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A Study on The Relationship Between Intraoperative Neuromonitoring and Hemoglobin Changes

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Abstract

This study was conducted in order to determine the effect of intraoperative hemoglobin changes on intraoperative neuromonitoring (IONM). This was a retrospective study that included 339 participants who underwent cerebrovascular surgery. We compared anesthetic agents, intraoperative hemoglobin, hematocrit, blood transfusion, and blood loss. We examined motor evoked potential and sensory evoked potential to patients. There were significant differences in hemoglobin changes, bleeding levels, transfusion, anesthesia time, and postoperative mobility disorders. Moreover, compared with patients who received transfusions, those who did not receive transfusion had a lower average hemoglobin level, as well as a higher bleeding amount, and a need of higher anesthesia time and anesthetic dose. Also, we found vasospasm occurred while surgery can bring adverse results after operation. This study showed that an intraoperative decrease in hemoglobin levels affects the function of cerebral perfusion, which could result in abnormal nerve monitoring results. However, as this study could not find a relation of anesthetics to IONM, there is a need for further research regarding the association between anesthetics and hemoglobin changes and IONM.

Keywords: *Anemia, Anesthesia, Blood transfusion, Hemoglobin, Bleeding, Intraoperative neuromonitoring*

1. Introduction

Intraoperative neuromonitoring is performed to prevent neurological damage to the patient and to yield information regarding the patient's condition [1]. It mostly involves tests based on motor- and sensory-evoked potentials with the possible involvement of an electroencephalogram, visual-evoked positives, brain stem auditory evoked positives, and electromyogram, as appropriate. Recent advances in technology have allowed an increase in the number of related studies [2]. Motor- and sensory-evoked potentials reflect the function of the cortical spinal cord in brain tissue, as well as peripheral neuropathy [3]. Here, electrodes are attached to the scalp surface to obtain an electrical signal from the brain that is converted into a waveform. Abnormal findings are indicative of compromised brain function. Therefore, intraoperative monitoring might yield abnormal findings in case of bleeding-induced anemia occurrence and degraded brain function [4]. Generally,

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in a significant intraoperative decrease in hemoglobin levels, blood transfusions are performed to minimize anemia-induced neurological damage. When blood transfusion is required due to low hemoglobin levels, the blood storage period and side effects of blood transfusion should be considered. Old packed red blood cells can increase patients' blood cell volume but not oxygen levels [5]. Moreover, breathing malfunction caused by acute pulmonary infarction can occur, which may reduce the oxygen supply in the brain and affect IONM [6]. Vasospasm is another factor that can affect monitoring. The risk of postoperative vasospasm is higher in cases with intraoperative cerebral aneurysm rupturing than in cases without [7]. Vasospasm of the main cerebral vessels increases the likelihood of ischemia in the brain tissue caused by blood flow disorders [8]. Therefore, a large amount of fluid is intraoperatively injected to prevent vasospasm, which lowers the blood cell density. The lower blood cell density reduces the hemoglobin per unit area, which can impair brain function in patients [9]. This study aimed to determine the effect of hemoglobin changes on IONM.

2. MATERIALS AND METHODS

2.1 Study Participants

In this paper, we considered 339 individuals who underwent cerebrovascular surgery at Seoul National University Bundang Hospital from October 2018 to December 2020. The study participants received explanations regarding the examination purpose; further, consent for data collection was sought. The study assessed 194 (57% of 339 patients) normal subjects, 145 (42% of 339 patients) patients with abnormal neuromonitoring test findings, and 34 (10% of 339 patients) patients with postoperative neurological deficits. There are about 80 to 90 patients in other studies that have conducted similar studies. All included participants lacked neurological disorders other than the main disease for surgery. Cases where the same person underwent a second surgery or another vascular operation at different time points were considered as duplicates. Among-group comparisons of the surgical time, hemoglobin levels, bleeding, transfusion, and anesthetics were performed to determine the extent of the variable effects on IONM.

Table 1 shows the main variables covered in this study and how they were analyzed. The average hemoglobin before, during and after surgery was mainly dealt with, and the anesthetic compared the dose of propofol and Remifentanyl.

