Effects of Controlled Hypotension on Cerebral Oxygenation in Tympanoplasty and Tympanomastoidectomy Surgery

Gulel Shabanova[1], Elvan Onan[2], Ebru Biricik[1], Feride Karacaer[1], Demet Laflı Tunay[1], Yasemin Güneş[1]

1 Department of Anesthesiology and Reanimation, Cukurova University Faculty of Medicine, Adana, Türkiye
2 Department of Otorhinolaryngology, Çukurova University Faculty of Medicine, Adana, Türkiye

Abstract

Aim: We aimed to evaluate the effects of controlled hypotension by using esmolol and nicardipine on cerebral oxygenation, hemodynamics, bleeding, surgical satisfaction and quality of recovery.

Methods: Sixty adult patients who were scheduled tympanoplasty and tympanomastoidectomy surgery were included. The mean arterial blood pressure was aimed to be <30% from baseline for controlled hypotension. Nicardipine infusion (1-5 µg/kg/min) was used in group N and esmolol infusion (50-300 µg/kg/min) was used in group E. Near-infrared spectroscopy (NIRS) values, surgical bleeding and surgical satisfaction, extubation and recovery time, postoperative side effects, antiemetic and additional analgesic medications were recorded.

Results: The NIRS values in N group were observed higher than E group at the 20th and 40th minutes on the left, and at the 25th, 30th, 35th, 40th, 45th and 60th minutes on the right ($p<0.05$). Mean arterial blood pressure at the 70th and 80th minutes, and heart rate at the 15th, 25th, 30th, 35th and 40th minutes were observed higher in N group when compared to the E group. In esmolol group, it was observed mild bleeding in 23 patients, moderate bleeding in 7 patients. In nicardipine group, it was observed mild bleeding in 11 patients, moderate bleeding in 18 patients, severe bleeding in 1 patient. Surgeon's satisfaction was higher in the esmolol group ($p<0.05$).

Conclusion: It was concluded that both nicardipine and esmolol could be applied for controlled hypotension during the otologic surgery. Surgical bleeding was less and surgeon's satisfaction was higher with the Esmolol group than the Nicardipine group.

***Keywords**: Esmolol, nicardipine, hypotensive anesthesia, tympanoplasty, tympanomastoidectomy*

1. Introduction

Controlled hypotension is a frequently preferred method in terms of reducing intraoperative bleeding, improving visualization of the surgical field, shortening the operation time, and reducing surgical complications. It is defined as reducing the systolic arterial pressure (SAP) to 70-80 mmHg, reducing and maintaining the mean arterial pressure (MAP) to 50-65, or reducing the initial MAP by 30%.[1-3] Controlled hypotension is preferred in oromaxillofacial surgery, endoscopic sinus, septoplasty, or middle ear microsurgery (tympanoplasty, mastoidectomy), spinal surgery, aneurysm, major orthopaedic surgery, prostatectomy, cardiovascular surgery and liver transplant surgery.[4,5] In middle ear surgery, control of the bleeding is essential and controlled hypotension is minimizing bleeding of surgical field.[6] Vasodilators such as sodium nitroprusside and nitroglycerin, β adrenergic blockers such as propranolol and esmolol, calcium channel blockers such as nicardipine, inhalation anaesthetics such as sevoflurane, isoflurane, desflurane, opioids such as remifentanil and fentanyl can be used for this purpose.[4-11] Esmolol is a highly cardioselective β1-blocker with rapid onset and short duration of clinical effects.[12] Its clearance is not dependent on renal or hepatic function because it is rapidly metabolized by plasma esterases. Nicardipine is another short-acting calcium channel blocker that has been found to be useful in controlling hemodynamics during intubation, intraoperatively, or during extubation.[13] Nicardipine has minimal dromotropic effect and has coronary and cerebral vasodilator activity.[14]

In our study, we aimed to evaluate the effects of controlled hypotension induced by esmolol and nicardipine on cerebral oxygenation, hemodynamics, intraoperative bleeding, surgical satisfaction and recovery in a prospective, randomized, controlled manner in

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patients scheduled for tympanoplasty and tympanomastoidectomy between July 2020 and July 2021. Nevertheless, we hypothesized that nicardipine would have positive effects on cerebral oxygenation.

