Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2021;46(4):1614-1623
DOI: 10.17826/cumj.986099

ARAŞTIRMA / RESEARCH

Changes in cerebral oxygenation and cognitive functions during controlled hypotension

Kontrollü hipotansiyon sırasında serebral oksijenasyon ve kognitif fonksiyonlarda meydana gelen değişiklikler

Bengü G. Aydın[1], Gamze Küçükosman[1], Özcan Pişkin[1], Necla Gülçek[2], Rahşan D. Okay[1], Hilal Ayoğlu[1]

[1]Bülent Ecevit University Faculty of Medicine, Department of Anesthesiology and Reanimation, Zonguldak, Turkey
[2]Midyat State Hospital, Clinic of Anesthesiology and Reanimation, Mardin, Turkey

Cukurova Medical Journal 2021;46(4):1614-1623

Abstract

Purpose: This study aimed to evaluate the effect of controlled hypotension on cerebral oxygen saturation and postoperative cognitive dysfunction (POCD) in patients undergoing nasal surgery.
Materials and Methods: Forty patients were randomized by a sealed envelope method into two drug groups: esmolol (Group E, n=20) or nitroglycerin (Group N, n=20) administration prior to surgical incision. The cognitive functions of the patients were evaluated by the Mini-Mental State Examination Test 1 day before and 1 day after the operation. Regional oxygen saturation was monitored with near-infrared spectroscopy to detect cerebral desaturation.
Results: The desired mean arterial blood pressure (50-65 mmHg) could be achieved in all groups. A decline in cognitive function occured in 16 patients (40%) at the 24th postoperative hour. There was no statistically significant difference between the groups in terms of POCD. There was a significant relationship between POCD and cerebral desaturation status.
Conclusion: Cerebral desaturation seen during hypotensive anesthesia may cause early POCD development, therefore we think that close cerebral and hemodynamic monitoring during hypotensive anesthesia may preserve cognitive functions.
Keywords:. Hypotensive anesthesia, cerebral oxygenation, cognitive function, esmolol, nitroglycerine

Öz

Amaç: Bu çalışmada, nazal cerrahi geçiren hastalarda uygulanan kontrollü hipotansiyonun serebral oksijen satürasyonu ve postoperatif kognitif disfonksiyon (POKD) üzerindeki etkisinin değerlendirmesi amaçlandı.
Gereç ve Yöntem: Kırk hasta kapalı zarf yöntemi ile esmolol (Grup E, n=20) ve nitrogliserin (Grup N, n=20) olmak üzere iki gruba ayrıldı. Hastaların kognitif fonksiyonları operasyondan 1 gün önce ve 1 gün sonra Mini Mental Durum Testi ile değerlendirildi. Serebral desatürasyonu saptamak için rejyonel serebral oksijen satürasyonu yakın kızılötesi spektroskopi ile izlendi.
Bulgular: Tüm gruplarda istenilen ortalama arteriyel kan basıncına (50-65 mmHg) ulaşıldı. Postoperatif 24. saatte 16 hastada (%40) kognitif fonksiyonlarda azalma meydana geldi. Postoperatif kognitif disfonksiyon açısından gruplar arasında istatistiksel olarak anlamlı fark yoktu. Postoperatif kognitif disfonksiyon ile serebral desatürasyon arasında anlamlı bir ilişki olduğu görüldü.
Sonuç: Hipotansif anestezi sırasında görülen serebral desatürasyon erken POKD gelişimine neden olabilmektedir, bu nedenle hipotansif anestezi sırasında yakın serebral ve hemodinamik monitorizasyon ile kognitif fonksiyonların korunabileceğini düşünmekteyiz.

Anahtar kelimeler: Hipotansif anestezi, serebral oksijenasyon, kognitif fonksiyon, esmolol, nitrogliserin

Yazışma Adresi/Address for Correspondence: Dr. Bengü G. Aydın, Bülent Ecevit University Faculty of Medicine, Department of Anesthesiology and Reanimation, Zonguldak, Turkey E-mail: bengukoksal@gmail.com
Geliş tarihi/Received: 23.08.2021 Kabul tarihi/Accepted: 22.10.2021 Çevrimiçi yayın/Published online: 21.11.2021

INTRODUCTION

Controlled hypotension, known as a hypotensive anesthesia procedure is the conscious and reversible reduction of arterial blood pressure to about 30-40% below its normal value, to at least 50-65 mmHg of mean arterial blood pressure (MAP) or as a reduction of the systolic blood pressure to 80–90mm Hg[1,2]. As the access to the nasal region in nasal surgeries is mainly from the nostrils and limited, not many surgical techniques can be used to control bleeding, and thus, applying controlled hypotension is an alternative method for reducing bleeding.

Although hypotensive anesthesia is an effective method, it is accompanied by the risk of reduced perfusion in vital organs, especially the brain. This may bring about potential complications such as permanent cerebral injury, delayed reanimation, cerebral thrombosis, brain ischemia and death[3,4]. Thus balancing surgical visibility with organ perfusion remains a difficulty[5-7].

Cerebral circulation has an autoregulation depending on the brain blood flow, oxygen and carbon dioxide concentration in the arterial blood and body temperature. In normal individuals, as the mean arterial pressure is in the range of 60-160 mmHg, the brain blood flow remains almost constant. If MAP decreases further, the brain blood flow is reduced. Decreased cerebral blood flow or advanced hypoxemia leads to a reduction in cerebral oxygen distribution. The duration and severity of the reduction in cerebral perfusion pressure may cause permanent neurological damage if it falls below critical values[8]. It is argued that intraoperative cerebral ischemia and cerebral oxygen desaturation are possible mechanisms for postoperative cognitive dysfunction[9,10].

