19 (1997) 176–180.
[21] J. Schuttler, H. Ihmsen, Population pharmacokinetics of propofol: a multicenter study, Anesthesiology 92 (2000) 727–738.
[22] C. Saint-Maurice, I.D. Cockshott, E.J. Douglas, et al., Pharmacokinetics of propofol in young children after a single dose, Br. J. Anaesth. 63 (1989) 667–670.
[23] Z. Chen, The effects of isoflurane and propofol on intraoperative neurophysiological monitoring during spinal surgery, J. Clin. Monit. Comput. 18 (2004) 303–308.
[24] C.J. Kalkman, J.C. Drummond, A.A. Ribberink, Low concentrations of isoflurane abolish motor evoked responses to transcranial electrical stimulation during nitrous oxide/opioid anesthesia in humans, Anesth. Analg. 73 (1991) 410–415.
[25] T. Sloan, Anesthesia and intraoperative neurophysiological monitoring in children, Childs Nerv. Syst. 26 (2010) 227–235.
[26] T.B. Sloan, E.J. Heyer, Anesthesia for intraoperative neurophysiologic monitoring of the spinal cord, J. Clin. Neurophysiol. 19 (2002) 430–443.
[27] L.H. Ubags, C.J. Kalkman, H.D. Been, Influence of isoflurane on myogenic motor evoked potentials to single and multiple transcranial stimuli during nitrous oxide/opioid anesthesia, Neurosurgery 43 (1998) 90–95.
[28] J.A. Lieberman, R. Lyon, J. Feiner, M. Diab, G.A. Gregory, The effect of age on motor evoked potentials in children under propofol/isoflurane anesthesia, Anesth. Analg. 103 (2006) 316–321.
[29] K. Ando, K. Kobayashi, K. Ito, et al., Wave change of intraoperative transcranial motor-evoked potentials during corrective fusion for syndromic and neuromuscular scoliosis, Oper. Neurosurg. (Hagerstown) 16 (2019) 53–58.