Table 1. Variables and comparisons model

Comparison	Variable	Analysis
Normal and Abnormal (intraoperative neurophysiological monitoring event)	Total Hemoglobin (g/dL)	F-test
	PreOP Hemoglobin (g/dL)	
	Max Hb-Min Hb (g/dL)	
	FFP transfusion(Pack, Unit)	Equal variance T-test
	Propofol (MAX, MIN)	
	Remifentanil(MAX, MIN)	
Normal and Postoperative neurologic deficits	Anesthesia Time (Hour: Min)	Unequal variance T-test
	Blood loss (mL)	

*IONM: intraoperative neuromonitoring; MIN: minimum; MAX: maximum; RBC: Red blood cells; FFP: Fresh frozen plasma; OP: operation; Hb: hemoglobin

2.2 Examination

We used the Xtek Protector (Natus Medical Inc., ExcelTech Ltd., Oakville, Ontario, Canada) as the test equipment. Based on the International 10-20 Electrode system, motor evoked potential (MEP) stimulation needles were inserted into the positive and negative stimulation needles at C2, C4, C1, and C3 to stimulate the right cerebral hemisphere, as well as at C1, C3, C2, and C4 to stimulate the left cerebral hemisphere. . C2, C4 is located in the right hemisphere centerline of the brain, and C1, C3 is located in the left hemisphere centerline of the brain. They are symmetrical with each other, C3 and C4 are located far left and right. The following stimulus parameters were used: biphasic polarity, continuative 5 pulse stimuli, 500 Hz of stimulation rate, 0.05 ms of stimulus duration, and 150–300 V for MEP. The MEP stimulation power was recorded in the abductor pollicis brevis and adductor digiti minimi, as well as in the tibialis anterior and abductor hallucis of the lower limbs. The upper somatosensory evoked potentials (SSEPs) were recorded at C3 and C4 by stimulating the median nerve (stimulation: 15 mA) while lower SSEPs were recorded at Cz by stimulating the post tibial nerve (stimulation : 20 mA). SSEP used current stimulation, MEP used Voltage stimulation. The abnormal group was comprised of patients whose waveform amplitude was reduced by > 50% or the incubation period was delayed by > 1 ms. The normal group was comprised of individuals without intraoperative changes in the waveform or with changes in the waveform smaller than those in the criteria. The transfusion group was comprised of individuals who received intraoperative blood transfusions due to low hemoglobin levels [10]. Patients with postoperative neurological deficits were considered having a postoperative decrease in muscle strength [11].

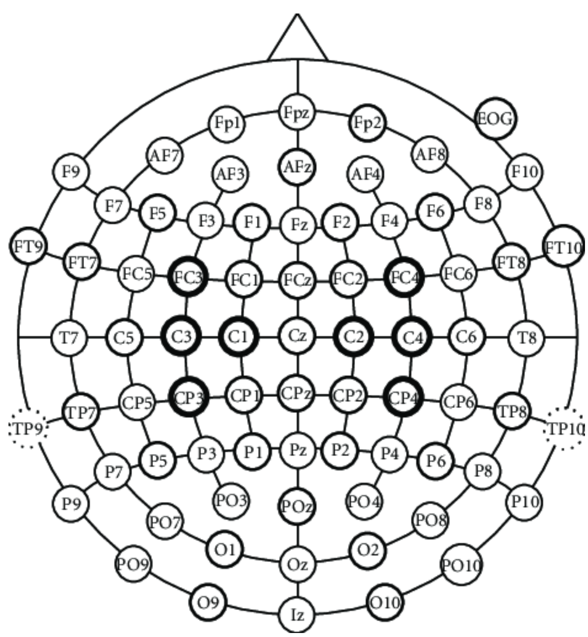

Figure 1. International 10-20 Electrode system

2.3 Statistical Analysis

The collected data were analyzed using Microsoft Excel 2010. Further, p and t values were compared using equal variances and two-variance t-tests. The average and standard deviation were calculated using technical statistics, and normal distribution was confirmed using the Shapiro–Wilk test. Further, the equivalence or bivariance was confirmed using the f test. The significance level for all statistics was set at a = 0.05 level.

3. RESULTS AND DISCUSSION

The characteristics of the overall patients are presented in Table 2. A total of 339 patients participated, with 243 women and 96 men. The average age of participants was 58.2, with cerebral aneurysm surgery accounting for the largest percentage of cerebrovascular surgery, followed by Byass(MCA-STA anastomosis) surgery. Cerebral aneurysm was most common in MCA, followed by Acom.

Table 2. Demographic characteristics of the participants

Demographic characteristics		Total No. (%)
	Participants	339
Sex	F	243
	M	96
Age		58.2 (± 9.9)
Surgery	Aneurysm clipping	330 (97.34)
	Bypass	14 (0.88)
	CEA	3 (0.88)
	AVM	3 (0.88)
Vessel	ICA	17 (5.01)
	MCA	200 (58.99)
	Acom	58 (17.10)
	Pcom	44 (7.37)
	ACA	25 (6.48)
	AchoA	22 (6.48)
	BA	1 (0.29)

*CEA: Carotid endarterectomy; AVM: arteriovenous malformation; ICA: internal carotid artery; MCA: Middle cerebral artery; Acom Anterior communicating artery; Pcom: Posterior communicating artery; AchoA: Anterior choroidal artery; BA: Basilar artery; ACA:

Table 3 is the hemoglobin of patients compared in this study. The difference between normal patients and patients with abnormalities during surgery can be clearly identified. P value was significant in the overall hemoglobin of surgery, postoperative hemoglobin, and subtraction of the highest and lowest hemoglobin.