2. Materials And Methods

Our study was carried out between 10 July 2020 and 10 July 2021 in Cukurova University Balcalı Hospital Central Operating Room. Sixty ASA I-II patients aged between 18-65 years who were to undergo endoscopic tympanoplasty or tympanomastoidectomy surgery were included in the study in a randomized and double-blind method. Written and verbal consents of the patients were obtained. Patients who were ASA III-IV, under 18 years of age, over 65 years of age, obese, pregnant, using anticonvulsant and antiarrhythmic drugs, having cerebrovascular disease, hypertension and cardiovascular problems, pulmonary, renal and hepatic disease, malignancy, a history of bleeding disorders or using anticoagulant drugs, having fever, having active infection and those who did not agree to participate in the study were excluded from the study.

Apfel scoring was used to determine the risk of postoperative nausea and vomiting.[15] PCR test for COVID-19 was performed to all cases two days before the operation. Demographical data of the patients were recorded.

The patients were admitted to the operating room without premedication and after venous access obtained 0.9% NaCl (5-7 ml/kg/hour) infusion was performed. Electrocardiogram (ECG), SAP, diastolic arterial pressure (DAP), MAP, heart rate (HR), peripheral oxygen saturation (SpO2) monitorization were performed to all patients. Non-invasive blood pressure values were measured three times before the induction, and the mean of these values was noted as baseline values. Before the induction of anaesthesia, Near-infrared spectroscopy (NIRS) probes were placed on the bilateral frontal region to measure the cerebral oxygen saturation (INVOS, Covidien, Somanetics, Troy, MI). NIRS values measured from the right and left frontal region were recorded as baseline.

Anesthesia induction was performed with propofol 2-2.5 mg/kg, remifentanil 0.5 µg/kg and rocuronium 0.6 mg/kg. Respiratory rate was adjusted to keep tidal volume of 6-7 mL/kg and end-tidal CO_2 values between 30-35 mmHg in mechanical ventilation. Anaesthesia was maintained with O_2/N_2O mixture 40%/60% and sevoflurane 2%. Low-dose remifentanil (0.03 µg/kg/min) infusion continued till the end of surgery. The depth of anesthesia was adjusted to an end-tidal MAC (EtMAC) value of 1-1.3 MAC. The remifentanil infusion dose was kept constant. Before placing the tympanic membrane graft, N_2O inhalation was stopped and ventilation was provided with O_2/air mixture 40%/60%.

Patients were divided into 2 groups at the 10th minute after induction. Power analysis was not applied in this study, and all patients who underwent tympanoplasty or tympanomastoidectomy surgery in our centre within 1 year were evaluated for eligibility for the study and assigned to groups with the 1-1 method.

Group N (n:30); The group which applied Nicardipine infusion. It was started with 1 µg/kg/min and the dose was increased at 5 minutes intervals until reaching the target is reached, maximum dose was 5 µg/kg/min.

Group E (n:30); The group which applied Esmolol infusion. It was started by 50 mcg/kg/min and the dose was increased at 5 min intervals until the target is reached, maximum dose was 300 mcg/kg/min.

During the operation, hemodynamic data of the patients (SAP, DAP, MAP, HR), SpO_2, $EtCO_2$ right and left cerebral NIRS values were recorded with 5 min intervals. It is aimed that the mean arterial pressure values are 30% less than the baseline values for controlled hypotension. If the mean arterial pressure was higher than the targeted values for more than 5 minutes, it was planned to increase the infusion doses by titration in both groups. If the mean arterial pressure was lower than the targeted value for more than 5 minutes, it was also planned to reduce the infusion drug doses by titration, to administer intravenous bolus fluid. If HR was less than 45 beats/min for more than 2 minutes, it was accepted as bradycardia. it was planned to reduce the drug dose and administered 0.5 mg atropine sulphate intravenous in case of inadequate response.

It was accepted as cerebral desaturation criterion if the reduction of rSO_2 (regional oxygen saturation) was more than 20% from baseline or it was more than 3000 seconds when desaturation time and the product of the rSO_2 value obtained by subtracting the 50 were multiplied. In this case, it was planned to perform same order as Denault et al.[16] (respectively, checking NIRS probes and patients head position; volume replacement and vasopressor administration). In addition, it was planned to increase the NIRS values by increasing FiO_2 and cerebral blood flow by optimizing the end-tidal CO_2 value.

All operations were performed by the same surgeon. Five step bleeding scale was used to check the amount of bleeding in the surgical region during the operation and the amount of bleeding was recorded with this scale.

