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RESEARCH

Comparison of the effects of hypotensive anesthesia techniques based on systolic and mean arterial pressure on cerebral perfusion, blood oxidant-antioxidant levels and HIF-1a levels

Sistolik ve ortalama kan basıncına göre uygulanan hipotansif anestezi tekniklerinin beyin perfüzyonu, kan oksidan-antioksidan seviyelerileri ve HIF-1a seviyeleri üzerindeki etkilerinin karşılaştırılması

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Abstract

Purpose: This study aims to compare and evaluate changes in tissue and cerebral perfusion when systolic blood pressure (SBP) or mean arterial pressure (MAP) is used as the reference parameter to achieve controlled hypotension.
Materials and Methods: Patients scheduled for planned rhinoplasty or jaw surgery requiring controlled hypotension were included in the study. The patients were categorized into two groups: Group 1 (systolic blood pressure group) and Group 2 (mean arterial pressure group). Before anesthesia induction and emergence, levels of total oxidant status (TOS), total antioxidant status (TAS), oxidative stress index (OSI), and hypoxia-inducible factor (HIF-1α) in the blood were measured. Perioperative cerebral perfusion monitoring was performed using near-infrared spectroscopy (NIRS).
Results: There was no significant difference between the two groups in preoperative and postoperative levels of TAS, TOS, OSI, and HIF-1α, which are used as indicators of oxidative stress. Similarly, there was no significant difference in RsO2 values between the groups. Surgical satisfaction scores were significantly higher in Group 2, while bleeding scores were significantly lower.
Conclusion: MAP-targeted controlled hypotension provides higher surgical satisfaction and lower bleeding scores without causing disadvantages in terms of cerebral oxygenation or oxidative stress.
Keywords: Hypotensive anesthesia, hypoxia, hypoxia-inducible factor, near-infrared spectroscopy

Öz

Amaç: Bu çalışmanın amacı, kontrollü hipotansiyon sırasında arteriyel kan basıncının ayarlanmasında referans parametre olarak sistolik kan basıncı (SKB) veya ortalama kan basıncının (OKB) kullanılması durumunda doku ve beyin perfüzyonundaki değişiklikleri değerlendirmektir.
Gereç ve Yöntem: Kontrollü hipotansiyon uygulanacak planlı rinoplasti ya da çene cerrahisi yapılacak hastalar çalışmaya dahil edildi. Hastalar, Grup 1 (sistolik kan basıncı grubu) ve Grup 2 (ortalama kan basıncı grubu) olarak kategorize edildi. Anestezi indüksiyonundan ve uyandırmadan önce kandaki toplam oksidan durumu (TOS), toplam antioksidan durumu (TAS), oksidatif stres indeksi (OSI) ve hipoksi inducible factör (HIF-1a) seviyeleri ölçüldü. Perioperatif beyin perfüzyonu monitörizasyonu near infraraed spectroscopy (NIRS) kullanılarak gerçekleştirildi.
Bulgular: İki grup arasında oksidatif stres göstergesi olarak kullanılan TAS, TOS, OSI, ve HIF-1α değerlerinde preoperatif ve postoperatif anlamlı bir fark bulunmadı. İki grup arasında RsO2 değerlerinde anlamlı fark bulunmadı. Grup 2'de cerrahi memnuniyet skorları anlamlı olarak daha yüksek, kanama skorları ise anlamlı olarak daha düşüktü.
Sonuç: OKB hedefli kontrollü hipotansiyonun, serebral oksijenasyon ve oksidatif stres açısından bir dezavantaj yaratmadan daha yüksek cerrahi memnuniyet ve daha düşük kanama skorları sağladığını göstermektedir.

Anahtar kelimeler: Hipotansif anestezi, hipoksi, hipoksi indüklenebilir faktör, yakın kızılötesi spektroskopisi

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INTRODUCTION

Controlled hypotension is employed to reduce bleeding and improve the quality of the surgical field[1]. Although there is no universally accepted blood pressure value for the implementation of controlled hypotension, it is generally defined as reducing the systolic blood pressure to 80-90 mmHg, the mean arterial pressure to 50-65 mmHg, or reducing the baseline values by approximately 30% in a healthy individual[2,3,4].

Controlled hypotension can be utilized in various fields, including orthopedic surgeries, spinal surgery, hepatic resection surgery, robotic surgery, maxillofacial surgery, rhinoplasty, and ear surgery[1,5]. Particularly in rhinoplasties, due to the limited surgical area, intraoperative bleeding complicates the reshaping of the nose and can lead to postoperative complications. This technique is particularly preferred in maxillofacial surgeries, such as rhinoplasty, this technique is preferred to ensure adequate surgical visibility, reduce bleeding, and minimize postoperative complications[3,5]. The implementation of controlled hypotension, particularly in vital organs such as the heart, kidneys, and brain, can inhibit the autonomic nervous system, leading to tissue ischemia. When implementing controlled hypotension, the goal should be to lower blood pressure in a way that does not compromise the microcirculation of vital organs[2,3,5].