Postoperative cognitive dysfunction (POCD) is a condition that emerges weeks or months after surgery and is generally characterized by short-term disorders in patients' memory, executive functions such as information perception and management, personality and sleep habits[11].

For cerebral autoregulation, changes observed in the cerebral blood flow by using methods such as middle cerebral artery Doppler or near-infrared spectroscopy (NIRS) are associated with changes in MAP, and this way, it is possible to determine the lower limit of autoregulation under the optimal cerebral perfusion pressure[12]. Regional cerebral saturation (rSO2) is measured by NIRS and prevalently utilized as it is not invasive and allows real-time and continuous monitoring of the cerebral tissue oxygen supply-demand balance. Cerebral oxygenation may change during various intraoperative factors such as ischemia, hypotension, hypovolemia, hemorrhage, shock or body position caused by surgical maneuvers, and for this reason, the clinician should consider NIRS monitorization to improve clinical outcomes especially in high-risk patients[13].

Many drugs are used to apply controlled hypotension. These agents need to have a short initial period, a fast-disappearing effect after the implementation ends and negligible influence on vital organs. Esmolol and nitroglycerin are agents that are frequently used for this purpose[14].

Our hypothesis is that brain perfusion may be affected during controlled hypotension, and as a result, postoperative cognitive function may be impaired. This prospective randomized study aimed to evaluate the effect of controlled hypotension on cerebral oxygen saturation and POCD in patients undergoing nasal surgery.

MATERIALS AND METHODS

Study group

The study (ClinicalTrials.gov: NCT04948957) was designed as prospective and observational and was conducted in Zonguldak Bulent Ecevit University Hospital, after its approval by the Local Ethics Committee (Zonguldak Bulent Ecevit University Clinic Research Ethics Committee, Meeting Protocol No. 2013-81-03/09) and written informed consents. Patients with ASA physical status of I–II, aged 18–65 years, required controlled hypotension scheduled for nasal surgeries from March 2014 to January 2016 were enrolled in this study. Age under 18 or above 65, ASA > II, coagulation disorders, history of cardiovascular and cerebrovascular disease, poor blood pressure control, anemia, pregnancy, addiction to opioids, body mass index (BMI) > 35, intraoperative systolic blood pressure < 65 mmHg, surgical duration less than 30 minutes or more than 160 minutes, need for an intraoperative sympathomimetic drug and the use of other hypotensive drugs, preoperative Mini-Mental State Examination (MMSE) score of 23 or less were excluded from the study.

Procedure

Upon arrival to the operating room, all cases received standard monitoring; Electrocardiogram, non-invasive blood pressure, heart rate (HR), peripheral oxygen saturation (SpO_2) and end-tidal carbon dioxide ($EtCO_2$) monitoring. Additionally, after Allen test from the non-dominant radial artery, arterial canulation was placed, and invasive arterial pressure monitoring was applied. Two near-infrared spectroscopy sensors connected to a regional oximetry system (O3™, Masimo, Irvine, CA) were placed on the patient's forehead to provide continuous measurement of regional oxygen saturation and intraoperative decreases in rSO_2 of 20% or greater were defined as cerebral desaturation. A bispectral index (BIS) sensor (Aspect Medical Systems, Newton, MA, USA) was connected to a monitor (BIS Vista™) for monitoring the depth of anesthesia. Intraoperative BIS values were targeted at 40-60. After preoxygenation, anesthesia was induced with propofol (2 mg/kg), lidocaine (1 mg/kg), fentanyl (1 mcg/kg), and rocuronium (0.6 mg/kg). After intubation, so that BIS would be 40-60, 50% O_2- 50% N_2O 1 MAC desflurane was used to start mechanical ventilation (6mL/kg tidal volume, 10 to 12 breaths/min, and 32 to 35mmHg $EtCO_2$). All patients were positioned in an approximately 30degree reverse Trendelenburg's position. The nasal mucosa was infiltrated with local anesthetic with epinephrine (1:100000, 0.0125mg/ml) mixture by the surgeon in all patients.

Forty patients were randomized into two drug groups as esmolol (Group E, n=20) or nitroglycerin (Group N, n=20) by sealed and opaque envelopes which were prepared using a computer program. Research assistant who was not included in the outcome evaluation was responsible for opening the envelope and preparing the study drug. The anesthesiologist administering the anesthesia and collecting the data were blinded to the study group allocation.

Drugs were administered before surgical incision. An infusion for Group E was continued with a bolus dose of esmolol by 500 µg/kg over 1 min and maintained at 50-300 µg/kg/min[1]; For group N, a titration of nitroglycerin at 0.5-2 µg/kg/min was administered. All infusions were titrated to maintain a MAP between 50 and 65 mmHg and discontinued at the end of the surgical procedure. Neuromuscular block was antagonized with neostigmine and atropine. Patients were extubated when they were able to maintain sufficient spontaneous breathing and their laryngeal reflexes fully returned.

