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The Effect of Cerebral Oxygen Saturation Changes on Early Postoperative Neuropsychological Function in Patients Undergoing Cranial Surgery

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ABSTRACT

AIM: To compare the incidence of postoperative neuropsychological dysfunction in patients managed with cerebral saturation monitoring versus traditional approaches.

MATERIAL and METHODS: A hundred patients undergoing elective intracranial surgery were divided into two groups to receive intraoperative management via cerebral saturation monitoring (Group O) or the conventional approach (Group C). The postoperative neuropsychological function was evaluated by the antisaccadic eye movement test (ASEM) and the Mini-Mental State Examination (MMSE). These tests were performed preoperatively and postoperatively on the first, second, and fifth days. The time for the modified Aldrete score to reach 9 (MAS 9), adverse effects, and pain using a Visual Analog Scale (VAS) scores were recorded.

RESULTS: Patient characteristics and surgery data were not statistically different. The MAS 9 of group O was significantly lower than that of group C ($p<0.001$). The MMSE at the postoperative 1, 2, and 5 days were significantly higher in Group O compared to Group C ($p<0.001$). ASEM was similar between groups. Group O was subdivided according to the type of surgery applied with diagnosis, and there were no statistically significant between-group differences in terms of areas under the curve for the cerebral regional oxygen saturation. There was no between-group difference regarding the mean arterial pressure at any time perioperatively. The heart rate at 80, 90, 100, and 110 min intraoperatively was significantly higher in group C than in Group O.

CONCLUSION: Intraoperative cerebral oxygenation monitoring can reduce patient mortality and morbidity by allowing early postoperative neurological evaluation to detect potential neurocognitive deficits.

KEYWORDS: Cerebral oxygenation, Postoperative cognitive dysfunction, Intracranial surgery

INTRODUCTION

Postoperative neuropsychological dysfunction is a common complication in patients undergoing intracranial surgery. Although the anesthetic techniques and undertaking intracranial surgeries have evolved over the years, postoperative neurologic and neuropsychological dysfunctions remain important causes of morbidity. The most significant changes in cerebral function include impaired attention and memory, depressed level of consciousness, and delayed recovery from anesthesia (11).

In intracranial surgery operations, monitoring the patient with the comprehensive parameters; It is important for early recognition of possible complications, taking precautions, intervention and planning for postoperative recovery. It is

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known that parameters such as peripheral oxygen saturation (SpO2), heart rate (HR), and mean arterial pressure (MAP) used during standard monitoring are not always sufficient to evaluated of patients. Tissue oxygenation has come to the fore studies conducted to overcome this deficiency in monitoring, and cerebral regional oxygen saturation (rSO_2) was started to be used in the surgical procedures. The values obtained by this method represent 75% venous, 20% arterial and 5% capillary compartment (5,13,20,24). Studies have reported that Near-infrared spectroscopy (NIRS) monitoring may determine decreased values in cerebral regional oxygen saturation in severe bleeding (22,23).

Postoperative cognitive dysfunction (POCD) is described as a reduction in many intellectual areas such as vigilance, understanding language, memory or mathematical function. A recent systematic cerebral oxygenation review showed only a weak association between severe intraoperative cerebral desaturation and POCD during non-cardiac surgery (17). This relationship was limited to certain surgeries. To our knowledge, there is no study indicating correlation between intraoperative cerebral oxygen desaturation and postoperative cognitive recovery, recovery from anesthesia in intracranial surgery. This study was aimed to compare cognitive dysfunction and anesthesia recovery in patients undergoing elective cranial surgery, managed according to traditional or cerebral saturation monitoring during the intraoperative period.

MATERIAL and METHODS

This single-center, prospective study was approved by Local Ethical Committee of Trakya University on 28 September 2016 (TUTF-BAEK 2016/225) and carried out on patients in the Trakya University Medical Faculty, from 2017 to 2020. The patients were informed about this study and written consents were gained (ClinicalTrials.gov Identifier: NCT03714347).