0: No bleeding
1:Mild bleeding, doesn't require aspiration
2:Mild bleeding, rarely requires aspiration
3:Minor bleeding requires frequent aspiration, the operation site can be seen for a few seconds after the aspiration.
4:Often requires aspiration, operation site can be seen only by means of aspiration
5:Major bleeding, continuous aspiration is required; the surgery can be performed difficultly.

Surgical satisfaction was asked to the surgeon evaluate after the operation. It was evaluated as "poor, fair, good, and excellent". All patients were received tramadol 2 mg/kg as an analgesic at least 30 minutes before end of the operation. Atropine sulfate 0.01-0.02 mg/kg and neostigmine 0.05-0.07 mg/kg were administered intravenously for reversal of neuromuscular blockage.

Patients were extubated when the tidal volume achieve the minimum 3ml/kg and oxygen saturation >96% in room air. Durations of the operation, anaesthesia, extubation time and recovery time of all patients were recorded. It was planned to administer intravenous ondansetron in case of persistent, moderate or severe nausea and vomiting in PACU (Post-anaesthesia Care Unit). The patients' length of stay in PACU and possible side effects (hypotension, hypertension, nausea, vomiting, insufficient analgesia, etc.) were recorded. Patients were evaluated according to the Postoperative Modified Aldrete scoring system. Paracetamol (1000 mg) was administered intravenously as a rescue analgesic to the patients when the visual analogue scale >4 in PACU. Patients with an Aldrete score >9 were sent to the Ear-Nose-Throat service.[17]

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board on 3th July, 2020 (approval number: 101)

2.1. Statistical analyses

SPSS (Statistical Package for the Social Sciences) 23.0 package program was used for the statistical analysis of the data. Descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) were used in the evaluation the research data. Shapiro-Wilk test was used to find if the continuous measurements conform to normal distribution. Mann-Whitney U test was used for the comparison of two groups of data not showing normal distribution. Pearson Chi-Square test, Fisher-Freeman-Halton Exact test and Fisher's Exact test were used in the comparison of categorical expressions. Statistical significance level was taken as 0.05 in all tests.

3. Results

There was no statistically difference in demographic data (age, gender, body weight, ASA scores) (p>0.05) Demographical and recovery data were presented in Table 1. It was seen that the SAP values at the 70th minute (p=0.045) and the DAP values at the 15th minute (p= 0.013) and 75th minutes (p=0.021) were higher in the Group N than in the Group E (p=0.045). In the Group N, it was determined that the target MAP was reached in a later period after the infusion. Mean arterial pressure values in the Group N were higher at the 15th minute (p=0.024), at the 70th minute (p=0.025) and 80th minute (p=0.045) than in the Group E (p<0.05). Nicardipine dose was increased up to maximum 4µg/kg/min in order to reach the target MAP in the patients. Systolic and mean arterial blood pressures during anesthesia was presented in Figure 1. It was found that this dose was up to maximum 120µg/kg/min in the Group E. Severe hypotension (MAP <55 mmHg) was observed in six patients in both groups. Intravenous bolus of norepinephrine (4 µg) was administered to these patients. A second bolus dose was required in 2 patients in the Group E and in 1 patient in the Group N. No patients required norepinephrine infusion. HR values at 15th, 25th, 30th, 35th and 40th min in the Group N were higher than in the Group E. (p=0.026, p=0.031, p=0.032, p=0.026, p=0.011) Intraoperative heart rates were presented in Figure 2. The incidence of bradycardia and hypotension in the groups were presented in Table 2.

Table 1

Demographical and Recovery Data

	Group E (n=30) (n, %)	Group N (n=30) (n, %)	Total (n=60) (n, %)	p
ASA				
I	12 (40)	18 (60)	30 (50)	0.121
II	18 (60)	12(40)	30 (50)	
Gender				
M	16 (53.3)	17 (56.7)	33 (55)	0.795
F	14 (46.7)	13 (43.3)	27 (40)	
Age (year, min-max)	48 (19-69)	45.5 (18-67)	47 (18-69)	0.450
Body weight (kg, min-max))	76 (51-100)	73.5 (55-114)	74 (51-113)	0.258
Duration of Anaesthesia	87.5 (50-212)	85 (40-185)	85.5 (40-212)	0.668
Duration of Surgery	81.5 (46-200)	79 (35-178)	80 (35-200)	0.706
Duration of Extubation	3 (1-10)	3 (1-6)	3 (1-10)	0.634
Duration of Recovery	3 (1-7)	3 (1-10)	3 (1-10)	0.312
Duration of staying in PACU	18.5 (10-30)	20 (15-30)	20 (10-30)	0.108
Postoperative Aldrete Recovery Score	10 (9-10)	10 (9-10)	10 (9-10)	0.394

*Data presented as number and percentage, Med: Median, Min: Minimum, Max: Maximum Mann Whitney u test, * p<0.05*

The left NIRS values of the groups at the 20th and 40th min and the right NIRS values at the 25th, 30th, 35th,40th,45th and 60th min was found significantly higher in the Group N than in the Group E. There was no statistically significant difference between the groups in the NIRS values at other times measured (p>0.05). Right and left NIRS values during anesthesia were presented in Figure 3.