Neurological assessment

Neurocognitive testing was performed preoperatively and postoperatively in all patients using the MMSE test. The MMSE test is the most common test for screening dementia developed by Folstein et al.[15] in 1975. Orientation, memory, attention, calculation, recall, language, motor function; and perception are tested. It is evaluated out of 30 points. Twenty-four to thirty points are normal, 18 to 23 points are mild dementia, and lower than 17 points are consistent with severe dementia. MMSE is valid and reliable in the diagnosis of mild dementia in the Turkish population by selecting the ideal threshold value of 23/24 [16]. All patients were awake during the MMSE evaluation. The cognitive functions of the patients were evaluated by the MMSE Test 1 day before and 1 day after the operation. The maximum score of the test is 30 points. If the MMSE value decreases by 2 points from the initial value, it is considered as a decline in cognitive function.

The surgical field was evaluated by a blinded same surgeon, using a 6-point category scale [17,18]. For the optimal surgical statuses, the ideal category scale was defined as ≤ 2. In our study, more than a 20% decrease in rSO_2 from the baseline was considered as significant change. When cerebral desaturation occurred, primarily the ventilator, anesthesia circuit and head position were checked. FiO_2 was increased, $EtCO_2$ was kept on the upper level of the normal range, and if there was no improvement, drugs for controlled hypotension were gradually reduced, fluid replacement was performed, and ephedrine was applied.

Statistical analysis

The approximate sample size was calculated before the study using the Power Analysis & Sample Size-11 software (NCSS statistical software, Kaysville, Utah, USA). In the sample size analysis performed with reference to 95% confidence interval and 80% power on the rSO_2 value (group 1: 81.49±9.5, group 2: 76.69±9.4), the minimum number of patients to be reached was found to be totally 33[5]. Considering a 15-20% attrition rate, the required sample size was determined to be 40. The data were analyzed by using IBM SPSS V23. Compliance with normal distribution was examined by Shapiro-Wilk test. In the comparison of the parameters based on the groups, independent-samples t-test for the normally distributed data and Mann-Whitney U test for the non-normally distributed data were used. In comparison of more than two time-dependent changes, repeated-measured analysis of variance (ANOVA) was used for the normally distributed data, while Friedman test was used for the non-normally distributed data. Chi-squared test and Fisher's Exact test were used to compare the categorical variables based on the groups. The analysis results are presented as mean ± SD and median (minimum - maximum) for the quantitative data and frequency (percentage) for the categorical data. $p<0.050$ was accepted as statistically significant.

RESULTS

A total of 40 patients were included and analysed in the study (Figure1). The demographic and surgical datas and BIS values of the patients in Groups E and N were found to be similar (Table 1).

Table 1. Demographic and clinical data of patients

	Group E (n:20)	Group N (n:20)	p
Age (year)	33.2 ± 12	36 ± 15,2	0.521
Gender (F/M, n)	11/9	7/13	0.204
Weight (kg)	72.70±13.39	75.65±12.99	0.67
Surgery time (min)	130.75±17.03	129±13.03	0.686
Anesthesia time (min)	139.25±13.59	134±10.71	0.237
BIS value	42.05±9.59	46.05±9.90	0.659
ASA (I/II)	18/2	16/4	0.661

Data are given as n or mean±SD, F/M: Female/Male, min:minute, BIS: Bispectral index score ASA: American Society of Anesthesiologists

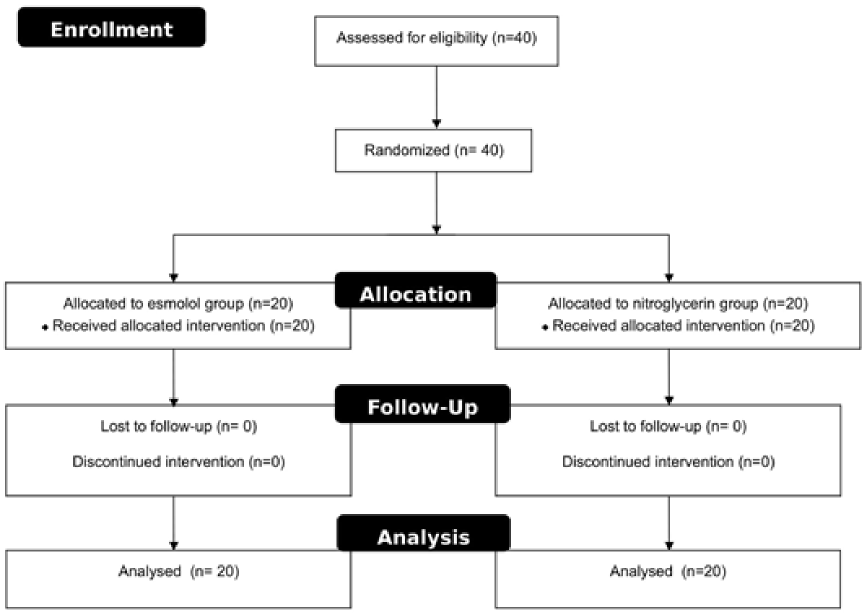

Figure 1. Trial flow diagram

There was a significant difference between the median values of the MAP parameter measured at the 10th minute based on the groups ($p=0.001$). The median value of Group N was smaller than that of Group E. There was no significant difference in the distributions of the MAP parameters measured at other times based on the groups ($p>0.05$). There were significant differences in the median values of the MAP parameters in Group E and Group N measured at different times ($p<0.001$) (Table 2).