Participants

The power of the study was calculated as 94.2% with an alpha level of 0.1% based on the MAS-9 values of the groups by post-hoc power analysis. 100 adult patients who planned on having elective intracranial surgery under general anesthesia, aged 25-75, fluent in Turkish and at minimum primary school graduates were included in the study. Exclusion criteria were alcohol abuse, language or hearing disabilities, psychiatric disorders, severe hepatic or renal dysfunction, symptomatic carotid stenosis, patients with a GCS below 15, heart failure, renal failure, liver failure, congenital neurological deficits. The patients were divided into two groups based on the technique used for intraoperative management—using cerebral saturation monitoring in Group O (n=50), and the traditional approach in Group C (control group, n=50).

Anesthesia was induced intravenously with 1-2 $\mu g.kg^{-1}$ fentanyl, 2-3 $mg.kg^{-1}$ propofol and 0.6 $mg.kg^{-1}$ rocuronium. Anesthesia was maintained with a combination of remifentanil infusion (0.25 $mg.kg^{-1}$), and sevoflurane titrated to effect. Ventilation was controlled at a tidal volume of 8 ml/kg, the fraction of inspired oxygen at 50%, and the ventilatory rate adjusted to maintain partial pressure of CO_2 ($PaCO_2$) at 30–35 mmHg.

Study Design

In Group C, the global hemodynamic goals were identified and achieved by monitoring the MAP, hemoglobin, and oxygen values (venous and arterial). However, monitoring in Group O was based on cerebral rSO_2 value measured using the O3-RO® (Masimo Corporation, Irvine, CA, USA) throughout the surgical process. Two disposable sensors were bilaterally applied to the patient's forehead before anesthesia induction. The sensor consisted of two photodetectors (extracranial and intracranial) and one light source. The reflected infrared light was detected by the two detectors. The shallower extracranial detector measured the reflected light from superficial tissues, such as the extracerebellar tissue reflections, and considerable variations of pigmentation, while the intracranial detector measured the hemoglobin oxygen saturation in the frontal cerebral cortex at a depth of 20 mm (9). This technique uses an optical method based on reflecting light from chromophores, such as oxy and deoxyhemoglobin in the brain, as it passes through the brain, skin, and bone at near-infrared wavelength.

A rSO_2 value of <50% or a decrease of >20% from baseline during surgery was considered an indicator for treatment intervention. We used Denault's cerebral desaturation algorithm for the interventions (7). The first step in this algorithm was to check the position of the patient's head and neck, followed by increasing the MAP and controlling the systemic oxygenation. Other steps of the algorithm comprised normalizing $PaCO_2$ and hemoglobin levels, assessing cardiac function, and reducing cerebral metabolic oxygen rate.

Neuropsychological Assessment

The patient's cognitive function was evaluated by a researcher, who was blinded to the group allocation, before surgery and on postoperative days 1, 2, and 5. The neuropsychological status of each patient was evaluated using Mini-Mental State Examination (MMSE) and a simplified antisaccadic eye movement test (ASEM). Repeated tests were postponed until the narcotic pain medication was stopped (6,10,26)

The MMSE evaluates five domains—recall (3 points), orientation (10 points), attention and calculation (5 points), registration (3 points), and language (9 points) resulting in a maximum score of 30 points (10). An MMSE score of <23 was indicative of abnormal cognition (10).

We used the clinical protocol for ASEM defined by Currie et al. for this study (6). ASEMs are voluntary eye movements made in the opposite direction of a peripheral stimulus that appears suddenly, which requires the suppression of any reflexive eye movement toward the stimulus. In this test, the patient sits across from the examiner whose hands are placed on the patient's right and left visual areas equidistant from the midline. The examiner's index fingers are extended to test visual areas by confrontation. The stimulus is repeated by flexing one of the examiner's index fingers. The correct antisaccadic response was moving the eye to the side opposite that of the moving finger. A correction made toward the finger that was not moving or any first eye movement toward the finger moving along the midline was recorded as half accurate. The ASEM test is not suitable in the case of a dysfunction of the frontal eye regions in the prefrontal cortex (12,19,26); nevertheless, it is easy, reliable, cheap, and strongly correlated with the standard MMSE (3,6). The ASEM test was explained to all patients and practice tests were performed before the actual test was administered. Ten trials of the test were performed for each patient, and the percentage in the score was calculated using the formula: (The total number of correct responses/ total number of trials) × 100. The postoperative ASEM values were compared with baseline values (26).