Several strategies and monitors have been developed to prevent cerebral ischemia. Near-infrared spectroscopy (NIRS) technology is a non-invasive method used to assess cerebral tissue oxygenation. The ratio of oxyhemoglobin to total hemoglobin in the area under the NIRS sensor is expressed as regional oxygen saturation (RsO_2). A decrease in RsO_2 below 40% or a drop of more than 25% from the baseline value is associated with neurological impairments and adverse outcomes[6].

Hypoxia-inducible factor (HIF) is the primary oxygen sensor in cells. Under hypoxic conditions, the HIF-1α subunit stabilizes, and its activity increases rapidly. HIF activation ensures cell integrity and optimal ATP production, making it an excellent marker of tissue hypoxia[7,8]. Total antioxidant status (TAS), total oxidant status (TOS), and the oxidative stress index (OSI) are markers of oxidative stress. Increases in these levels are observed when the balance of antioxidant defenses is disrupted due to an increase in reactive oxygen species (ROS), which cause molecular damage in the cell[9]. Therefore, TAS, TOS, OSI, and HIF-1α are considered strong markers for assessing the effects of hypoxia/hyperoxia.

Our literature review reveals no consensus on how controlled hypotension should be applied. It is commonly defined as a reduction of systolic blood pressure (SBP) to 80-90 mmHg, mean arterial pressure (MAP) to 50-65 mmHg, or a 30% decrease from baseline values. However, many studies have focused on MAP, with target ranges varying across different studies. In our study, we aim to compare controlled hypotension based on MAP-targeted (50-65 mmHg) and systolic-targeted (80-90 mmHg) approaches in terms of cerebral perfusion, global tissue perfusion, as well as the amount of bleeding and surgical satisfaction scores.

Our study evaluates different target blood pressure techniques used in controlled hypotension in terms of cerebral and tissue perfusion, intraoperative bleeding, and surgical satisfaction scores. Our hypothesis is that MAP-targeted controlled hypotension is superior to SBP-targeted controlled hypotension in terms of cerebral perfusion, tissue perfusion, bleeding, and surgical satisfaction scores. The parameters we used to evaluate tissue perfusion (TAS, TOS, OSI, HIF-1a) have not been previously examined in controlled hypotension applications. Furthermore, two different controlled hypotension techniques have not been compared in terms of cerebral perfusion. Evaluation and comparison of techniques in the literature for controlled hypotension in terms of organ perfusion will contribute to clinical practice.

MATERIALS AND METHODS

Sample

Patients scheduled for elective rhinoplasty and jaw surgery, in which controlled hypotension would be applied, were included. Written informed consent was obtained from the patients after explaining the effects of controlled hypotension during the operation and the need for blood samples. Inclusion criteria were defined as patients aged 18-75, classified as ASA I-II, non-smokers, and undergoing rhinoplasty or jaw surgery. Exclusion criteria were definde as smoking, morbid obesity, hypertension, cerebrovascular disease, and cardiovascular disease.

This study was designed as a single blind (the surgeon performing the surgery was not informed). Randomization was performed by an independent investigator (IS) using computer software. Patients were randomly assigned to the systolic blood pressure or mean blood pressure group in a 1:1 ratio. The surgeon performing the operation was not informed about which technique would be applied. Therefore, the surgeon remained unaware of the controlled hypotension technique applied.

The sample size was calculated using G power 3.1. In the power analysis using the sample study, if we assign the significance of 1.5 units of HIF-1 measurement between the groups according to the literature, assuming that the standard deviation is 2 units, it was calculated that 29 cases were required in each group for a 95% confidence level and 80% power. Considering the possibility of dropout, it was decided to include 1 case in each group. No patient was excluded from the study during the course of the trial. In both groups, 30 patients were included in the study.

Procedure

This study was designed as a prospective randomized controlled trial and conducted in accordance with CONSORT guidelines. Ethical approval was obtained from the Bezmialem Vakıf University Faculty of Medicine Ethics Committee with protocol number 71306642-05.01.04 on 14.11.2018. Additionally, a clinical trial registration was completed (clinicaltrials.gov: NCT04174417).

Before the procedure, patients who had been restricted from oral intake for 8 hours had a venous cannula inserted through the hand. Prior to anesthesia induction, 3 ml of blood was drawn from the venous cannula to measure HIF-1α, TAS, and TOS levels and placed in MiniCollect® tubes. The collected blood samples were centrifuged at 2000 x g for 10 minutes, and the serum was sent to the biochemistry laboratory to be stored at -80°C until analysis.In the operating room, patients were monitored using an electrocardiogram (ECG), peripheral oxygen saturation (SpO_2), non-invasive blood pressure (NIBP), Bispectral Index (BIS) (E-BIS-00, GE Healthcare, Finland), and Near-Infrared Spectroscopy (NIRS) (INVOS 5100, Medtronic). Values were recorded prior to anesthesia induction. During the operation, continuous NIRS monitoring was performed and the values were recorded at 5 min intervals. If the value fell below 40% for more than one minute during surgery, or by more than 25% from baseline, the dose of remifentanil and propofol was reduced, fluid replacement and intravenous ephedrine were administered, and an increase in blood pressure was planned. If there was no response, fluid and inotropic support was continued and the patient's withdrawal from the study was to be planned.

