의학석사 학위논문

Predictive factors of unpredicted movement in motor evoked potential during intraoperative neurophysiologic monitoring in adult patients undergoing brain surgery

뇌수술을 받는 성인환자에서 수술 중 신경생리학적 감시를 위한 운동유발전위 검사 시 예측하지 못한 움직임에 영향을 미치는 인자

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뇌수술을 받는 성인환자에서 수술 중 신경생리학적 감시를 위한 운동유발 전위 검사 시 예측하지 못한 움직임에 영향을 미치는 인자

Predictive factors of unpredicted movement in motor evoked potential during intraoperative neurophysiologic monitoring in adult patients undergoing brain surgery

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Abstract

Background: Despite advances in neuroendovascular techniques, several complications can occur by brain surgery. Among them, the most frightful complication is the postoperative motor deficit. Motor evoked potential (MEP) as a kind of intraoperative neurophysiologic monitoring (IONM) is a safe monitoring method for detecting the motor deficit, but this could inadvertently cause harms. It can cause excitotoxicity, electrochemical injury, thermal injury, bite injuries, seizures, invasive electrode complications, unpredictable and unacceptable movement-induced injury, and arrhythmia. The unpredictable and unacceptable can cause injuries in site of rigid pin fixation of the head, cervical spine injuries, excessive surgical field movement, and deterioration of surgical outcome. However, risk factors associated with unpredictable and unacceptable movement remain unclear. The aim of this retrospective study was to evaluate risk factors associated with unpredictable and unacceptable movement in the patients who underwent brain surgery with MEP monitoring under general anesthesia while using partial neuromuscular blocker (NMB).

Methods: We recorded demographic data including age, sex, height, weight, body mass index, diagnosed disease, performed surgical procedure, duration of anesthesia, duration of surgery, underlying disease (e.g. hypertension, diabetes, neurologic disease, respiratory disease), preoperative anticonvulsant infusion. Laboratory data immediately after induction of anesthesia was also collected including arterial blood gas analysis, hematocrit, hemoglobin, sodium, potassium, glucose, ionized calcium, ionized magnesium, and lactate. We retrospectively compare the data of patients with and without unpredictable and unacceptable movement during surgery.

Results: The study was enrolled and analysis 768 patients, an unpredictable and unacceptable movement was observed 278 patients (36.2%). The incidence of unpredictable and unacceptable movement was significantly higher in patients in normocalcemia group than in those in hypocalcemia group ($P < 0.001$). Ionized calcium (odds ratio [OR] 368.519, 95% confidence interval [CI] 25.391, 5348.585) was independent risk factors for an unpredictable and unacceptable movement. Age (odds ratio [OR] 0.987, 95% confidence interval [CI] 0.965, 0.992), height (odds ratio [OR] 1.059, 95% confidence interval [CI] 1.033, 1.085), weight (odds ratio [OR] 0.969, 95% confidence interval [CI] 0.952, 0.987), and neurologic disease (odds ratio [OR] 0.205, 95% confidence interval [CI] 0.049, 0.911) were other independent risk factors for an unpredictable and unacceptable movement.

Conclusion: Serum ionized calcium concentration was the risk factors associated with unpredictable and unacceptable movement in the patients who underwent brain surgery with MEP monitoring under general anesthesia while using partial NMB.

Keywords: Motor evoked potential, Unpredicted movement, Brain surgery, Ionized calcium.

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INTRODUCTION

Despite advances in neuroendovascular techniques, several complications can occur by brain surgery. Among them, the most frightful complication is the postoperative motor deficit within or adjacent to the motor areas and pathways caused by ischemia, embolization, and cell injury during surgery. If a motor impairment occurs, postoperative recovery is delayed, the quality of life of the patient is deteriorated, and personal, and social economic losses are also increased. Therefore, for neurosurgeons and anesthesiologists, it is a major concern to describe and monitor surgical lesion for maintaining structural and functional integrity as well as achieving maximal cytoreduction in lesion, and modifying the management of patients on the process of surgery. For example, microvascular Doppler sonography, indocyanine green angiography, intraoperative digital subtraction angiography, and intraoperative neurophysiologic monitoring (IONM) are used for this purpose [1].