The Modified Aldrete Score (MAS) was used to assess patients' recovery from anesthesia rated on a scale from 0 to 2. MAS was recorded every 3 min in the recovery unit; a patient having a MAS score of ≥9 was transferred to the clinic. The time for MAS to reach 9 was recorded.

Patients were assessed for pain with visual analogue scale (VAS) at 1, 2, and 4 hours postoperatively by an anesthesiologist who was not included in the study. Intravenous paracetamol (1000 mg) was given for analgesia when VAS scores were >4 in each two group within 4 h.

Statistical Analysis

The student's t test was used for comparison of normally distributed variables between groups, and Mann Whitney U test was used to compare variables that did not exhibit a normal distribution between groups. A paired t test was used to compare pre-post measurements within groups. The Chi-square test was used to compare categorical data. The area under the curve (rSO2 AUC) was calculated for each group according to the trapezoidal rule. The Kruskal Wallis test was used to compare the rSO_2 (AUC) area under the curve between subgroups. Statistical significance was accepted as p value less than 0.05.

RESULTS

One hundred patients were included in this study (Figure 1). The groups were similar with respect to gender, age, BMI, ASA scores, duration of surgery, duration of anesthesia and patient characteristics (Table I). The total amount of intraoperative remifentanil and postoperative tramadol consumption was statistically similar in both groups (Table II).

The MAS 9 was significantly lower in group O than in group C (p<0.001). The mean VAS score in the first 24 h postoperatively was significantly higher in Group O than in Group C (p<0.001) (Table II). Details of the side effects are presented in Table II. There were no differences with respect to shivering and agitation.

Table I: Surgical and Demographic Characteristics of the Patients

	Group O (n=50)	Group C (n=50)	p-value
Age (years)	54.2 ± 12.6	51.8 ± 13.9	0.377
BMI	26.6 ± 4.3	27.4 ± 4.7	0.351
Gender, F/M	22/28	24/26	0.688
ASA, I/II/III	29/21/10	27/23/	0.840
Duration of surgery (min)	149.6 ± 39.2	146.3 ± 34	0.505
Duration of anesthesia (min)	161.6 ± 34.5	157 ± 35.5	0.441
Diabetes mellitus, Yes	20 (40.0)	19 (38.0)	1.000
Hypertension, Yes	20 (40.0)	19 (38.0)	1.000
Level of education (>8 years)	17 (34.0)	12 (24.0)	0.378

Data are mean ± SD or number of patients. ***BMI:*** *Body mass index,* ***ASA:*** *American society of anesthesiology,* ***M:*** *Male,* ***F:*** *Female,* ***VAS:*** *Visual analog scale, MAS modified Aldrete score, *Statistically significant.*

Table II: Total Intraoperative Opioid Consumption, Postoperative Visual Analog Scale (VAS) Scores, and Side Effects

	Group O (n=50)	Group C (n=50)	p-value
Total Remifentanil consumption (mg)	48.6 ± 12.9	49.5 ± 12.9	0.720
Total Tramadol consumption (mg)	27.9 ± 7.5	29.3 ± 8.5	0.446
MAS 9 time (min)	14 ± 3.4	17.4 ± 2.5	**<0.001**
VAS (Average of 0-24 hours)	2.9 ± 0.6	1.8 ± 0.7	**<0.001**
Shivering, Yes	8 (16.0)	10 (20.0)	0.795
Agitation, Yes	8 (16.0)	12 (24.0)	0.453