Anesthesia induction and maintenance

Patients received premedication with 0.03 mg/kg intravenous midazolam. After administering 1 mg/kg of lidocaine, anesthesia induction was performed using propofol at a dose of 2-3 mg/kg, fentanyl at 1.5 mcg/kg, and rocuronium at 0.5 mg/kg. Anesthesia maintenance was achieved through intravenous infusion of propofol at 5-8 mg/kg/h and remifentanil at 0.01-0.50 mcg/kg/min.

Patients undergoing rhinoplasty were intubated orotracheally, while those undergoing jaw surgery were intubated nasotracheally. Tidal volume was set to 6 mL/kg, with a positive end-expiratory pressure (PEEP) of 5 cmH2O, inspired oxygen fraction (FiO_2) at 50%, fresh gas flow at 3 L/min, and end-tidal carbon dioxide ($EtCO_2$) maintained between 30-35 mmHg. The respiratory rate was adjusted accordingly.Bispectral index (BIS) values were maintained between 40-60 by adjusting the propofol infusion, while remifentanil infusion was administered to achieve a systolic blood pressure of 80-90 mmHg for Group 1 patients and a mean arterial pressure of 50-65 mmHg for Group 2 patients. To achieve the target blood pressure, additional intravenous boluses of 0.002 mcg/kg glyceryl trinitrate (Perlinganite) were administered as needed. We preferred glycerol trinitrate because it is a short-acting agent and nitrate group drugs have been used in previous studies to induce controlled hypotension[10,11]. If the hypotension was deeper than expected, the dose of remifentanil was reduced and a 5 mg bolus of ephedrine was scheduled. In the absence of a response, positive inotropic support was initiated and the patient's withdrawal from the study was to be planned.

During the surgery, all patients received intravenous infusion of balanced electrolyte solution (Isolyte-S) at a rate of 5-8 ml/kg/hour. Hemodynamic parameters (heart rate, systolic blood pressure, mean arterial pressure), BIS, SpO_2, and NIRS were recorded at 5-minute intervals.

Ten minutes before awakening, an additional 3 ml of blood was drawn from the arm that did not receive medication to measure HIF-1α, TAS, TOS, and OSI levels, and these samples were sent to the biochemistry laboratory. The values obtained from preoperative samples were designated as T0, while those obtained after the operation were designated as T1.

All patients received 50 mg of ranitidine and 8 mg of dexamethasone intravenously. At the end of the surgery, 2 mg/kg of sugammadex was administered intravenously to reverse the effects of the neuromuscular blocker.

Patients received intravenous paracetamol at a dose of 15 mg/kg 30 minutes before the end of the surgery. In the postoperative care unit, patients with a Visual Analog Scale (VAS) pain score greater than 4 were administered tramadol at a dose of 1 mg/kg.

Evaluation of surgeon satisfaction and bleeding score

The surgeon was not informed about which controlled hypotension technique was applied before or during the surgery. To minimize variability in surgical satisfaction and bleeding scores, the same surgeon performed all operations. At the end of the surgery, a bleeding and surgical satisfaction score form was provided to the surgeon for completion.

The bleeding level was assessed using the Fromme and Boezart bleeding score (0: No bleeding, 1: Slight bleeding - no suctioning required, 2: Slight bleeding - occasional suctioning required, 3: Slight bleeding - frequent suctioning required; operative field visible for some seconds after evacuation, 4: Moderate bleeding - frequent suctioning required; operative field only visible immediately after evacuation, 5: Severe bleeding - constant suctioning required; bleeding appears faster than can be removed by suction; surgery is hardly possible, and sometimes impossible Surgeon satisfaction was evaluated using a Likert scale (5: Excellent, 4: Good, 3: Satisfactory, 2: Poor, 1: Very poor [12].

Primary and secondary outcomes

The primary outcome measures of our study were the change in NIRS values during controlled hypotension and comparison between groups, and the comparison of changes in TAS, TOS and HIF 1a values between groups after controlled hypotension. Secondary outcomes were to compare the effects of controlled hypotension implementation techniques on surgical satisfaction and bleeding scores.

Statistical analysis

In this study, statistical analyses were performed with NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) package programme. In the evaluation of the data, in addition to descriptive statistical methods (mean, standard deviation, median, interquartile range), the distribution of the variables was examined with the Shapiro-Wilk normality test, paired one-way analysis of variance was used for time comparisons of normally distributed variables, Newman Keuls multiple comparison test was used for subgroup comparisons, surgical time , Independent t test was used for comparison of normally distributed binary groups such as height and weight, Wilcoxon test was used for comparison of non-normally distributed variables between two times, Mann Whitney U test was used for comparison of binary groups such as bleeding and satisfaction scores, drug consumption amounts, chi-square test was used for comparison of qualitative data such as gender and ASA score. The results were evaluated at a significance level of $p<0.05$.