Motor evoked potential (MEP) as a kind of IONM is a relatively recent introduction and its use and the awareness of the necessity are increased as a valuable monitoring method to improve the outcome. It is known that MEP has higher diagnostic accuracy than SSEP and about 90% accurate in predicting postoperative motor deficit [2, 3]. MEP is a safe monitoring method for clinical practice if it is performed by a specialist with proper care [4, 5], but this could inadvertently cause harms. Safety issues correlate with MEP are excitotoxicity, electrochemical injury, thermal injury, bite injuries, seizures, invasive electrode complications, unpredictable and unacceptable movement-induced injury, and arrhythmia [6].

The incidence of unpredictable and unacceptable movement is relative low [7]. However, the results are so horrendous that they can cause injuries in site of rigid pin fixation of the head, cervical spine injuries, excessive surgical field movement, and deterioration of surgical outcome. Thus, there are many institutes that use partial neuromuscular blocker (NMB) because full omission of the NMB may cause a risk of unexpected patient movement. However, risk factors associated with unpredictable and unacceptable movement remain unclear. If risk factors are known in advance, the safety of the patient can be achieved and the outcome of the surgery can be improved. Towards this purpose, the aim of this retrospective study was to evaluate risk factors associated with unpredictable and unacceptable movement in the patients who underwent brain surgery with MEP monitoring under general anesthesia while using partial NMB.

METHODS

Study design and inclusion criteria

This study was approved by the Institutional Review Board at Seoul National University Bundang Hospital (Seongnam-si, South Korea, approval on January 1, 2018, B-1801-444-102). We retrospectively analyzed collected data for consecutive patients of American Society of Anesthesiologists (ASA) physical status classes I-II, aged 19-74 years who underwent brain surgery with MEP monitoring under general anesthesia while using partial NMB in Seoul National University Bundang Hospital from January 2014 to August 2017. ‘Unpredictable and unacceptable movement’ was defined as a condition in which the patient’s spontaneous movement or breathing is observed or as the case where the smooth progress of the operation was difficult to proceed the operation smoothly due to the movement of the microscopic field.

Anesthesia and MEP monitoring

The surgical and anesthetic procedures were consistent according to our institutional protocol. As a premedication, all patients were received with intravenous midazolam at 0.03 mg/kg at reception area. On arrival at the operating room, standard monitoring with pulse oximetry, non-invasive blood pressure, and electrocardiography was applied. The bispectral index (A-2000 BISTM monitor: Aspect Medical Systems, Inc., Natick, MA, USA) was also monitored. Anesthesia was induced with propofol (effect-site concentration: 4–6 mg/ml) or etomidate 0.2 mg/kg, continuous infusion of remifentanil (target effect-site concentration controlled infusion 3 ng/ml; Orchestra infusion pumps: Fresenius Vial, Brezins, France), and rocuronium (0.6 mg/kg) and maintained continuous infusion of propofol (effect-site concentration: 3-4 mg/ml] and remifentanil (target effect-site concentration controlled infusion 2-3 ng/ml). After endotracheal intubation, lungs were mechanically ventilated with 50% oxygen and medical air and adjusted to maintain an end-tidal carbon dioxide tension of 35-40 mmHg. The temperature was measured with an esophageal stethoscope and maintained at least 35 ℃. The concentrations of propofol and remifentanil were adjusted to maintain intraoperative systolic arterial pressure within 20% of baseline value and the BIS at 40-60. If necessary, phenylephrine (20–30 mcg) was administered or continuously infused (0.25–0.5 mcg/kg/ min) to maintain systolic arterial pressure. Intraoperative haemoglobin concentration was maintained above 10 g/dl.

After endotracheal intubation, no additional NMB was administrated to obtain baseline signals of MEP. After obtaining baseline signals, continuous infusion of rocuronium (0.3 mg/kg/hr) was started for partial neuromuscular blocking according to our institutional protocol. If unpredictable and unacceptable movement is detected, the continuous infusion rate of rocuronium was increased by 0.1 mg/kg/hr. In addition, to avoid movement of the microsurgical field during critical surgical procedure, prior to major surgical procedure, the Stimulus intensity and evoked potential responses was checked and no changes in the continuous infusion rate of rocuronium were observed during major critical surgical procedure.