Table 3. Comparison among the normal group, abnormal group, and postoperative deficit group

Variables	Normal	Abnormal	P-value	T-value
	Mean (± SD)			
Total hemoglobin (g/dL)	12.1 (1.2)	11.5 (1.5)	0.0003	3.689
PreOP hemoglobin (g/dL)	12.2 (1.1)	11.8 (1.3)	0.001	3.219
RBC transfusion (Pack, Unit)	1.9 (0.8)	3.1 (4.8)	0.002	-3.201
FFP transfusion (Pack, Unit)	3.5 (1.7)	4.6 (5.6)	0.024	-2.280
Blood loss (mL)	506.1 (326.6)	859.5 (1287.7)	0.007	-2.721
Max Hb-Min Hb (g/dL)	1.4 (1.0)	1.8 (1.7)	0.002	-3.081

Anesthesia Time (Hour: Min)	5:20	6:09	0.00009	-3.955
Propofol (μg/mL, MIN)	3.7 (0.4)	3.5(1.6)	5.236	9.088
Propofol (μg/mL, MAX)	4.1 (2.0)	4.0(2.0)	0.111	1.599
Remifentanil (μg/mL, MIN)	1.9 (0.9)	1.8(1.1)	4.004	5.603
Remifentanil (μg/mL, MAX)	3.2 (1.2)	3.0(1.6)	5.379	6.369

Variable	Normal	Post op neurologic deficit	P-value	T-value
	Mean (± SD)			
Total hemoglobin (g/dL)	12.1 (1.2)	11.4 (1.5)	0.013	2.513
PreOP hemoglobin (g/dL)	12.2 (1.1)	11.8 (1.42)	0.134	1.532
RBC transfusion (Pack, Unit)	1.9 (0.8)	5.7 (7.7)	0.010	-2.878
FFP transfusion (Pack, Unit)	3.5 (1.7)	7.2 (8.7)	0.040	-2.363
Blood loss (mL)	506.1 (326.6)	1634.4 (2313.9)	0.014	-2.594
Max Hb-Min Hb (g/dL)	1.4 (1.0)	2.1 (1.9)	0.003	-3.023
Anesthesia Time (Hour: Min)	5:20	7:14	1.585	-5.413
Propofol (μg/mL, MIN)	3.7(0.4)	3.5(0.4)	0.133	1.507
Propofol (μg/mL, MAX)	4.1(2.0)	4.1(1.9)	0.501	-0.674
Remifentanil (μg/mL, MIN)	1.9(0.9)	1.8(1.0)	0.763	0.302
Remifentanil (μg/mL, MAX)	3.2(1.2)	3.1(1.0)	0.541	-0.612

*MIN: minimum; MAX: maximum; RBC: Red blood cells; FFP: Fresh frozen plasma

Table 4 compared Transfusion groups with Non-transfusion groups. Significant statistical significance was expressed in anesthesia time, hemoglobin, blood loss, propofol dose. The number of IONM events also recorded a higher number of transfusions.

Compared with normal patients, those with abnormal IONM findings showed a decrease in the average hemoglobin level by 0.6 g/dL; moreover, this group had a higher proportion (by 16.4%) of patients with hemoglobin levels below 11.0 g/dL ($p < 0.05$). Compared with the normal group, the abnormal group had longer surgical time by 49 minutes, as well as greater difference in the bleeding volume, maximal thrombocyte level, and minimum hemoglobin level ($p < 0.05$). The abnormal group had lower blood pressure than the normal group. There was no significant between-group difference in the anesthesia and stimulation strength of the neuromonitoring test. A comparison between individuals with postoperative neurological deficits and normal individuals did not yield remarkable findings. There was no significant between-group difference in the preoperative hemoglobin and anesthesia time ($p > 0.05$).