RESULTS

There was no statistically significant difference between the groups in terms of age, gender distribution, height, weight, body mass index, ASA scores, type of surgery, duration of surgery, and consumption of propofol and remifentanil ($p>0.05$ for all values; Table 1).

Throughout all time points, there were no statistically significant differences in average anesthesia depth, SpO_2, and MAP among the groups ($p>0.05$). No statistically significant difference was observed in the average SBP among the groups at all times ($p>0.05$) (Figure 1). However, the average MAP values for Group 2 at 15 minutes, 20 minutes, 30 minutes, 70 minutes, 90 minutes, and 10 minutes before extubation were found to be statistically significantly lower than those of Group 1 ($p<0.05$) (Figure 2).

The mean TOS of T1 measurement of group 1 was statistically significantly lower than the mean TOS of T0 measurement ($p=0.017$) (Table 2). The mean HIF-1a of T1 measurement of group 2 was statistically significantly lower than the mean HIF-1a of T0 measurement ($p=0.013$) (Table 2) There was no statistically significant difference between the mean TAS measurements of T0 and T1 of group 1 and group 2 (p>0. 05) (Table 2) The mean OSI of T1 measurement of group 1 was statistically significantly lower than the mean TOS of T0 measurement (p=0,017) (Table 3)

Table -1 Characteristic s of patients, surgery type and duration, anaesthetic drug consumption, surgeon satisfaction and bleeding scores

Demographics		**Group 1 n:30**		**Group 2 n:30**		**p value**
Age (years)		25.9±8.66		28.13±10.44		0.371*
Gender	Male	9	30.00%	11	36.67%	
	Female	21	70.00%	19	63.33%	0.584+
Height (cm)		170.63±18.53		169.77±8.05		0.815*
Weight (kg)		66,2±13.72		67.8±14.67		0.664*
BMI kg/m2		23.07±4.73		23.39±3.89		0.777*
ASA	1	29	96.67%	26	86.67%	
	2	1	3.33%	4	13.33%	0.161+
Surgery type	Jaw surgery	6	20.00%	8	26.67%	
	Dental İmplant	1	3.33%	4	13.33%	
	Rhinoplasty	23	76.67%	18	60.00%	0.260+
Surgery duration (minutes)		119.4±23.19		120.33±20.3		0.869*
Surgery satisfaction score		2.97±0.62		3.33±0.55		**0.018‡**
Bleeding score		1.97±0.77		1.50±0.73		**0.019‡**
Propofol consumption amount (mg)		1002.8±892.49		1323.13±819.99		0.153‡
Remifentanil consumption amount (mcg)		3400.67±2012.68		3198.73±2050.48		0.702‡

*Independent t test ‡Mann Whitney U test + chi-square test

Table 2. Preoperative and postoperative TAS, TOS, HIF-1a measurements of the groups

		Group1 n:30	**Group2 n:30**	**p‡**
TAS	T0	1.55±0.33	1.72±0.76	0.971‡
	T1	1.78±0.83	1.80±0.78	0.652‡
	p†	0.376	0.885	
TOS	T0	33.60±25.22	37.73±27.31	0.525‡
	T1	20.37±20.67	26.73±21.10	0.120‡
	p†	**0.017**	0.119	
H1F-1a	T0	0.60±0.59	1.63±5.63	0.917‡
	T1	0.45±0.51	1.20±3.96	0.805‡
	p†	0.123	**0.013**	

‡Mann Whitney U Testi †Wilcoxon Test TAS; Total antioxidant status, TOS; Total oxidant status, HI1-1a; Hypoxia inducible factor

Table-3 Preoperative and postoperative OSI measurements of the groups

	Group1 (n=30)		**Group 2 (n=30)**		**p value**
	Ort±Ss	Min-Max (Median)	Ort±Ss	Min-Max (Median)	
OSI T0	22.25±17.28	0-79.02 (16.89)	23.75±16.94	0-64.48 (18.63)	0.735
OSI T1	13.77±13.5	0-59.52 (10.46)	16.25±12.68	0-61.19 (12.98)	0.466

[b]Independent Sample t Test OSI; Oxidative stress index

Table-4 Data of desaturated and non-desaturated patients of the groups

Cerebral Desaturation	**Group 1 n:30**		**Group 2 n:30**		**p value**
Cerebral Desaturation (-)	17	56.67%	21	70.00%	0.284+
Cerebral Desaturation (+)	13	43.33%	9	30.00%	

+Chi square test

Overall, there were no statistically significant differences in the average TAS, TOS, OSI values among all measurements between the groups ($p>0.05$) (Tables 2 and 3). Similarly, there were no statistically significant differences in the average HIF-1α values among all measurements between the groups ($p>0.05$) (Table 2). In Group 1, 17 patients and in Group 2, 9 patients exhibited a greater than 25% decrease in RsO_2 values compared to baseline (Table 4). The lowest average RsO_2 value was 56 in Group 1 and 63 in Group 2 (Figure 3). When these values were statistically compared between the two groups, there was no significant difference in the distribution of cerebral desaturation ($p=0.284$, $p>0.05$)(Table 4). The surgical satisfaction score for Group 2 was found to be statistically significantly higher than that of Group 1 ($p=0.018$) (Table 1). Additionally, the bleeding score for Group 2 was statistically significantly lower than that of Group 1 ($p=0.019$) (Table 1).