MEP stimulation were generated by multipulse transcranial electrical stimulation (Xltek Protector; Natus Medical Incorporated Excel-Tech Ltd, Oakville , Ontario Canada) at sites 2 cm anterior to the C1 and C2 positions of the international 10-20 system using 3~7 square-wave, monophasic, anodal, constant-voltage electrical pulses of 0.5 msec duration with an interstimulus interval of 2~4 msec. MEP were recorded (32-channel Xltek Protector) from the bilateral upper and lower extremities simultaneously with needles placed in bilateral abductor pollicis brevis and abductor digiti minimi, tibialis anterior and abductor hallucis muscles. MEPs were monitored and recorded within a 100 msec epoch after being filtered (band-pass 10~1,000Hz) and amplified (X10,000). Stimulus intensity was increased by 10~50 V increments from 100 V to a maximum of 300 V until evoked potential responses were detectable in the lower extremities above a minimum of approximately 0.1 mV. MEPs were monitored every 10 minutes throughout surgery and more frequently during critical surgical manipulation. To prevention of movement of the microsurgical field during critical surgical procedure, brief surgical pauses (a few seconds) for monitoring of MEPs were coordinated between the neurosurgery, anesthesia, and electrophysiology teams. Video monitoring was also used to assist the electrophysiology team in timing stimulation in coordination with surgery.

Data collection

The electronic medical records of enrolled patients were reviewed retrospectively. We recorded demographic data including age, sex, height, weight, BMI, diagnosed disease, performed surgical procedure, duration of anesthesia, duration of surgery, underlying disease (e.g. hypertension, diabetes, neurologic disease, respiratory disease), preoperative anticonvulsant infusion. Laboratory data immediately after induction of anesthesia was also collected including arterial blood gas analysis, hematocrit, hemoglobin, sodium, potassium, glucose, ionized calcium, ionized magnesium, and lactate. When the unpredictable and unacceptable movement was observed, the surgeon informed the anesthesiologist and neurophysiologic specialist, and the anesthesiologist increased the sustained rate of rocuronium as previously described. Therefore, when the elevation of the infusion rate of rocuronium was ascertained in the patient's electronic medical records, we determined that an unpredictable and unacceptable movement was occurred.

Statistical analysis

We retrospectively compare the data of patients with and without unpredictable and unacceptable movement during surgery. Values are mean ± standard deviation or number (percent). A statistical analysis was performed using IBM SPSS Statistics version 21.0 (SPSS Inc., Chicago, Illinois, USA). For continuous variables, values were compared using the independent t-test. Differences in proportions were compared using chi-square test. Variables with P-values < 0.1 in the primary test were selected and univariate binary logistic regression analyses were conducted to identify the factors predictive of an unpredictable and unacceptable movement. P-value < 0.05 was considered statistically significant.

RESULTS

The study was enrolled and analysis 768 patients, an unpredictable and unacceptable movement was observed 278 patients (36.2%). Baseline characteristics of the patient group, assorted according to the presence or absence of an unpredictable and unacceptable movement, are presented in Table 1. Age was significantly higher in patients without an unpredictable and unacceptable movement than in those with ($P < 0.001$). Height was significantly higher in patients with an unpredictable and unacceptable movement than in those without ($P < 0.001$). The proportion of male patients was significantly higher in patients with an unpredictable and unacceptable movement than in those without ($P=0.001$). Laboratory data immediately after induction of anesthesia of the patient group, assorted according to the presence or absence of an unpredictable and unacceptable movement, are presented in Table 2. Ionized calcium was significantly higher in patients with an unpredictable and unacceptable movement than in those without ($P < 0.001$).

Anticonvulsant might have an effect on the sensitivity of the neuromuscular junction to muscle relaxants. Therefore, secondarily, patients were classified according to the presence or absence of an unpredictable and unacceptable movement except for patients who did not received a preoperative anticonvulsant infusion. Baseline characteristics and laboratory data of the patient group received a preoperative anticonvulsant infusion were compared according to the presence or absence of an unpredictable and unacceptable movement but there was no statistical difference with or without anticonvulsant infusion.

Lastly, according to the logistic regression analysis presented in Table 3, age (odds ratio [OR] 0.987, 95% confidence interval [CI] 0.965, 0.992), height (odds ratio [OR] 1.059, 95% confidence interval [CI] 1.033, 1.085), weight (odds ratio [OR] 0.969, 95% confidence interval [CI] 0.952, 0.987), neurologic disease (odds ratio [OR] 0.205, 95% confidence interval [CI] 0.049, 0.911), and ionized calcium (odds ratio [OR] 368.519, 95% confidence interval [CI] 25.391, 5348.585) were independent risk factors for an unpredictable and unacceptable movement.