Table 4. Comparison between the transfusion and non-transfusion groups

Variable	Transfusion	Non-transfusion	P-value	T-value
	Mean (± SD)			
Age (year)	58.3 (9.0)	58.9 (11.5)	0.564679	-0.576
Blood loss (mL)	410.4 (238.4)	1091.6 (1412.4)	0.000002	-4.978
Anesthesia Time (hour: min)	5:04 (112)	6:54 (2:19)	0.000000	-9.516
Hemoglobin (g/dL)	12.2 (1.2)	11.0 (1.5)	0.000000	7.187
MEP Stim (voltage)	289.1 (93.0)	275.3 (86.1)	0.350261	0.936
SSEP Stim (mA)	18.0 (2.7)	18.1 (2.7)	0.679541	-0.413
Propofol μg/mL, Mean)	3.8 (0.3)	3.3(0.8)	0.000000	5.997
Remifentanil (μg/mL, Mean)	2.4 (0.7)	2.4 (0.8)	0.631505	-0.480
IONM event	75 (51.4%)	64 (61.0%)		

*MEP: Motor evoked potential, SSEP: Somatosensory evoked potential, IONM: Intraoperative neuromonitoring

There were significant differences in the anesthetic dose, anesthesia time, bleeding, and hemoglobin levels between patients with and without blood transfusion ($p < 0.05$).

4. DISCUSSION

Our study showed that the decline of hemoglobin concentration during cerebrovascular surgery may impair brain function, which in turn may affect IONM. [12]. Hemoglobin is crucially involved in supplying oxygen to the entire human tissue [13,14]. Even if the oxygen supply is cut off for only five minutes, nonreversible damage can occur. When the brain suffers from ischemic damage, the amplitude of the IONM waveform can be reduced or an extension latency can be observed. This study has found a significant correlation between hemoglobin levels and abnormal neuromonitoring results ($p < 0.05$).

In many hospitals, intraoperative blood transfusions are performed to preserve the patient's vital signs. However, it is difficult to control hemoglobin decrease after onset and effectively prevent brain ischemia [15]. In this study, most patients who received blood transfusions did not show recovery compared with the preoperative state because the hemoglobin loss due to bleeding cannot be compensated by blood transfusion. The lower preoperative hemoglobin levels in the abnormal group are associated with a more sensitive response to bleeding-induced intraoperative hemoglobin loss [16]. The adequate range of intraoperative hemoglobin levels remains unclear. In our institution, blood transfusions are performed to patients with a hematocrit reduction ≥ 30% and a hemoglobin level < 10 g/dL [9]. Previous studies have reported that approximately 5.6%-27.2% of patients receive blood transfusions during brain aneurysm surgery [17]. In this study, 30.7% of patients received intraoperative blood transfusions. There seems to be a large deviation between performing transfusion or not depending on aneurysm rupture. In this study, none of the patients who received blood transfusions presented related side effects. In addition, the blood storage period could not be confirmed; therefore, its effect on hemoglobin could not be determined [18].

During intraoperative bleeding, blood leaks into the surrounding tissues with hemolysis occurring over time. Then, components that can cause vasospasm are created. To prevent vasospasm, large fluid amounts are injected, and the patient's blood pressure is increased reducing hemoglobin density and causing anemia [19]. In this study, most patients with postoperative neurologic deficits who present suspected vasospasm (slowed blood flow speed) have low hemoglobin levels ($P<0.05$).

Although extensive intraoperative bleeding could increase the anesthetic dose [20], there were no significant between-group differences in the anesthetic dose. However, the propofol dose was significantly higher in patients undergoing transfusion than those that were not ($p<0.05$). Propofol, which is generally the basic anesthetic of brain surgery anesthesia, exerts a calming effect on the autonomic nervous system and cerebral blood interactions, which adversely affects brain perfusion [21]. If the patient's brain perfusion is restricted by anesthetic agents, the patient's blood circulation can worsen, and medical interventions could be necessary. There is a need for future studies on this subject.

After surgery, 34 out of 145 patients in the abnormal group presented radiological abnormalities; among them, 16 patients had cerebral infarction. The hemoglobin levels and bleeding amount in patients with abnormal radiological findings differed from those in the normal group ($p < 0.05$). This finding confirmed the association of bleeding with postoperative radiological abnormalities [22-24]. A severe intraoperative bleeding can affect neuromonitoring and adversely affect surgical outcomes. Neuromonitoring examiners should be aware of the associations among hemoglobin levels, cerebral perfusion, and electrophysiological tests, as well as of the need to clearly distinguish them from other intraoperative factors.

5. CONCLUSION

In this study we demonstrate that a reduction in hemoglobin levels during cerebrovascular surgery can impair brain function, which may affect IONM. Moreover, intraoperative bleeding may negatively affect postoperative prognosis. Although blood transfusions cannot entirely prevent the bleeding-induced degradation of brain perfusion, they may produce better results in cases of severe intraoperative hemoglobin loss despite their side effects. If the patient's brain is not supplied with enough blood, brain tissue can deteriorate and, in severe cases, ischemic infarction may occur. Abnormal findings occur during IONM may indicate the disruption of the patient's brain perfusion and should prompt efforts to improve the patient's condition following the temporary suspension of the surgery, transfusion of blood, or administration of hypertensive agents. If we study with hemoglobin in the future, we will be able to improve the completeness of this study.

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