Table 2. Intergroup and intragroup comparison of the MAP parameter

Time (min)	Group E (n:20)	Group N (n:20)	p
Control	98.5 (76 - 165)^{a}	96 (67 - 129)^{c}	0.607
10	69 (50 - 143)^{ac}	61 (50 - 69)^{b}	0.001
20	60.5 (52 - 76)^{bc}	60 (52 - 82)^{ba}	0.734
30	63.5 (46 - 72)^{bc}	63.5 (54 - 70)^{ba}	0.745
45	57.5 (45 - 70)^{b}	62.5 (51 - 70)^{ba}	0.136
60	59 (50 - 71)^{b}	62 (50 - 69)^{ba}	0.083
90	62 (50 - 71)^{bc}	62 (48 - 70)^{ba}	0.871
120	61.5 (50 - 84)^{bc}	60 (50 - 68)^{b}	0.349
p	<0.001	<0.001	

Datas are presened as median (minumum-maximum), a-c: No statistically significant difference between times with the same superscript letter

There was a significant difference between the groups in terms of the median values of the HR parameter measured at the 30th minute ($p= 0.029$). The median value of Group N was higher than that of Group E. There was no significant difference between the groups in the distributions of the HR parameter measured at other times ($p>0.050$). There were significant differences in the median values of the HR parameters in Group E and Group N measured at different times ($p<0.001$) (Table 3).

Table 3. Intergroup and intragroup comparison of the HR parameter

Time (min)	Group E (n:20)	Group N (n:20)	p
Control	89 (60 - 114)^{a}	77 (55 - 118)^{ad}	0.093
10	76.5 (50 - 106)^{ab}	77 (52 - 116)^{ad}	0.756
20	67.5 (50 - 92)^{b}	69 (51 - 113)^{bcd}	0.542
30	63.5(51 - 77)^{b}	69.5 (54 - 102)^{bcd}	0.029
45	64.5 (51 - 75)^{b}	64.5 (53 - 98)^{bc}	0.903
60	66.5 (52 - 80)^{b}	64.5 (48 - 93)^{c}	0.818
90	65.5 (50 - 78)^{b}	70.5 (52 - 95)^{bcd}	0.151
120	70 (55 - 89)^{b}	72.5 (52 - 98)^{bcd}	0.233
p	<0.001	<0.001	

Datas are presened as median (minumum-maximum), a-d: No statistically significant difference between times with the same superscript letter

The changes in the NIRS right/left results are shown in Figure 2. The cerebral desaturation had a decrease of 21-29% in Group N and 20-25% in Group E. The mean arterial pressure at the highest amount of decrease in comparison to the basal NIRS value (29%) was 49 mmHg and observed in Group N. Cerebral desaturation was observed in 3 patients in group E and 6 patients in group N. There was no significant difference between the groups in terms of their desaturation distributions ($p>0.05$). The mean desaturation duration was 43.11±6.23 seconds. There was no statistically significant difference between the groups in terms of their mean MMSE scores measured preoperatively and at the 24th postoperative hour ($p>0.050$). There were significant differences in the mean MMSE scores in Groups E and N measured at different times ($p<0.001$) (Table 4). A decline in cognitive function occurred in 16 patients (40%) at the 24th postoperative hour. While POCD was observed in 9 patients in Group N and 7 patients in Group E, there was no statistically significant difference between the groups ($p>0.05$).

There was a significant relationship between POCD and cerebral desaturation status ($p<0.001$). Among those with POCD, 81.3% had cerebral desaturation (Table 5).

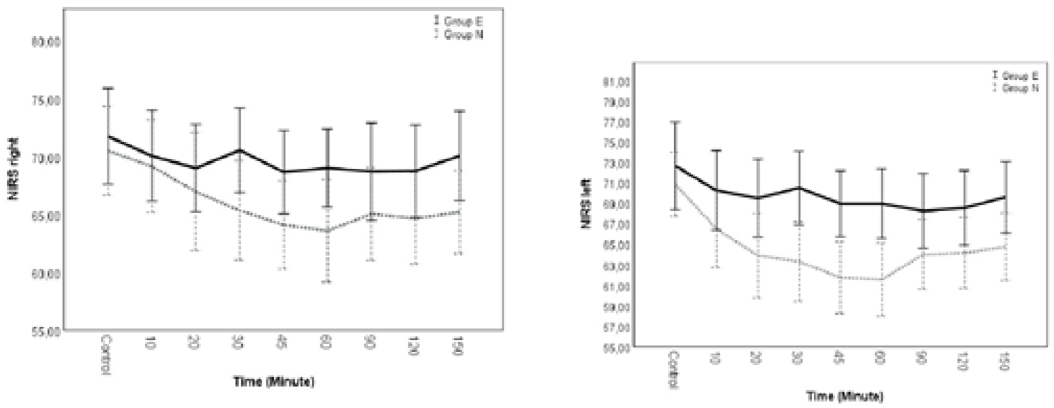

Figure 2. Changes in right/left NIRS

Table 4. Intergroup and intragroup comparison of the MMSE scores

Time	Group E (n:20)	Group N (n:20)	Total	p
Preoperative	28.3 ± 2^a	28.6 ± 1.9^a	28.4 ± 1.9	0.684
Postoperative 24th h	26.8 ± 2.6^b	25.9 ± 2^b	26.3 ± 2.3	0.202
p	<0.001	<0.001		

Data are presented as mean ± SD, a-b: No significant difference between the times with the same superscript letter.