Table 1. Baseline patient characteristics

		No movement (n=490, 63.8%)	Movement (n=278, 36.2%)	P-value
Age (year)		56.54±11.63	52.18±12.08	.000*
Sex				0.001*
	Male	162 (33.1)	127 (45.7)	
	Female	328 (66.9)	151 (54.3)	
Height (cm)		160.04±8.87	163.18±8.80	.000*
Weight (kg)		62.88±11.39	63.19±11.55	0.715
BMI (kg/m^2)		24.46±3.36	23.64±3.28	0.001*
Duration of surgery (min)		266.29±106.06	281.29±106.00	0.060
Duration of anesthesia (min)		338.31±114.20	351.45±117.91	0.130
Type of surgery				0.458
	Vascular surgery	351 (71.6)	206 (74.1)	
	Tumor	137 (28.0)	72 (25.9)	
	Other	2 (0.4)	0 (0)	
HTN				0.070
	No	275 (56.2)	175 (62.9)	
	Yes	214 (43.8)	103 (37.1)	

DM				0.082
	No	438 (89.4)	259 (93.2)	
	Yes	52 (10.6)	19 (6.8)	
Respiratory disease				0.359
	No	478 (97.6)	268 (96.4)	
	Yes	12 (2.4)	10 (3.6)	
Neurologic disease				0.018
	No	473 (96.5)	276 (99.3)	
	Yes	17 (3.5)	2 (0.7)	
Preoperative anticonvulsant infusion				0.240
	No	29 (5.9)	11 (4.0)	
	Yes	461 (94.1)	267 (96.0)	

Values are mean ± standard deviation or number (percent). *, P-value was < 0.05.

Table 2. Laboratory data immediately after induction of anesthesia of total enrolled patients

	No movement (n=490, 63.8%)	Movement (n=278, 36.2%)	P-value
Ionized calcium (mmol/L)	1.12±0.59	1.14±0.60	.000*
Ionized magnesium (mmol/L)	0.46±0.52	0.47±0.52	0.147
pH	7.40±0,38	7.40±0.35	0.342
pCO2 (mmHg)	36.40±4.29	36.47±4.19	0.836
pO2 (mmHg)	231.77±80.85	241.30±74.40	0.106
Hematocrit (%)	35.69±3.57	36.35±3.60	0.015
Na (mmol/L)	138.47±2.57	138.33±2.39	0.442
K (mmol/L)	3.68±0.40	3.73±0.38	0.062
Hemoglobin (g/dl)	11.89±1.18	12.12±1.21	0.011
Glucose (mg/dl)	109.34±28.16	106.95±23.02	0.255
Lactate (mmol/L)	1.21±0.63	1.16±0.63	0.352

Values are mean ± standard deviation. *, P-value was < 0.05.

Table 3. Logistic regression analysis of unpredictable and unacceptable movement

Dependent factor	Independent factor	Exp (B) (95% C.I.)	P-value
Movement	Age	0.987 (0.965-0.992)	0.002*
	Height	1.059 (1.033-1.085)	0.000*
	Weight	0.969 (0.952-0.987)	0.001*
	Neurologic disease	0.205 (0.046-0.911)	0.037*
	Preoperative anticonvulsant infusion	2.095 (0.995-4.414)	0.052
	Ionized calcium	368.519 (25.391-5348.585)	0.000*

Exp(B) : the exponentiation of the B coefficient, C.I. : confidence interval

*, P-value was < 0.05.

DISCUSSION

This retrospective study found that concentration of age, height, weight, neurologic disease, and ionized calcium were independent risk factors for an unpredictable and unacceptable movement in the patients who underwent brain surgery with MEP monitoring under general anesthesia while using partial NMB.

MEP is one kind of IONM and has higher diagnostic accuracy than somatosensory evoked potential (SSEP) and can show positive findings when no change in SSEP because receives some blood supply of motor pathway are a little bit different from that of sensory pathway [8]. MEP is a reliable monitoring method that improves the surgical outcome for brain tumor, cerebral aneurysm and cerebrovascular surgery such as endarterectomy [9-11]. To strengthen the accuracy of MEP results, it is most desirable not to use neuromuscular blocker because of false negative results [12]. Notwithstanding, some institutes support the use of partial neuromuscular blocker during MEP monitoring since an unpredictable and unacceptable movement causes fatal injuries [13-15]. In previous studies, the incidence of an unpredictable and unacceptable movement during MEP monitoring with partial neuromuscular blocker or no neuromuscular blocker are 3.2% to 10% [7, 8, 12, 16]. In our study, according to study’s definition, the incidence of an unpredictable and unacceptable movement was about 38%. The reason for higher incidences than previous studies is that our definition has a wide range of inclusions and so much it included all the moves that were considered a little dangerous. So, in fact, the adjustment of the continuous infusion rate of rocuronium had already been finished before the main surgical procedure and in the most critical surgical procedure, there were no an unpredictable and unacceptable movement.