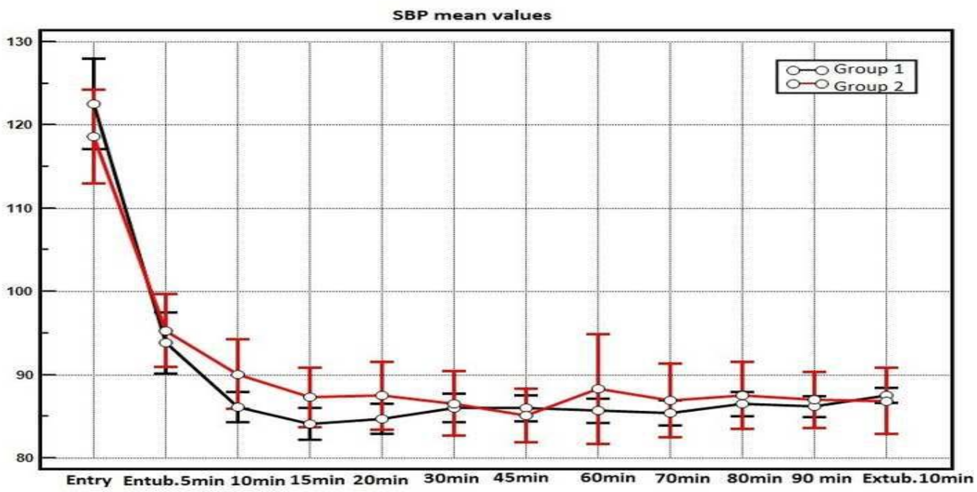

Figure 1. Systolic blood pressure (SBP) mean values of the groups.

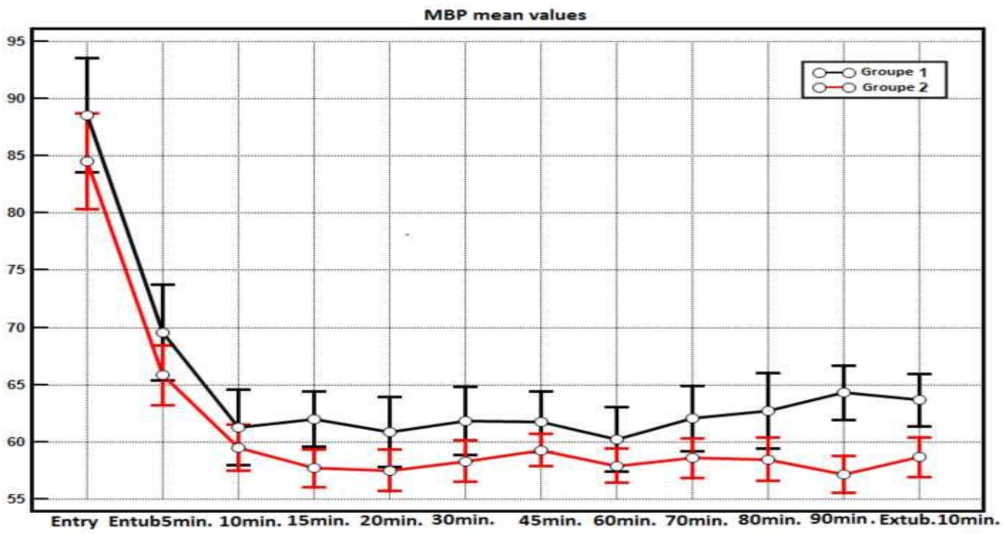

Figure 2. Mean blood pressure (MBP) mean values of the groups.