Table 5. Relationship between POCD and cerebral desaturation

Desaturation	POCD -	POCD +	Total	p
No	23 (95.8%)	3 (18.8%)	26 (65%)	0.018*
Yes	1 (4.2)	13 (81.3%)	14 (35%)	

POCD: Postoperative cognitive dysfunction

There was no significant difference between the groups based on their mean SpO_2 and $EtCO_2$ parameters measured at different times ($p>0.05$). There was also no significant difference between the SPO_2 and $EtCO_2$ parameters measured at different times in Groups N and E ($p>0.05$). When surgical site bleeding in the hypotensive period was examined, no significant difference was found between the groups. ($p>0.05$). The 6-point category scale was ≤ 2 at all-time in both groups.

DISCUSSION

This study examined the effects of hypotensive anesthesia on cerebral oxygenation and POCD. The targeted mean arterial pressures were obtained and it was determined that patients with cerebral desaturation had significantly more POCD during hypotensive anesthesia.

One of the most important goals in the perioperative period is to maintain sufficient cerebral perfusion. It was reported that, if MAP falls below 50 mmHg, ischemia may develop. In addition to this, as there are several definitions of "hypotension" in the literature, it is difficult to define a sufficient MAP value [19]. Ha TN. et al. [20] investigated the effect of blood pressure and cardiac output on surgical site quality and middle cerebral blood flow during endoscopic sinus surgery and stated that moderate hypotension provided a better view of the surgical field but keeping MAP below 60 mmHg may increase the risk of cerebral hypoperfusion. In our study, MAP was maintained between 50-65.

Various agents are used in application of controlled hypotension. Nitroglycerin is a nonspecific agent that does not have a toxic metabolite which has a direct vasodilator effect on venous capacitance blood vessels. It causes a reduction in venous return and cardiac output, as well as tachycardia[14]. Cottrell et al. [21] stated that the intracranial pressure increase seen as a result of controlled hypotension with nitroglycerin is connected to dilatation of capacitance vessels followed by an increase in the cerebral blood volume. In contrast, Sulz et al.[22] measured the effects of nitroglycerin which is an exogenous nitric oxide source on right middle cerebral arterial blood flow rate and general blood flow. Their study showed that vasodilatation occurred in the right middle cerebral artery as a response to exogenous nitric oxide. Moreover, they reported that the brain blood flow generally remained unchanged as the blood flow rate also decreased. In another controlled hypotension study where nitroglycerin and labetalol were compared, in the group that was applied nitroglycerin, among the tissue perfusion marker values, the perfusion index was higher, and the serum lactate levels were lower [23]. Esmolol is a short acting β1-adrenoceptor that lowers cardiac output by reducing the heart rate. It causes a reduction in arterial pressure by lowering the serum renin activity and catecholamine levels[5]. A study where esmolol was used to stabilize the hemodynamic changes occurring during electroconvulsive treatment reported that the blood flow rate in the middle cerebral artery was not affected by the use of esmolol [24]. Heinke et al.[25] revealed the effect of the drug by the method of blood-oxygen-level-dependent functional magnetic resonance imaging. As a result, they demonstrated that cerebral blood flow and cerebral vasoreactivity remained unchanged during moderate blockage and did not intervene with cognitive processing in volunteers who were awake in their study on the effects of esmolol on cerebral blood flow, cerebral vasoreactivity and cognitive performance. In our study, controlled hypotension was achieved with esmolol and nitroglycerin, and cerebral desaturation was observed between 20-29%. Although there was no significant difference between the two groups, the incidence of cerebral desaturation was less in the esmolol group.

To make a diagnosis of POCD, first of all, one needs to have information on the preoperative cognitive function of the patient. Identification of POCD is confirmed through comparison of cognitive statuses as a result of basic cognitive performance tests conducted before and after the surgery[26]. In our study, we applied the MMSE test 1 day before preoperatively and 1 day after postoperatively.

The incidence of POCD may differ based on the patient group that is studied, the definition of POCD that is used, the tests that are used to make a diagnosis and statistically analyze the results and the timing of the tests[27]. Monk et al.[28] documented the incidence of POCD at discharge from the hospital among patients that undergone major noncardiac surgery as 36.6% in patients at the ages of 18-39, 30.4% in patients at the ages of 40-59 and 41.1% in patients at the age of 60 or older. They determined that, after three months, the POCD still continued in 12.7% of the patients at or over the age of 60. Their study used the Beck Depression Inventory, MMSE and State-Trait Anxiety Inventory tests. In a study where controlled hypotension (MAP 50-60 mmHg) was provided with propofol and remifentanil infusion, a decrease in cognitive function was observed in 46% of patients as a result of MMSE scoring[29]. In the study of Niazi et al. [30] that included patients at the ages of 21-50 who had septoplasty operations, after hypotension (MAP 50-60 mmHg) induced by increasing isoflurane minimum alveolar concentration, there was a significant decrease in comparison to the group followed as normotensive in the MMSE scores measured at the postoperative 30th minute, 60th minute and 24th hour. The incidence of POCD in the postoperative 24th hour in the hypotensive group was found as 6.6%. POCD was not observed in any patient in the normotensive patient group. A study using esmolol and remifentanil to induce controlled hypotension applied MMSE in the 30th preoperative minute, 30th postoperative minute, 60th postoperative minute and 24th postoperative hour. When the MMSE results in the preoperative 30th minute and postoperative 30th minute were compared, it was determined that POCD developed in one patient in the esmolol group and four patients in the remifentanil group. It was reported that remifentanil and esmolol provided similar operational conditions in tympanoplasty, and their effects on cognitive functions in the postoperative short term were similar [31]. Choi et al.[7] compared the effect of nitroglycerin and nicardipine for inducing hypotension on patients undergoing orthognathic surgery. It was concluded that no patient was observed to develop POCD as a result of mini mental test conducted after one postoperative week. In our study, a decline in cognitive function occurred in 16 patients (40%) at the postoperative 24th hour. We think that the differences in the incidences may have been caused by applying MMSE at different postoperative times or because of the differences in the age distributions, characteristics and operation types of the studied patients. We tried to keep MAP in the range of 50-65 mmHg. At the 10th, the MAP in Group N was significantly lower than that in Group E. When the preoperative 1st day and postoperative 1st day MMSE results were compared, while there was no significant difference between the groups, POCD was observed in seven patients in Group E and nine patients in Group N. There were two patients where the MAP was in the range of 45-50 mmHg only in the nitroglycerin group.