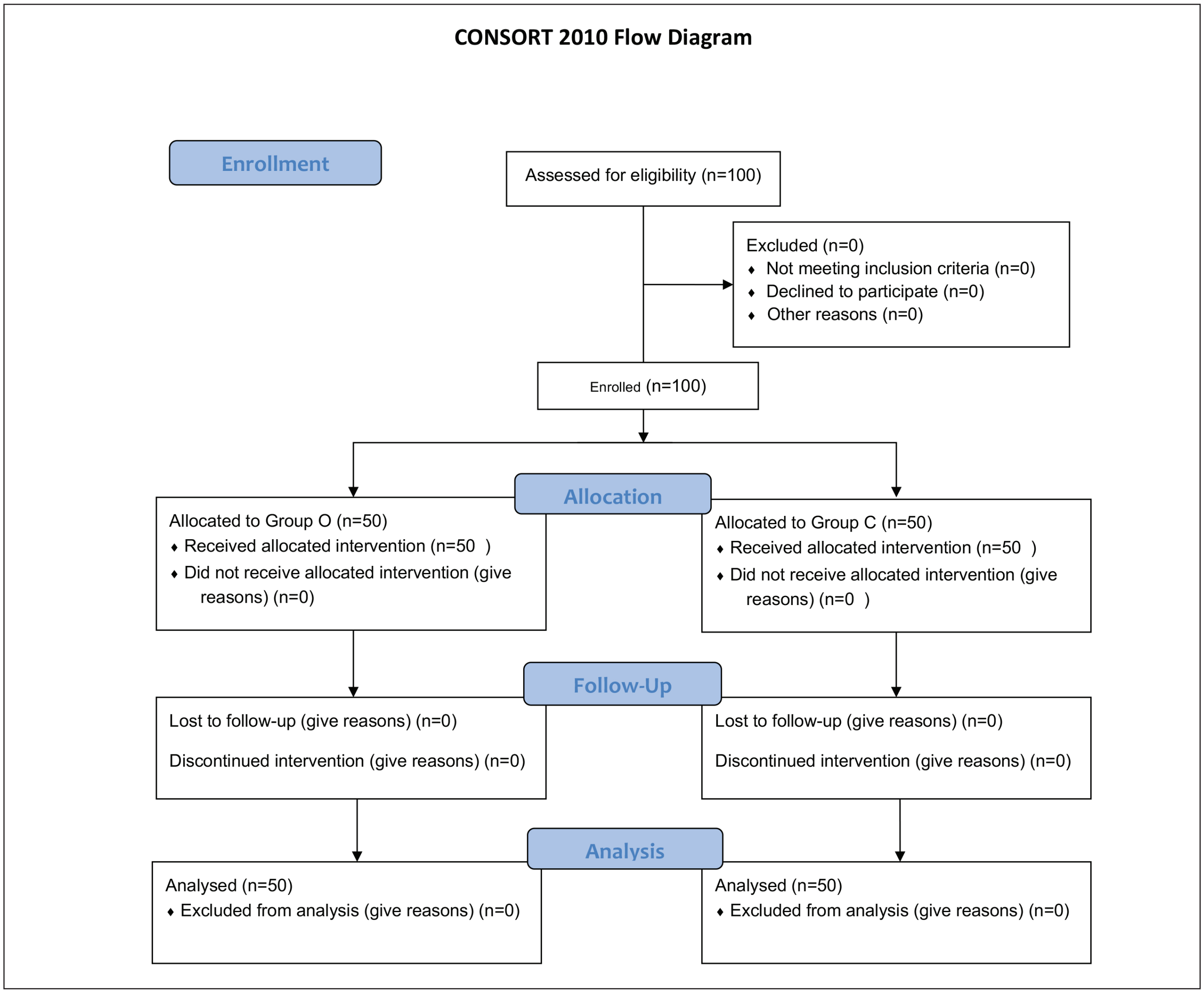

Figure 1: Flow diagram.

Moreover, there was no statistically significant between-group or within-group differences regarding the ASEM value measured on postoperative days 1, 2, and 5 compared to the preoperative values. When the preoperative MMSE was evaluated between the groups, there was no statistically significant difference (p=0.807). MMSE was significantly decreased at 1., 2. and 5 day compared to the preoperative values in group O and group C (p<0.001) (Table III). MMSE value at 1, 2, and 5 days postoperatively were significantly higher in Group O than in group C (p<0.001) (Table III).

Group O was divided into subgroups according to the type of surgery applied with diagnosis; Group O1: Pituitary, Group O2: Cranial mass, Group O3: Cerebellar mass, Group O4: Aneurysm. There was no significant difference between the subgroups in terms of areas under the curve of rSO_2 (Table IV, Figure 2).