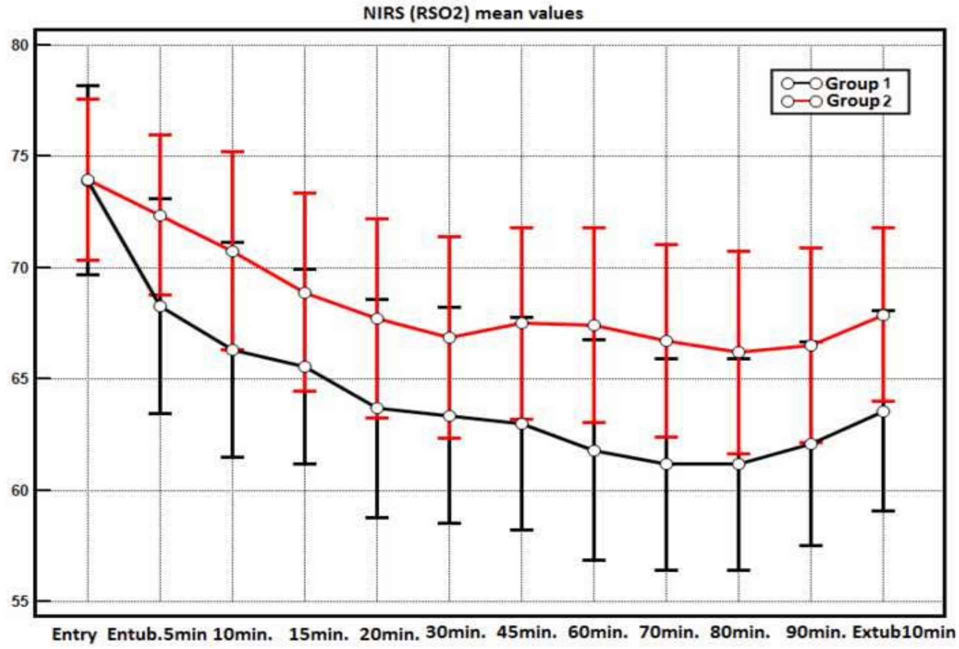

Figure-3 Regional oxygen saturation (RsO_2) mean values of the groups.

DISCUSSION

Looking at the controlled hypotension strategies we used, our study showed that target mean arterial pressure (MAP) and systolic blood pressure (SBP) were not superior to each other in terms of cerebral oxygenation, hypoxia-induced markers and perioperative complications. However, it was observed that the MAP group had less perioperative bleeding.

Controlled hypotension has been defined in many studies as a decrease in systolic blood pressure to 80-90 mmHg, mean arterial pressure to 50-65 mmHg or a%30 decrease from baseline values. It is known that cerebral blood flow is maintained in MAP range of 50-150 mmHg. These ranges are generally used as targets to minimize bleeding and improve vision in surgeries performed in narrow spaces such asthe nasal and oral cavities. A more restrictive strategy would make it difficult to keep patients in this range and would have risked increasing the number of patients unnecessarily excluded from the study. However, studies have shown that when controlled hypotension is applied according to different threshold values, there is no significant difference in cognitive tests within the MAP range 50-65 mmHg. In light of these data, we have used the MAP range of 50-65 mmHg, as our study involves surgery in confined spaces such as the nasal and oral cavities[10,13,14,15,16]. The aim of controlled hypotension is to maintain blood pressure at a level that does not disrupt the autoregulation of microcirculation in vital organs [3]. To achieve this goal, NIRS technology is used to continuously and non-invasively monitor cerebral oxygenation during the perioperative period[17].

In a study conducted by Erdem et al., NIRS was used in patients undergoing controlled hypotension with a mean arterial pressure (MAP) of 50-65 mmHg. Cerebral desaturation was detected in 10% of the patients. All patients underwent preoperative and postoperative Mini-Mental State Examination (MMSE) to evaluate cognitive function, and a decrease in the MMSE score was observed in all patients at 24 hours postoperatively compared to preoperative values. This decrease was reported to be more pronounced in patients with cerebral desaturation[3]. In another study by Jose et al., controlled hypotension was applied to patients undergoing shoulder surgery in a sunbed position with systolic blood pressure (SBP) less than 100 mmHg at heart level. Intraoperative cerebral blood flow, cerebral saturation, and postoperative neurocognitive status were evaluated. Cerebral desaturation and neurocognitive changes were detected in 25% of the patients[18]. In a separate study by Lee et al. on patients undergoing shoulder surgery, controlled hypotension was applied with NIRS monitoring to maintain MAP at 60-65 mmHg at the level of the external auditory canal, and a significant decrease in RsO_2 values was reported[19].

Thanaboriboon et al. applied controlled hypotension using NIRS monitoring in patients undergoing shoulder surgery, maintaining a mean arterial pressure (MAP) >70 mmHg in those without hypertension and inducing a 20% reduction from baseline in those with hypertension. They reported that in 43% of the patients developed cerebral desaturation[20].

Zhang et al. conducted a study in patients undergoing endoscopic sinus surgery, using controlled hypotension by reducing MAP by approximately 30% from baseline while using NIRS monitoring. They reported that cerebral desaturation occurred in 5% of the patients[21].

In our study, we observed that 43% of patients in group 1 and 30% in group 2 experienced a decrease in RsO_2 values of more than 25%. The duration of these decreases was longer than 15 seconds but shorter than 60 seconds and was reversible. These data showed no statistically significant difference between the two groups.