Mild surgical bleeding which did not and rarely required aspiration (score 1 and 2) was observed in 23 patients in the Group E and 11 patients in the Group N.

Minor bleeding which required frequent aspiration and operation site could be seen for a few seconds after the aspiration (score 3) was observed 7 patients in Group E and 18 patients in the Group N. Bleeding which required frequent aspiration and in operation site could only be seen by means of aspiration (score 4) was observed in 1 patient in the Group N.

Surgical satisfaction was evaluated by the surgeon who performed the surgery. The rate of surgical satisfaction as "good and excellent" was higher in the Group E (38.33%) than in the Group N (18.34%) (p=0,003).

Table 2

The Incidence of Bradycardia and Hypotension in the Groups

	Group E (n=30)	Group N (n=30)	Total (n=60)	p
	n(%)	n(%)	n(%)	
Bradycardia				
Yes	2(6.7)	0(0)	2 (3.3)	0.150
Hypotension				
No	9 (30)	6 (20)	15 (25)	0.371

Table 3

Perioperative Data about Nausea and Vomiting

	Group E (n=30)	Group N (n=30)	Total (n=60)	p
	n(%)	n(%)	n(%)	
Apfel Score				
Low risk	6 (20.3)	4 (13.3)	10 (16.7)	0.530
Moderate risk	15 (50)	13 (43.3)	28 (46.7)	
High risk	9 (30.0)	13 (43.3)	22 (36.7)	
Postoperative Nausea and Vomiting				
No	13 (43.3)	18 (60)	31 (51.7)	0.219
Mild	15 (50)	11 (36.7)	26 (43.3)	
Moderate	2 (6.7)	0 (0)	2 (3.3)	
Severe	0 (0)	1 (3.3)	1 (1.7)	
Antiemetic				
Yes	9(30)	10(33.3)	19(31.7)	
No	21(70)	20(66.7)	41(68.3)	NA

** p<0,05, chi-square test, NA: p value could not be calculated.*

Figure 1

Systolic and Mean Blood Pressures in Groups Gr E= Group Esmolol, Gr N= Group Nicardipine