The MMSE <23 incidence was not significantly different between the subgroups. However, MMSE <23 incidence at 1., 2. and 5 days postoperatively were significantly lower in Group O than in group C (Table V).

Lastly, when the two groups were compared in terms of preoperative, intraoperative, and postoperative MAP, there was no significant difference, but a general decrease in MAP was found. The HR at 80, 90, 100, and 110 min intraoperatively were significantly higher in Group C than in Group O; no statistically significant difference was found for other time points.

DISCUSSION

The present study suggested that better early postoperative neurological evaluations can provided by cerebral saturation monitoring than by conventional approach following intracra-

Table III: Summary of Neuropsychological Tests

	Group O (n=50)	Group C (n=50)	p-value
ASEM $_{preoperative}$	93.9 ± 8.8	92.6 ± 7.7	0.290
ASEM $_{1\ th\ day}$	92.8 ± 9.4	92.9 ± 7	0.740
ASEM $_{2\ th\ days}$	92.8 ± 9.1	93 ± 7	0.947
ASEM $_{5\ th\ days}$	92.6 ± 10.3	93 ± 7	0.628
p	0.774	0.194	
MMSE $_{preoperative}$	24.8 ± 1.5	25 ± 1.4	0.807
MMSE $_{1\ th\ day}$	22.9 ± 3.54	20.1 ± 2.7	**<0.001**
MMSE $_{2\ th\ days}$	23.2 ± 2.9	20.4 ± 2.5	**<0.001**
MMSE $_{5\ th\ days}$	23.4 ± 2.4	21 ± 2.3	**<0.001**
p	<0.001	<0.001	

***MMSE:** Mini-Mental State Examination, **ASEM:** Antisaccadic eye movement test.*

Table IV: Results for the Area Under the Curve (AUC) in Terms of rSO2 in Subgroups

	Group O_1 Pituitary (n=12)	Group O_2 Cranial mass (n=13)	Group O_3 Cerebellar mass (n=13)	Group O_4 Aneurysm (n=12)	P-value
rSO_2 (AUC)	9395 ± 840	9241 ± 1186	8865 ± 727	9182 ± 1140	0.518

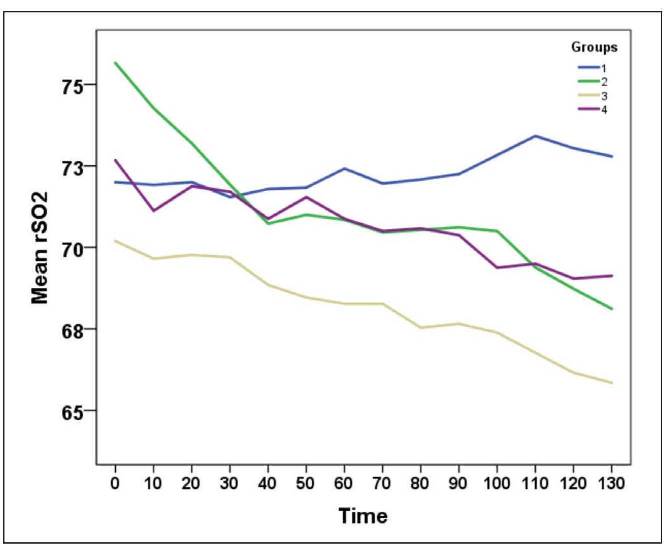

Figure 2: Comparing rSO_2 between subgroups.

Table V: Between-Group Comparison of the Incidence of Mini-Mental State Examination (MMSE) < 23

MMSE<23		Group O (n=50)	Group C (n=50)	p-value
1th	day	21 (42.0)	43(86.0)	**<0.001**
2nd	days	20 (40.0)	43(86.0)	**<0.001**
5th	days	19 (38.0)	41(82.0)	**<0.001**

nial surgery. In addition, MAS 9 of Group O was lower than the Group C at postoperatively.