In this study, we used 0.6 mg/kg of rocuronium for intubation and no additional NMB was used until obtaining baseline signals of MEP. After that, continuous infusion of rocuronium (0.3 mg/kg/hr) was started for partial neuromuscular blocking and infusion rate was adjusted depending on the occurrence of an unpredictable and unacceptable movement. This allows almost degree of neuromuscular block of all enrolled patients to maintain a train-of-four (TOF) 2/4–3/4. According to previous studies [12, 14, 17-22], appropriate degree of partial neuromuscular block has been reported variously from first evoked response of TOF between 5% and 50% of baseline or one or two twitches in TOF electrical stimulation to 0.5 twitch height of the second evoked response of TOF stimulation compared with the baseline control twitch. Compared with above previous studies, degree of partial neuromuscular block in our study was considered to have maintained the middle degree of the block presented above. In addition, although the comparison of SSEP and MEP is very limited, the degree of partial neuromuscular blocking used in this study did not seem to affect negatively the specificity or sensitivity based on our institute SSEP data [23].

In our study, ionized calcium was the best predictor of the occurrence of the unpredictable and unacceptable movement during MEP in patient underwent brain surgery. This is because calcium has astonishing numbers of regulatory functions and especially in the neuromuscular junction it plays a significant role in triggering of neuromuscular transmission [24]. Calcium channels are presented both in presynaptic and postsynaptic membrane. Action potential arriving at presynaptic membrane opens calcium channels and causes the influx of calcium ion. And calcium triggers the release of neurotransmitter such as acetylcholine from synaptic vesicles into the synaptic cleft. At the postsynaptic membrane, neurotransmitter molecules union with membrane-bound receptor and binding of the neurotransmitter to the receptor triggers a postsynaptic response. The postsynaptic responses are excitatory or inhibitory. Receptors coupled to sodium or calcium channels are excitatory and receptors coupled to chloride or potassium channels are inhibitory [25-30]. If neurotransmitter molecule binds to receptor coupled to calcium channels, it produces a depolarization of the postsynaptic membrane.

Several studies have investigated the overall impact of ionized calcium on neuromuscular transmission and neuromuscular blockade. In previous in vivo and in vitro animal experiments, calcium has been shown to emphasize the desensitization of depolarizing agent [31], and to reduce affinity of the receptor for tubocurarine and pancuronium [32, 33] in postsynaptic space. Hypercalcemia has been antagonized tubocurarine and succinylcholine and hypocalcemia decreased the twitch tensions of rats' phrenic nerve-hemidiaphragm [34]. In cats, hypercalcemia also has been shown to antagonize the blocking effects of atracurium and vecuronium [35]. In human case report, patients with hypercalcemia due to hyperparathyroidism showed an upward tendency to increases the requirement for non-depolarizing muscle relaxants [36, 37]. In comparison study with healthy patients, vecuronium requirement in patients with hypercalcemia due to hyperparathyroidism was increased and the onset of neuromuscular blockade was delayed [38]. In addition, calcium coadministered with neostigmine for neuromuscular recovery enhanced neuromuscular recovery from nondepolarizing neuromuscular blockade [39]. On the contrary, calcium channel antagonists have enhanced the neuromuscular blockade. In animal studies, high-dose verapamil induced neuromuscular blockade [40].In human healthy volunteers. verapamil and amlodipine impaired neuromuscular transmission [41] and pretreatment with nicardipine before intubation improves intubation conditions and shortens the onset of action of rocuronium [42].

Overall, considering the results of the above, ionized calcium has the effect of reversal of neuromuscular blockade and relative high concentration of ionized calcium can be alter the effect of neuromuscular block agents and neuromuscular transmission. Therefore, it is thought that ionized calcium can be it can affect the results of MEP or may cause a jerky dangerous response than expected for MEP stimulation in spite of partial neuromuscular blockade such as an unpredictable and unacceptable movement in our study. And it is possible that serum ion calcium concentration in patients with shallow neuromuscular blockade, administration of ionized calcium may induce it is presumed that there is a possibility that false negative or false positive results of MEP can be seen a patient who has taken a calcium channel blocker for a long period of time or has hypercalcemia due to hyperparathyroidism. Or in patient with hypocalcemia, use of partial neuromuscular blockade can interfere with accurate results of MEP.