In another study by Behrooz et al, controlled hypotension was used in patients undergoing endoscopic sinus surgery. MAP was maintained at 55-60 mmHg. They evaluated the changes between $EtCO_2$, MAP, and RsO_2 values and reported that RsO_2 remained within a safe range at MAP >55 mmHg [1]. In contrast to this study, our findings indicated that both groups maintained $EtCO_2$ and SpO_2 values within normal limits throughout the operation and were considered reliable reference values. In the statistical analysis of our study outcomes, we did not establish a threshold blood pressure value that would ensure RsO_2 remained within a safe range. Furthermore, the decrease in RsO_2 was observed to be heterogeneous across different MAP and systolic blood pressure values in both groups.

Hypoxia-induced factors are a family of nuclear transcription factors that act as master regulators of the adaptive response to hypoxia. HIF-1a levels increase with hypoxia in ischaemic tissue. HIFs act as master regulators of impaired oxygen haemostasis in circulatory disorders and cancer. For example, they play a protective role in myocardial ischaemia due to coronary artery disease or limb ischaemia due to peripheral arterial disease. HIF-1a levels increase dramatically when cellular oxygen is reduced[7,22,23]. Oxidative stress occurs when the balance between the production of reactive oxygen species (ROS) and antioxidant mechanisms and cellular defence is disturbed. TAS, TOS and OSI are biomarkers of oxidative stress. Surgical stress, general anaesthesia and surgical inflammation and ischaemia-reperfusion can cause ROS production[9,24] . In line with these data, we considered that oxidative stress may also occur during controlled hypotension and evaluated the changes in these markers in our study. According to the results of our study, there were no statistically significant differences in the mean values of TAS, TOS, OSI and HIF-1a between the two groups. However, we found studies investigating the effects of propofol, a commonly used anaesthetic in daily practice, on these parameters[24,25,26]. These studies reported that propofol could affect these laboratory values. However, the use of propofol in our study groups was similar and there were no statistical differences.

The primary goal of implementing controlled hypotension is to reduce intraoperative bleeding and provide a clear surgical view[5]. The secondary outcomes of our study were the assessment of surgical satisfaction and bleeding scores between the two groups. According to our results, the bleeding score was statistically significantly lower in group 2, while the surgical satisfaction score was statistically significantly higher. Mean pressures in the SBP group did not fall below 50 mmHg in any measurement and were statistically significantly higher than in the MAP group. This explains the higher bleeding and dissatisfaction with surgery in the SBP group. The literatüre includes many studies evaluating bleeding amounts and surgical satisfaction during controlled hypotension applications. In these studies, the effects of drugs used in controlled hypotension on bleeding amounts and surgical satisfaction scores were investigated[15,27,28]. In our study we compared two different tecniques and we achieved better results in the MAP group.

Our study has several limitations. Evaluation of the clinical implications of the observed cerebral desaturation with specific tests may contribute to the widespread use of NIRS during controlled hypotension. Furthermore, considering that oxidative stress markers may be influenced by anaesthetic agents, we believe that conducting clinical studies free from these effects would also contribute to clinical practice.

In conclusion, we have shown in our study, as in similar studies, that cerebral desaturation can be observed in patients during the application of controlled hypotension. In terms of cerebral perfusion and its effects, similar effects of controlled hypotension were observed compared to MAP and SBP. There was no difference in oxidative stress markers between the two groups. In terms of surgical satisfaction and bleeding scores, the use of controlled hypotension was more advantageus than MAP.

Controlled hypotension provides better surgical visualisation and less haemorrhage, without disadvantage in terms of tissue and cerebral perfusion, when applied to MAP. It can be used safely in selected procedures and patients. Monitoring of cerebral perfusion during controlled hypotension increases the safety of its use.

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Ethical Approval: Ethical approval for the study was obtained from the Bezmialem Vakıf University Faculty of Medicine Ethics Committee with protocol number 71306642-05.01.04 on 14.11.2018.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
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REFERENCES