In laboratory studies and clinical research, it was found that cerebral oxygen saturation measured by NIRS is clinically appropriate for cerebral blood flow in monitoring of autoregulation[32]. A study where NIRS and transcranial Doppler were used in patients receiving liver transplantation showed the correlation between disrupted cerebral blood flow autoregulation and low NIRS values[33].The normal values of rSO_2 before oxygen application are 60-75%. However, initial rSO_2 values measured with NIRS vary from person to person, and thus, it is clinically important to monitor how initial values change in time. A cerebral oximeter should be used as a trend monitor[34].

While the relationship between cerebral perfusion pressure and cognitive dysfunctions in the early postoperative period is not clear, the hypotension level that may be seen during anesthesia and its duration may negatively affect cognitive functions[35]. When Aguirre et al.[36] applied intravenous anesthesia and controlled hypotension in shoulder surgery, they observed that cerebral desaturation was at a rate of 25%, and the decrease in blood pressure, rSO_2 and middle cerebral arterial blood flow rate was higher in the group that showed cerebral desaturation than the group that did not have cerebral desaturation 5 minutes after the sunbed position. They reported that cerebral desaturation events lead to disruption of brain blood flow and neurobehavioral functions 1 day after the operation. In a study which assessed neuropsychological outcomes with the MMSE test and the Anti-Saccadic Eye Movement (ASEM) test, it was found that rSO_2 values of <40% were a single predictor factor for impairment in both postoperative ASEM and MMSE tests[37]. In the study they applied controlled hypotension, Erdem et al.[29] reported as a result of MMSE they conducted in the postoperative 24th hour that POCD developed in all patients where cerebral desaturation was observed. The highest decrease in rSO_2 in comparison to the baseline was 28%, while at that moment, MAP was 57 mmHg. In our study, we determined cerebral desaturation by a decrease of 20% of more in the trend of rSO_2 rather than its % value. Cerebral desaturation was observed in 35% of the patients. The SpO_2 values of these patients were in the range of 98-100%. The changes in NIRS in terms of cerebral desaturation in Group N were in the form of a decrease of 21-29% and those in Group E were in the form of a decrease of 20-25%. During the highest decrease in comparison to the basal NIRS value (29%), the mean arterial pressure was 49 mmHg. There was no statistically significant difference between the groups in terms of their desaturation distributions. As CO_2 is an important parameter for cerebral perfusion, $EtCO_2$ was kept between 32 and 35 mmHg in all patients. 81.3% of the patients who developed POCD also had cerebral desaturation.

Data suggesting that interventions to repair low rSO_2 values reduce neurological complications (stroke, delirium or POCD) are conflicting[38]. It was observed that, by application of ephedrine for treatment of hypotension developing as a result of spinal anesthesia, cerebral oxygen saturation also went back to normal values[39]. In our study, all patients with cerebral saturation were treated with intravascular fluid administration and ephedrine (5-10 mg). The mean duration of desaturation was 43.11±6.23 seconds.

One of the purposes of applying controlled hypotension is to provide a bloodless operation field. Bajwa et al.[40] demonstrated that dexmedetomidine and esmolol showed better hemodynamic stability and operation site visibility in comparison to nitroglycerin during functional endoscopic sinus surgery. It was shown in orthognathic surgery that esmolol reduced blood loss and improved the quality of the surgical site better in comparison to sodium nitroprusside[41]. A study where nitroglycerin and labetalol were applied for controlled hypotension reported that, in the nitroglycerin group, the mean arterial blood pressures were significantly lower, while surgeon satisfaction was higher [42]. In our study, both groups were found to be adequate in terms of the ideal surgical site visibility.

The limitations of the current study are that cognitive functions were looked at only at the end of the 1st postoperative day, and this situation was not assessed in the following times. All patients in whom cerebral desaturation developed were intervened with, but it could not be determined whether or not the applied interventions would improve the neuropsychological outcomes as the study did not include a control group. We believe, as cerebral monitoring did not continue in the postoperative period, the hemodynamic changes in this period might have also affected the MMSE results.

In conclusion, cerebral desaturation seen during hypotensive anesthesia may cause early POCD development**,** therefore we think that close cerebral and hemodynamic monitoring during hypotensive anesthesia may preserve cognitive functions.