As far as our knowledge, our study is the first study which evaluated the predictors of an unpredictable and unacceptable movement during MEP monitoring. Although it was retrospective study, it found that concentration of ionized calcium could be an independent risk factor for an unpredictable and unacceptable movement in the patients who underwent brain surgery with MEP monitoring under general anesthesia while using partial NMB. Therefore, patients with high ionized calcium should consider maintaining a slightly higher dose of muscle relaxant to reduce the incidence of unpredictable and unacceptable movement during MEP monitoring. Furthermore, prospective and randomized study and effects of calcium on MEP will be needed for understanding the effect of ionized calcium on MEP monitoring better.

REFERENCES

1. Raabe A, Seidel K. Prevention of ischemic complications during aneurysm surgery. J Neurosurg Sci 2016; 60: 95-103.

2. Yamada Y, Kato Y, Nouri M, Ganaha T, Oheda M, Ishihara K, Moriya S, Sadato A, Inamasu J, Hirose Y. Predictive Value of Motor Evoked Potential Monitoring during Surgery of Unruptured Anterior Circulation Cerebral Aneurysms. Asian J Neurosurg. 2017; 2: 44-647.

3. Thomas B, Guo D. The Diagnostic Accuracy of Evoked Potential Monitoring Techniques During Intracranial Aneurysm Surgery for Predicting Postoperative Ischemic Damage: A Systematic Review and Meta-Analysis. World Neurosurg. 2017; 103: 829-840.

4. MacDonald DB. Safety of intraoperative transcranial electrical stimulation motor evoked potential monitoring. J Clin Neurophysiol. 2002; 19: 416-29.

5. MacDonald DB, Al-Zayed Z, Stigsby B, Al-Homoud I. Median somatosensory evoked potential intraoperative monitoring: recommendations based on signal-to-noise ratio analysis. Clin Neurophysiol. 2009;120: 315-2.

6. Macdonald DB1, Skinner S, Shils J, Yingling C; American Society of Neurophysiological Monitoring. Intraoperative motor evoked potential monitoring - a position statement by the American Society of Neurophysiological Monitoring. Clin Neurophysiol. 2013 Dec;124(12):2291-316.

7. Hemmer LB, Zeeni C, Bebawy JF, Bendok BR, Cotton MA, Shah NB, Gupta DK, Koht A. The incidence of unacceptable movement with motor evoked potentials during craniotomy for aneurysm clipping World Neurosurg. 2014 Jan;81(1):99-104.

8. Neuloh G, Schramm J. Monitoring of motor evoked potentials compared with somatosensory evoked potentials and microvascular Doppler ultrasonography in cerebral aneurysm surgery. J Neurosurg. 2004;100:389-99.

9. Landazuri P, Eccher M. Simultaneous direct cortical motor evoked potential monitoring and subcortical mapping for motor pathway preservation during brain tumor surgery: is it useful? J Clin Neurophysiol. 2013 Dec;30(6):623-5.

10. Malcharek MJ, Kulpok A, Deletis V, Ulkatan S, Sablotzki A, Hennig G, Gille J, Pilge S, Schneider G. Intraoperative multimodal evoked potential monitoring during carotid endarterectomy: a retrospective study of 264 patients. Anesth Analg. 2015 Jun;120(6):1352-60.

11. Yamada Y, Kato Y, Nouri M, Ganaha T, Oheda M, Ishihara K, Moriya S, Sadato A, Inamasu J, Hirose Y. Predictive Value of Motor Evoked Potential Monitoring during Surgery of Unruptured Anterior Circulation Cerebral Aneurysms. Asian J Neurosurg. 2017 Oct-Dec;12(4):644-647.

12. Kim WH1, Lee JJ, Lee SM, Park MN, Park SK, Seo DW, Chung IS. Comparison of motor-evoked potentials monitoring in response to transcranial electricalstimulation in subjects undergoing neurosurgery with partial vs no neur omuscular block. Br J Anaesth. 2013 Apr;110(4):567-76.

13. Szelenyi A, Langer D, Kothbauer K, et al. Monitoring of muscle motor evoked potentials during cerebral aneurysm surgery: intraoperative changes and postoperative outcome. J Neurosurg 2006;105: 675–81.

14. Kalkman CJ, Drummond JC, Kennelly NA, et al. Intraoperative monitoring of tibialis anterior muscle motor evoked responses to transcranial electrical stimulation during partial neuromuscular blockade. Anesth Analg 1992;75:584–9. [9]

15. Sloan TB, Janik D, Jameson L. Multimodality monitoring of the central nervous system using motor-evoked potentials. Curr Opin Anaesthesiol 2008;21:560–4.