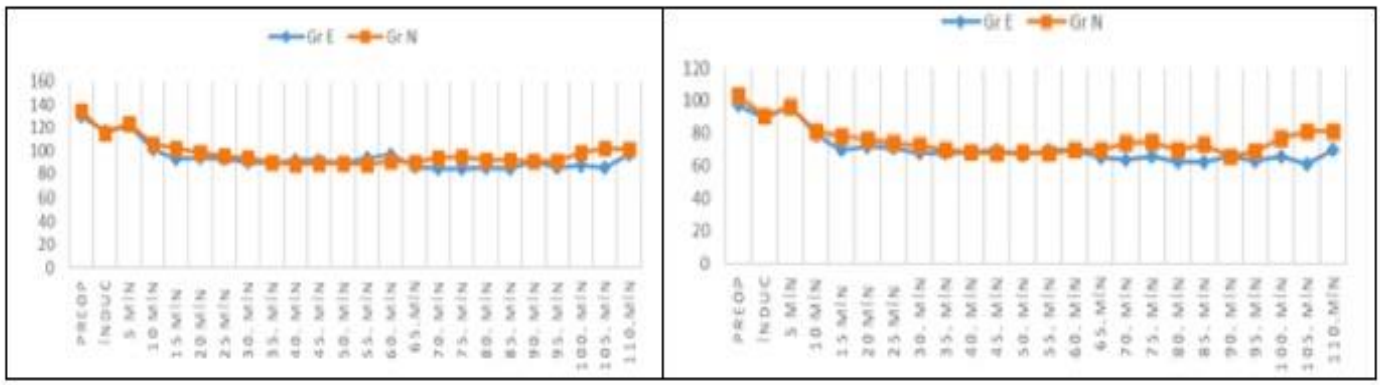


Figure 2

Heart Rates during Anesthesia Gr E= Group Esmolol, Gr N= Group Nicardipine

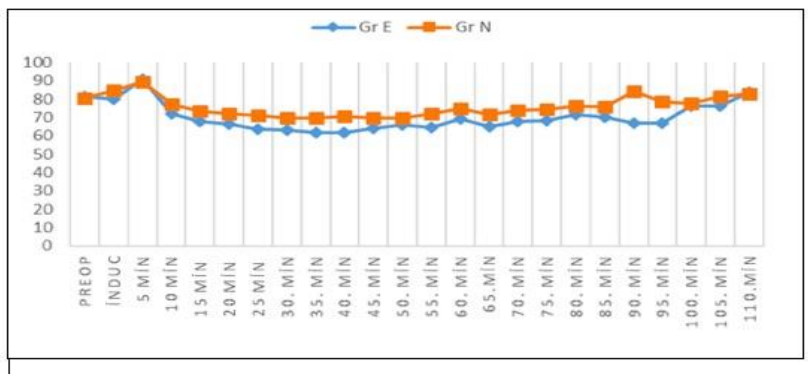
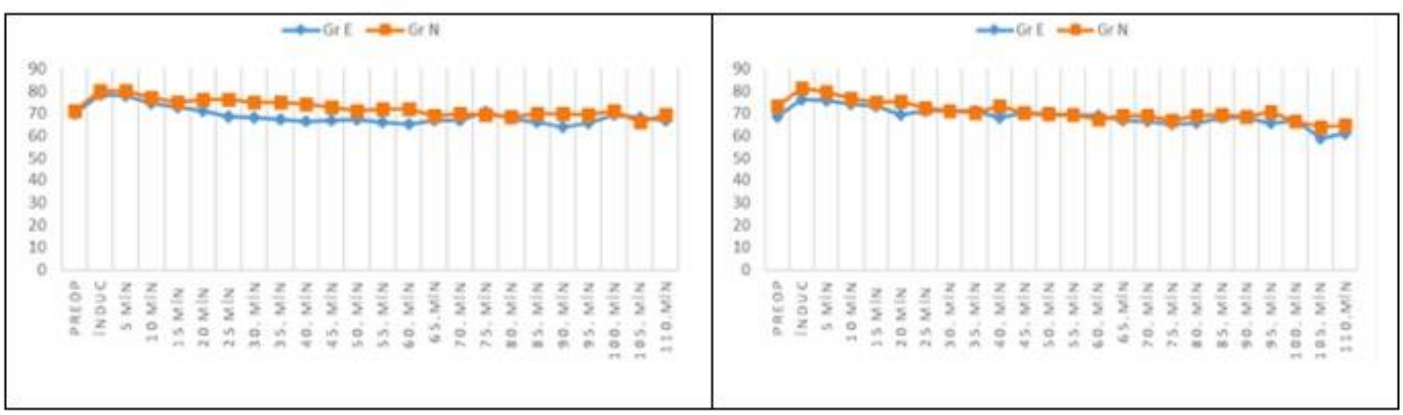


Figure 3

Right and Left NIRS values during Anesthesia Gr E= Group Esmolol, Gr N= Group Nicardipine, NIRS= Near İnfrared spectroscopy



There was no significant difference between the anaesthesia and surgery durations, extubation time, recovery time, length of staying in the recovery room and postoperative Modified Aldrete Scores of the groups. Severe bradycardia was observed in two patients in the Esmolol group. No difference was observed between two groups in terms of postoperative hypotension (p>0.05). Five patients in each group required additional analgesic (paracetamol 1000 mg). Mild postoperative nausea and vomiting were observed in 15 patients in the Esmolol group and in 11 patients in the Nicardipine group. Moderate nausea and vomiting were observed in 2 cases in the Esmolol group, and severe nausea and vomiting were observed in 1 case in the Nicardipine group. (Table 3) Antiemetic (ondansetron 4 mg) was administered to 9 patients in the Group E and 10 patients in the Group N (p>0.05).