Yazar Katkıları: Çalışma konsepti/Tasarımı: BGA, GK; Veri toplama: NG, ÖP; Veri analizi ve yorumlama: ÖP, BGA; Yazı taslağı: BGA, GK; İçeriğin eleştirel incelenmesi: HA, RDO; Son onay ve sorumluluk: BGA, GK, ÖP, NG, RDO, HA; Teknik ve malzeme desteği: NG, RDO; Süpervizyon: RDO, HA; Fon sağlama (mevcut ise): yok.
Etik Onay: Bu çalışma için Bülent Ecevit Üniversitesi Klinik Araştırmalar Etik Kurulu Başkanlığından 05.11.2013 tarih ve 2013/17 sayılı kararı ile etik onay alınmıştır.
Hakem Değerlendirmesi: Dış bağımsız.
Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.
Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.
Author Contributions: Concept/Design : BGA, GK; Data acquisition: NG, ÖP; Data analysis and interpretation: ÖP, BGA; Drafting manuscript: BGA, GK; Critical revision of manuscript: HA, RDO; Final approval and accountability: BGA, GK, ÖP, NG, RDO, HA; Technical or material support: NG, RDO; Supervision: RDO, HA; Securing funding (if available): n/a.
Ethical Approval: For this study, ethical approval was obtained from the Bülent Ecevit University Clinical Research Ethics Committee with the decision dated 05.11.2013 and numbered 2013/17.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

REFERENCES

1. Degoute CS, Ray MJ, Manchon M, Dubreuil C, Banssillon V. Remifentanil and controlled hypotension; comparison with nitroprusside or esmolol during tympanoplasty. Can J Anaesth. 2001;48:20-7.
2. Van Aken H, Miller D. Delibrate hypotension. In: Miller RD, editor. Anesthesia. New York, USA: Churchill Livingstone Inc.; 2000;1470-90.
3. Choi WS, Samman N. Risks and benefits of deliberate hypotension in anaesthesia: a systematic review. Int J Oral Maxillofac Surg. 2008;37:687-703.
4. Cincikas D, Ivaskevicius J. Application of controlled arterial hypotension in endoscopic rhinosurgery. Medicina (Kaunas). 2003;39:852-9.
5. L. Strunin. Organ perfusion during controlled hypotension. Br J Anaesth. 1975;47:793-8.
6. M. J. Lindop. Complications and morbidity of controlled hypotension. Br J Anaesth 1975;47:799-803.
7. Choi SH, Lee SJ, Jung YS, Shin YS, Jun DB, Hwang KH et al. Nitroglycerin- and nicardipine-induced hypotension does not affect cerebral oxygen saturation and postoperative cognitive function in patients undergoing orthognathic surgery. J Oral Maxillofac Surg. 2008;66:2104-9.
8. Pohl A, Cullen DJ. Cerebral ischemia during shoulder surgery in the upright position: a case series. J Clin Anesth. 2005;17:463–9.
9. Lei L, Katznelson R, Fedorko L, Carroll J, Poonawala H, Machina M et al. Cerebral oximetry and postoperative delirium after cardiac surgery: a randomised, controlled trial. Anaesthesia. 2017;72:1456–66.
10. Yu Y, Zhang K, Zhang L, Zong H, Meng L, Han R. Cerebral near-infrared spectroscopy (NIRS) for perioperative monitoring of brain oxygenation in children and adults. Cochrane Database Syst Rev. 2018;1:CD010947.
11. Kotekar N, Shenkar A, Nagaraj R. Postoperative cognitive dysfunction -current preventive strategies. Clin Interv Aging. 2018;13:2267–73.
12. Fantini S, Sassaroli A, Tgavalekos KT, Kornbluth J. Cerebral blood flow and autoregulation: current measurement techniques and prospects for noninvasive optical methods. Neurophotonics. 2016;3:031411.
13. Hayashi H, Kawaguchi M. Intraoperative monitoring of the brain. In Textbook of Neuroanesthesia and Neurocritical Care Volume I - Neuroanesthesia (Eds Prabhakar H, Ali Z.) :43-8. Singapore, Springer, 2019.
14. Degoute CS. Controlled hypotension: a guide to drug choice. Drugs. 2007;67:1053-76.
15. Folstein MF. Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12:189–98.
16. Güngen C, Ertan T, Eker E, Yaşar R, Engin F. Standardize Mini Mental Test'in Türk toplumunda hafif demans tanısında geçerlik ve güvenilirliği. Turk Psikiyatri Derg. 2002;13:273-81.
17. Nair S, Collins M, Hung P, Rees G, Close D, Wormald PJ. The effect of beta-blocker premedication on the surgical field during endoscopic sinus surgery. Laryngoscope. 2004;114:1042-6.
18. Boezaart AP, van der Merwe J, Coetzee A. Comparison of sodium nitroprusside and esmolol-induced controlled hypotension for functional endoscopic sinus surgery. Can J Anaesth. 1995;42:373-6
19. Bijker JB, van Klei WA, Kappen TH, van Wolfswinkel L, Moons KG, Kalkman CJ. Incidence of intraoperative hypotension as a function of the chosen definition: literature definitions applied to a retrospective cohort using automated data collection. Anesthesiology. 2007;107:213–220.
20. Ha TN, van Renen RG, Ludbrook GL, Wormald PJ. The effect of blood pressure and cardiac output on the quality of the surgical field and middle cerebral