16. Szelenyi A, Kothbauer K, de Camargo AB, et al. Motor evoked potential monitoring during cerebral aneurysm surgery: technical aspects and comparison of transcranial and direct cortical stimulation. Neurosurgery 2005;57:331–8.

17. Sloan TB, Heyer EJ. Anesthesia for intraoperative neurophysiologic monitoring of the spinal cord. J Clin Neurophysiol 2002; 19: 430–43

18. van Dongen EP, ter Beek HT, Schepens MA, et al. Effect of nitrous oxide on myogenic motor potentials evoked by a six pulse train of transcranial electrical stimuli: a possible monitor for aortic surgery. Br J Anaesth 1999; 82: 323–8

19. Sloan TB. Anesthesia and motor evoked-potentials monitoring. In: Deletis V, Shils J, eds. Neurophysiology in Neurosurgery: A Modern Intraoperative Approach. San Diego: Academic Press, 2002: 175–81

20. Gugino LD, Aglio LS, Segal NE, Gonzalez AA, Kraus KH, Woodard EJ. Use of transcranial magnetic stimulation for monitoring spinal cord motor paths. Semin Spine Surg 1997; 9: 315–36

21. Lee WY, Hou WY, Yang LH, Lin SM. Intraoperative monitoring of motor function by magnetic motor evoked potentials. Neurosurgery 1995; 36: 493 – 500

22. Yang LH, Lin SM, Lee WY, Liu CC. Intraoperative transcranial electrical motor evoked potential monitoring during spinal surgery under intravenous ketamine or etomidate anaesthesia. Acta Neurochir (Wien) 1994; 127: 191 –8

23. Byoun HS, Bang JS, Oh CW, Kwon OK, Hwang G, Han JH, Kim T, Lee SU, Jo SR, Kim DG, Park KS. The incidence of and risk factors for ischemic complications after microsurgical clipping of unruptured middle cerebral artery aneurysms and the efficacy of intraoperative monitoring of somatosensory evoked potentials: A retrospective study. Clin Neurol Neurosurg. 2016 Dec;151:128-135.

24. Neher E, Sakaba T. Multiple roles of calcium ions in the regulation of neurotransmitter release. Neuron. 2008 Sep 25;59(6):861-72.

25. Santafe MM, Garcia N, Lanuza MA, et al. Presynaptic muscarinic receptors, calcium channels, and protein kinase C modulate the functional disconnection of weak inputs at polyinnervated neonatal neuromuscular synapses. J Neurosci

Res 2009; 87:1195–1206.

26. Ginsborg BL, Jenkinson DH. Transmission of impulses from nerve to muscle. In: Zaimis E, Maclagan J, editors. Neuromuscular junction. Berlin, Heidelberg: Springer Berlin Heidelberg; 1976. pp. 229–364.

2. Südhof TC. Calcium control of neurotransmitter release. Cold Spring Harb Perspect Biol. 2012 Jan 1;4(1):a011353.

28. Catterall WA. Voltage-gated calcium channels. Cold Spring Harb Perspect Biol. 2011 Aug 1;3(8):a003947.

29. Purves D, Augustine GJ, Fitzpatrick D, et al., editors. Neuroscience. 3nd edition. Sunderland, MA, Sinauer Associates, Inc., 2004Chapter 5 Synaptic Transmission 93-128.

30. Losavio A, Muchnik S. Spontaneous acetylcholine release in mammalian neuromuscular junctions. Am J Physiol 1997;273:1835–41.

31. Manthey AA. The effect of calcium on the desensitization of membrane receptors at the neuromuscular junction. J Gen Physiol. 1966 May;49(5):963-76.

32. Jenkinson DH. The antagonism between tubocurarine and substances which depolarize the motor end-plate. J Physiol. 1960 Jul;152:309-24.

33. Waud BE, Waud DR. Interaction of calcium and potassium with neuromuscular blocking agents. Br J Anaesth 1980; 52:863–86

34. Okamoto T. Effects of magnesium and calcium on muscle contractility and neuromuscular blockade produced by muscle relaxants and aminoglycosides (Japanese). Masui 1992; 41: 1910–22.

35. Gramstad I_, Hysing ES. Effect of ionized calcium on the neuromuscular blocking actions of atracurium and vecuronium in the cat. Br J Anaesth 1990; 64: 199-206.