Cerebral oxygenation monitoring can be used in diseases such as cardiac surgery (deep hypothermic circulation arrest, aortic arch surgery), carotid endarterectomy, head trauma and subarachnoid hemorrhage. However, data supporting the usefulness of intraoperative cerebral rSO_2 measurements are lacking for other types of surgery. It is reported that NIRS can effectively detect minimal changes before the intracranial pressure (ICP) varies in patients with delayed traumatic hematoma (11). Leal-Noval et al. described that rSO_2 was moderately accurate for identifying severe intracerebral hypoxemia but had low accuracy for detecting moderate intracerebral hypoxia (15). Therefore, regular intraoperative cerebral oxygenation monitoring can help prevent cerebral hypoxia and allow accurate early neurological evaluation by providing safe recovery from anesthesia after the surgery.

Yao et al. reported that cerebral oxygen desaturation (rSO_2 <40%) is associated with early period after surgery ASEM and MMSE impairments in patients undergoing cardiopulmonary bypass (26). Although the results of this study sufficiently supported monitoring and maintaining adequate cerebral oxygenation, it was not entirely clear whether the interventions aimed at maintaining adequate cerebral oxygenation during cardiac surgery have any bearing on the patient's cognitive outcomes. Similarly, Nollert et al. reported that neuropsychological deficits develop due to intraoperative cerebral hypoxia (18). In our study, we found that recovery from anesthesia and postoperative cognitive functions were better in the patient who were observed for cerebral oxygenation monitoring.

The recently systematic review, Yu et al. identified 15 randomized-controlled trials to assess the effect of perioperative NIRS monitoring on brain oxygenation in children and adults (27). They reported uncertainty regarding the impact of perioperative cerebral oxygenation monitoring with NIRS on postoperative death, cognitive dysfunction, or stroke since the evidence supporting the use of NIRS for decreasing the occurrence of mild short-term POCD is of low quality.

Computed tomography (CT) is the gold standard in the diagnosis and management of traumatic brain injury and intracranial hematoma. However, classifying these patients accurately is of great importance when CT is not available. Perioperatively, the operation table and recovery rooms are areas where rapid CT scans cannot be performed. In these circumstances, NIRS can be extremely helpful as it can detect the slightest change before any obvious change occurs in the ICP of patients with delayed traumatic hematoma, besides being portable and predictive of intracranial hematoma (4). Braun et al. showed that NIRS technology can also be used in penetrating and blunt traumatic brain injuries, emergency room conditions, and military medical rescue centers, i.e., in places where CT scan is not readily available (4).

Cerebral oxygenation monitoring has been generally applied in cardiovascular surgery in patients under anesthesia, but rarely intraoperatively in intracranial masses or other intracranial surgeries under anesthesia. Studies on cerebral oxygenation monitoring have been carried out in various intensive care followups of intracranial surgeries or neurology and neurosurgery services. An intraoperative decrease in brain oxygenation during intracranial surgery under anesthesia may adversely affect the patient's recovery from anesthesia by causing brain edema, which is indicative of detrimental outcomes. Additionally, neurologically deteriorating patients in recovery from anesthesia or during postoperative recovery may require an urgent CT scan and reoperation. Therefore, both patient mortality and morbidity can be reduced by predicting, preventing, and treating neurological deterioration with brain oxygenation followups.

Maintaining cerebral tissue oxygenation is the primary goal while administering anesthesia since brain ischemia or hypoxia is the chief cause of brain damage requiring immediate restoration of perioperative cerebral perfusion and monitoring (11). Since many neurological damages are preventable, detecting harmful intracerebral events timely and while they are manageable is extremely important during brain surgery to improve postoperative neurological outcomes. In this regard, intraoperative cerebral saturation monitoring may be crucial in allowing early postoperative recovery and reducing complications. Intracranial hematomas that develop in the early postoperative period are important curable causes of secondary brain injury in patients with head trauma. Early detection and treatment of these lesions can improve neurological outcomes (11).

Furthermore, postoperative cognitive impairment is an important factor affecting the patient's quality of life and health economics. While the cerebral rSO_2 is preserved in patients undergoing minor surgery, such as appendectomy and mastectomy, it is reported to decrease in operations involving body positioning procedures, such as anti-Trendelenburg used for laparoscopic and shoulder surgeries. Many times, cerebral desaturation occurring after any noncardiac surgery has been associated with increased formation of POCD (17). However, to the best of our knowledge, there is a dearth of literature regarding the evaluation of recovery between intraoperative and postoperative cerebral rSO_2 values in intracranial surgery.