1. Farzanegan B, Eraghi M G, Abdollahi S, Ghorbani J, Khalili A, Moshari R et al. Evaluation of cerebral oxygen saturation during hypotensive anesthesia in functional endoscopic sinus surgery. J Anaesthesiol Clin Pharmacol. 2018;34:503-6.
2. Upadhyay SP, Samant U, Tellicherry SS, Mallik S, Saikia PP, & Mallick PN Controlled hypotension in modern anaesthesia: a review and update. Int. J. Biol. Pharm. Res. 2015;6:532-42.
3. 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.
4. Javaherforooshzadeh F, Monajemzadeh SA, Soltanzadeh M, Janatmakan F, Salari A, Saeed HA Comparative study of the amount of bleeding and hemodynamic changes between dexmedetomidine infusion and remifentanil infusion for controlled hypotensive anesthesia in lumbar discopathy surgery: A double-blind, randomized, clinical trial. Anesth Pain Med. 2018;8:e66959.
5. Barak M, Yoav L, Abu el-Naaj I Hypotensive anesthesia versus normotensive anesthesia during major maxillofacial surgery: a review of the literature. ScientificWorldJournal. 2015;2015;480728.
6. Edmonds HL Jr, Ganzel BL, Austin EH 3rd. Cerebral oximetry for cardiac and vascular surgery. Semin Cardiothorac Vasc Anesth. 2004;8:147-66.
7. Chen R., Lai UH, Zhu L, Singh A, Ahmed M, Forsyth NR Reactive oxygen species formation in the brain at different oxygen levels: The role of hypoxia inducible factors. Front Cell Dev Biol. 2018;6:132.
8. Coimbra-Costa D, Alva N, Duran M, Carbonell T, Rama R Oxidative stress and apoptosis after acute respiratory hypoxia and reoxygenation in rat brain. Redox Biol. 2017;12:216-25.
9. Kundovic SA, Rasic D, Popovic L, Peraica M, Crnjar K Oxidative stress under general intravenous and inhalation anaesthesia. Arh Hig Rada Toksikol. 2020;71:169-77.
10. Sajedi P, Rahimian A, Khalili G. Comparative evaluation between two methods of induced hypotension with infusion of remifentanil and labetalol during sinus endoscopy. J Res Pharm Pract. 2016;5:264-71.
11. Alkan A, Honca M, Alkan A, Güleç H, Horasanlı E. The efficacy of esmolol, remifentanil and nitroglycerin in controlled hypotension for functional endoscopic sinus surgery. Braz J Otorhinolaryngol. 2021;87:255-59.
12. Parvizi A, Haddadi S, Habibi AF, Nemati S, Akhtar N, Ramezani H. Dexmedetomidine efficacy in quality of surgical field during endoscopic sinus surgery. Iran J Otorhinolaryngol.2019;31:281.
13. Giriyapur P, Madhusudhana R. Controlled hypotension for functional endoscopic sinus surgery with two different doses of fentanyl. Cureus.2023;15:e33859. doi:10.7759/cureus.33859.
14. Boonmak P, Boonmak S, Laopaiboon M. Deliberate hypotension with propofol under anaesthesia for functional endoscopic sinus surgery. Cochrane Database Syst Rev. 2016;10:CD006623.
15. Karami A, Fattahi Saravi Z, Hosseini H et al. Comparison of labetalol and lidocaine in induction of controlled hypotension in tympanoplasty: a randomized clinical trial. Braz J Otorhinolaryngol. 2024;90:101-403.
16. Nowak S, Oldak A, Kluzik A, Drobnik L. Impact of Controlled Induced Hypotension on cognitive functions on patients undergoing functional

endoscopic sinus surgery. Med Sci Monit. 2016;22:898-907.
17. Scheeren TW, Saugel B. Monitoring cerebral oxygenation and autoregulation. J Clin Monit Comput. 2017;31:241-46.
18. 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.
19. Lee JH, Min KT, Chun YM, Kim EJ, Choi SH. Effects of beach-chair position and induced hypotension on cerebral oxygen saturation in patients undergoing arthroscopic shoulder surgery. Arthroscopy. 2011;27:889-94.
20. Thanaboriboon C, Vanichvithya P, Jinaworn P. What is the risk of intraoperative cerebral oxygen desaturation in patients undergoing shoulder surgery in the beach chair position? Clin Orthop Relat Res. 2021;1;479:2677-87.
21. Zhang L, Yu Y, Xue J, Lei W, Huang Y, Li Y et.al. Effect of deliberate hypotension on regional cerebral oxygen saturation during functional endoscopic sinus surgery: A randomized controlled trial. Front Surg. 2021;8:681471.
22. Semenza GL. Oxygen sensing, hypoxia-inducible factors, and disease pathophysiology. Annu Rev Pathol. 2014;9:47-71.
23. Suresh MV, Balijepalli S, Solanki S, Aktay S, Choudhary K, Shah YM et al. Hypoxia-inducible factor 1α and its role in lung injury: adaptive or maladaptive. Inflammation. 2023;46:491-508.
24. Ucar M, Ozgul U, Polat A, Toprak HI, Erdogan MA, Aydogan MS et.al. Comparison of antioxidant effects of isoflurane and propofol in patients undergoing donor hepatectomy. Transplant Proc. 2015;47:469-72.
25. Braz MG, Braz LG, Freire CMM, LucioL MC. Braz JRC, Tang G et.al. Isoflurane and propofol contribute to increasing the antioxidant status of patients during minor elective surgery: A randomized clinical study. Medicine (Baltimore). 2015;94:e1266.
26. Bellanti, Mirabella L, Mitarotonda D, Blonda M, Tamborra R, Cinnella G et.al. Propofol but not sevoflurane prevents mitochondrial dysfunction and oxidative stress by limiting HIF-1alpha activation in hepatic ischemia/reperfusion injury. Free Radic Biol Med. 2016;96:323-33.
27. Eberhart LH, Folz BJ, Wulf H, Geldner G. Intravenous anesthesia provides optimal surgical conditions during microscopic and endoscopic sinus surgery. Laryngoscope. 2003;113:1369-73.
28. Elsharnouby NM, Elsharnouby MM. Magnesium sulphate as a technique of hypotensive anaesthesia. Br J Anaesth. 2006;96:727-31.