36. Al-Mohaya S, Naguib M, Abdelatif M, et al. Abnormal responses to muscle relaxants in a patient with primary hyperparathyroidism. Anesthesiology 1986;

65:554–556.

37. Narimatsu H, Nishikawa Y, Namiki A. Vecuronium-induced neuromuscular blockade in two patients with hyperparathyroidism and a patient with hypoparathyroidism (Japanese). Masui 1992; 41: 136–9.

38. Roland EJ, Wierda JM, Eurin BG, Roupie E. Pharmacodynamic behaviour of vecuronium in primary hyperparathyroidism. Can J Anaesth 1994; 41: 694–8.

39. Ju JW, Kim HC, Yoon S, Hong DM, Park HP. Effects of calcium chloride coadministered with neostigmine on neuromuscular blockade recovery: A double-blind randomised study. Eur J Anaesthesiol. 2017 Sep;34(9):617-622.

40. Nagaral J, Gh S, K J, et al. Study on neuromuscular blockade action of verapamil in albino rats. J Clin Diagn Res 2013; 7:1617–1619.

41. Ozkul Y. Influence of calcium channel blocker drugs in neuromuscular transmission. Clin Neurophysiol 2007; 118:2005–2008.

42. Lee SY, Kim YH, Ko YK, et al. Effects of nicardipine on the onset time and intubation conditions of rocuronium-induced neuromuscular blockade. J Clin Anesth 2016; 32:112–118.

국문 초록

서론: 신경내혈관 기술의 발전에도 불구하고 뇌 수술을 통해 여러 합병증이 발생할 수 있다. 그 중에서도 가장 무서운 합병증은 수술 후 발생하는 운동 장애이다. 수술 중 신경생리학적 모니터링의 일종인 운동유발전위 검사는 운동 장애를 감지하는 안전한 검사이지만, 역으로 위해를 가할 수도 있다. 이는 신경흥분독성, 전기화학적 손상, 열손상, 물림 손상, 발작, 침습적 전극에 의한 합병증, 예측할 수 없는 움직임에 의한 손상, 부정맥을 유발할 수 있다. 이런 예측할 수 없고 받아들이기 어려운 움직임은 두부의 핀 고정 부위의 손상, 경추 손상, 과도한 수술 시야의 움직임을 유발할 수 있고, 나쁜 수술 결과를 초래할 수 있다. 그러나 이런 움직임에 대한 위험 요소는 알려져 있지 않다. 따라서 이 후향적 연구의 목적은 부분적 신경근 차단제를 사용하며 전신마취 하에 운동유발전위를 감시하며 뇌 수술을 받은 환자의 예측 불가능하고 받아들이기 어려운 움직임과 관련된 위험 요소를 알아보는 것이다.

방법: 본 연구에서 연구자는 후향적으로 대상 환자의 연령, 신장, 체중, 체질량 지수, 진단명, 수술명, 마취 시간, 수술 시간, 기저 질환 (예 : 고혈압, 당뇨, 신경계 질환, 호흡기계 질환), 수술전 항경련제 투여여부를 조사하였다. 또한 마취 유도 직후 동맥혈 채혈검사를 통해 헤모글로빈,

헤마토크릿, 나트륨, 칼륨, 포도당, 이온화된 칼슘, 이온화된 마그네슘, 젖산염 수치도 수집하였다. 수술 중 예측할 수 없고 받아들일 수 없는 움직임이 있는 환자와 없는 환자에서 얻은 위 데이터를 후향적으로 비교하였다.

결과: 본 연구에서는 총 768명 환자를 조사하였으며, 예측할 수 없는 움직임이 발생한 군이 278명 (36.2%)이었다. 예측할 수 없는 움직임이 발생한 빈도는 저칼슘혈증군 보다 정상칼슘혈증군에서 유의하게 높았으며(P<0.001), 이온화된 칼슘은 예측할 수 없는 움직임에 대한 독립적인 위험 요소였다(odds ratio [OR] 368.519, 95% 신뢰구간 [CI] 25.319, 5348.585). 나이, 키, 몸무게, 신경계 질환도 예측 불가능한 움직임의 다른 독립적인 위험 요인이었다.

결론: 부분적인 신경근 차단제를 사용하며 전신마취 하에 운동유발전위 검사를 감시하며 뇌수술을 받는 환자에서 발생하는 예측할 수 없는 움직임에서 혈청 이온화 칼슘 농도는 이런 움직임과 관련된 위험 인자였다.

주요어: 운동유발전위, 뇌수술, 예측하지 못한 움직임, 칼슘이온

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