In our study, postoperative neuropsychological dysfunction was defined with MMSE and ASEM tests. Although MMSE and ASEM are not a part of the standard neurocognitive testing sequence for the assessment of neurocognitive function, these tests were used because of the ease of conducting them at the bedside in common clinical practice. The ASEM test is a practical measure for evaluating high cortical functions in terms of deliberate eye movements in the opposite direction of a sudden environmental stimulus (16,26). In addition to generating excitatory and inhibitory oculomotor signals, it also invokes the use of representative memory of what the target means, rather than using direct stimulation. Therefore, ASEM seems to be appropriate to confirm the effects of deoxygenation. Impaired ability to perform the test is associated with lesions involving both the basal ganglia and frontal cortex as it is expected to involve the corticotectal pathways originating from the prefrontal cortex, including the frontal eye areas (12,16,21,26). MMSE, however, is a screening test that quantitatively evaluates cognitive function. In this study, the MMSE was preferred because of its ease and brevity of application both pre and postoperatively. Many studies have used the MMSE to assess cognitive function after general anesthesia (25,26). Anthony et al. reported that the MMSE was 82% specific and 87% sensitive for detecting dementia and delirium (2). Andropoulos et al. and Kussmann et al. had supported the use of NIRS monitoring to reduce long-term cognitive deficits after cardiac surgery (1,14). In our study, the fact that there was no significant difference between the two groups regarding the pre and postoperative ASEM values may be significant in terms of eliminating pathology-induced cognitive damage. Moreover, there was no statistically significant difference between the subgroups (pituitary, cranial mass, cerebellar mass, and aneurysm) in terms of AUC of rSO_2 and MMSE <23 incidences. However, the incidence of MMSE <23 on postoperative days 1, 2, and 5 was significantly lower in Group O than in Group C.

Although surgical resection is the gold standard for treating meningiomas, the risk of postoperative deficits is uncertain. Ehresman et al. found that there was a 3.4% incidence of new cognitive deficit after meningioma resections (8). This incidence increased to 7.2% in operations where the tumor was removed from the anterior skull base. The factors independently associated with postoperative cognitive impairment were history of stents/coronary artery bypass grafting (CABG) and age. However, there was no preoperative evaluation of neurocognitive function in this study. Nevertheless, knowledge of these risk factors may allow surgeons to better inform patients about the risk of deficits and adjust their strategies to minimize postoperative neurological deficits (8). Accordingly, due consideration of the factors associated with deficits that occur after intracranial surgery can guide treatment strategies with specific monitoring to be applied perioperatively. Cerebral oxygen monitoring can be an important tool in this regard.

There were no serious adverse effects observed in either group during or after the intracranial surgery in our study. Shivering and agitation postoperatively were alike between the two groups. Both groups were clinically similar with respect to MAP. However, the HR was significantly higher in Group C than in Group O and there was a general increase in HR. Moreover, the average VAS score during the first 24-h postoperatively was significantly higher in Group O than in Group C, which may be attributed to an early onset of awareness.

There were some limitations in the study. First, cerebral saturation monitoring was not used "blindly" in the groups. Second, we did not follow cerebral oxygenation postoperatively.

CONCLUSION

In conclusion, intraoperative cerebral oxygenation monitoring allows for effective early postoperative neurological evaluation and outcomes. Additionally, it can be said that intraoperative cerebral oxygenation monitoring can reduce mortality and morbidity by offering an early indication of potential postoperative neurological and neurocognitive function deficits in patients undergoing intracranial surgery.

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AUTHORSHIP CONTRIBUTION

Study conception and design: SHS, EC, ED

Data collection: SHS, EC, ED, BT, FS

Analysis and interpretation of results: SHS, NS, GS, AC

Draft manuscript preparation: SHS, EC, ED, AC

Critical revision of the article: SHS, EC, ED, BT

All authors (SHS, EC, ED, BT, NS, AC, GS, FS) reviewed the results and approved the final version of the manuscript.

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