artery blood flow during endoscopic sinus surgery. Int Forum Allergy Rhinol. 2016;6:701-9.
21. Cottrell JE, Gupta B, Rappaport H, Turndorf H, Ransohoff J, Flamm ES. Intracranial pressure during nitroglycerin-induced hypotension. J Neurosurg. 1980;53:309-11.
22. Schulz JM, Al-Khazraji BK, Shoemaker JK. Sodium nitroglycerin induces middle cerebral artery vasodilatation in young, healthy adults. Exp Physiol. 2018;103:1047-55.
23. Zayed M, Nassar H, Hasanin A, Saleh AH, Hassan P, Saad D et al. Effects of nitroglycerin versus labetalol on peripheral perfusion during deliberate hypotension for sinus endoscopic surgery: a randomized, controlled, double-blinded trial. BMC Anesthesiol. 2020;20:85.
24. Saito S, Nishihara F, Akihiro T et al. Landiolol and esmolol prevent tachycardia without altering cerebral blood flow. Can J Anaesth. 2005;52:1027-34.
25. Heinke W, Zysset S, Hund-Georgiadis M, Olthoff D, von Cramon DY. The effect of esmolol on cerebral blood flow, cerebral vasoreactivity, and cognitive performance: a functional magnetic resonance imaging study. Anesthesiology. 2005;102:41-50.
26. Li D, Liu H. Cognitive function assessment should be included in preoperative evaluation. J Biomed Res. 2017;32:161–3.
27. Ghoneim MM, Block RI: Clinical, methodological and theoretical issues in the assessment of cognition after anaesthesia and surgery: a review. Eur J Anaesthesiol. 2012;29:409–22.
28. Monk TG, Weldon BC, Garvan CW et al. Predictors of cognitive dysfunction after major noncardiac surgery. Anesthesiology. 2008;108:18–30.
29. Erdem AF, Kayabasoglu G, Tas Tuna A, Palabiyik O, Tomak Y, Beyaz SG. Effect of controlled hypotension on regional cerebral oxygen saturation during rhinoplasty: a prospective study. J Clin Monit Comput. 2016;30:655-60.
30. Niazi AA. Postoperative cognitive function and controlled hypotensive anesthesia in patients undergoing septoplasty. Egypt J Anaesth. 2016;32:61-6.
31. Celebi N, Artukoglu F, Dal D, Saricaoglu F, Celiker V, Aypar U. Effect of hypotensive anesthesia on cognitive functions. A comparison of esmolol and remifentanil during tympanoplasty. Saudi Med J. 2007;28:1357-61.
32. Brady KM, Lee JK, Kibler KK, Smielewski P, Czosnyka M, Easley RB et al. Continuous time-domain analysis of cerebrovascular autoregulation using near-infrared spectroscopy. Stroke. 2007;38:2818-25.
33. Zheng Y, Villamayor AJ, Merritt W, Pustavoitau A, Latif A, Bhambhani R et al. Continuous cerebral blood flow autoregulation monitoring in patients undergoing liver transplantation. Neurocrit Care. 2012;17:77-84.
34. Denault A, Deschamps A, Murkin JM. A proposed algorithm for the intraoperative use of cerebral near-infrared spectroscopy. Semin Cardiothorac Vasc Anesth. 2007;11:274-81.
35. Caverni V, Rosa G, Pinto G. Hipotensive anesthesia and recovery of cognitive function in long term craniofacial surgery. J Craniofac Surg 2005;16:531-6.
36. Aguirre JA, Etzensperger F, Brada M, Guzzella S, Saporito A, Blumenthal S et al. The beach chair position for shoulder surgery in intravenous general anesthesia and controlled hypotension: Impact on cerebral oxygenation, cerebral blood flow and neurobehavioral outcome. J Clin Anesth. 2019;53:40-8.
37. Yao FS, Tseng CC, Ho CY, Levin SK, Illner P. Cerebral oxygen desaturation is associated with early postoperative neuropsychological dysfunction in patients undergoing cardiac surgery. J Cardiothorac Vasc Anesth. 2004;18:552-8.
38. Zheng F, Sheinberg R, Yee MS, Ono M, Zheng Y, Hogue CW. Cerebral near-infrared spectroscopy monitoring and neurologic outcomes in adult cardiac surgery patients: a systematic review. Anesth Analg. 2013;116:663-76.
39. Foss VT, Christensen R, Rokamp KZ, Nissen P, Secher NH, Nielsen HB. Effect of phenylephrine vs. ephedrine on frontal lobe oxygenation during caesarean section with spinal anesthesia: an open label randomized controlled trial Front Physiol. 2014;5:81.
40. Bajwa SJ, Kaur J, Kulshrestha A, Haldar R, Sethi R, Singh A. Nitroglycerine, esmolol and dexmedetomidine for induced hypotension during functional endoscopic sinus surgery: A comparative evaluation. J Anaesthesiol Clin Pharmacol. 2016;32:192-7.
41. Blau WS, Kafer ER, Anderson JA. Esmolol is more effective than sodium nitroprusside in reducing blood loss during orthognathic surgery. Anesth Analg. 1992;75:172-8.
42. Ghodraty M, Khatibi A, Rokhtabnak F, Maleki M, Parsa F. Comparing labetalol and nitroglycerine on inducing controlled hypotension and intraoperative blood loss in rhinoplasty: a single-blinded clinical trial. Anesth Pain Med. 2017;7:e13677.