4. Discussion

In our study, we investigated to the effect of nicardipine and esmolol on cerebral oxygenation, hemodynamics, bleeding in the surgical region, surgeon satisfaction and recovery during hypotensive anesthesia. We measured higher NIRS values in patients receiving nicardipine than in those receiving esmolol, but we did not observe cerebral desaturation in any patient. Additionally, we found that esmolol can provide better hemodynamic stability, surgeon satisfaction and less surgical bleeding during hypotensive anesthesia in endoscopic tympanoplasty and tympanomastoidectomy surgery. It is not clear about what the target value is in controlled hypotension. Erdem et al.[18] aimed MAP as 50-60 mmHg in ASA I patients who underwent rhinoplasty. Degaute et al.[10] accepted systolic blood pressure of 80 mmHg as the target in 30 ASA I-II patients in their study on tympanoplasty surgery and reported that combination of propofol and remifentanil reduces middle ear blood flow, provides better surgical vision and is a good option for creating hypotension in tympanoplasty surgery.

In various studies, it was shown that the volume of bleeding was less in the hypotension group compared to the normotensive group. Kol et al.[19] reported that esmolol or dexmedetomidine limit the volume of bleeding in operation side in desflurane anaesthesia. Salman et al.[20] observed that esmolol provides better surgical bleeding control and less blood and fluid replacement.

In our study, hemodynamic parameters were found to be similar, except that the MAP values were higher at the 15th, 70th and 80th minutes and the heart rate was higher at the 15th, 25th, 30th, 35th and 40th minutes in the Group N. We attributed this result to nicardipine vasodilation effect. Besides heart rates were higher in Group N than Group E, we assumed that this result is conclusion of stimulation of the sympathetic nervous system with Nicardipine.[21] Hypotension, haemorrhage, ischemia, pH imbalances, and temperature variables can greatly affect tissue oxygenation. It is important to remember that tissue perfusion may not correlate with changes in blood pressure and maintain the oxygenation of the brain tissue during controlled hypotension. Evidence suggests that cerebral tissue desaturation may occur undetected in the presence of normal vital signs. Therefore, it is important to monitoring of brain tissue oxygenation during the hypotension. One of the best indicators of cerebral perfusion is NIRS monitoring which shows regional brain tissue oxygenation.[22-28] Low values always mean a failure of brain perfusion and oxygenation and increased oxygen demand. Cox et al.[29] reported that the desaturation is correlated with intraoperative blood pressure in shoulder arthroscopy performed on sitting position.

Shear et al.[30] reported that controlled hypotension range of 55-65 mmHg has no effect on regional cerebral oxygen saturation in pediatric patients. Similarly, Salman et al.[20] emphasized that controlled hypotension induced by esmolol does not affect regional cerebral oxygen saturation in myomectomy operation. Erdem et al.[18] consider a decrease of more than 20% in cerebral oxygenation as desaturation in rhinoplasty surgery. Besides, Al-Rawi et al.[31] showed that a 13% decrease in saturation is an indicator of cerebral ischemia.

In our study, it was found that right and left cerebral oxygenation is preserved in both groups during controlled hypotension induced by Esmolol and Nicardipine. It was determined that NIRS values were higher in the nicardipine group during periods of high heart rate. This result was thought to be related to the increased heart rate, myocardial contractility, cardiac output and cerebral blood flow due to Nicardipine. No desaturation was observed in NIRS measurements. This was accepted as the preservation of cerebral perfusion.

There are studies in the literature suggesting that Nicardipine increases surgical bleeding. Hersey SL et al.[32] reported that nicardipine caused more bleeding than nitroprusside in spinal fusion surgery (761 +/- 199 mL and 1297.5 +/- 264 mL). In our study, it was observed bleeding that required frequent aspiration in 7 patients in the Group E and in 18 patients in the Group N a major bleeding that required frequent aspiration in 1 patient in the Nicardipine group. This result was associated with the vasodilation effect of Nicardipine. At the same time, surgical satisfaction was determined better (good and very good) in esmolol group. We thought it is because of the provision of a bloodless surgical field.

The groups were comparable in terms of anesthesia, surgery, extubation and recovery times. In the early postoperative period, bradycardia was encountered in two patients in the esmolol group.

There were some limitations of the present study. Firstly, our study was conducted during the COVID-19 pandemic. Therefore, it was carried out with a limited number of patients. The study could have been conducted with a larger group of patients. Second, arterial blood pressures could have been followed by placing arterial line but it was not performed because of overcosting. Third, intraoperative and postoperative urine follow-up and renal functions of the patients could have been monitored. Fourth, comparisons could be made by choosing non-medicated normotensive patients as the control group.

5. Conclusion

In conclusion, it was considered that both nicardipine and esmolol can be administered in controlled hypotension in sevoflurane-remifentanil anesthesia, cerebral oxygenation was maintained at applied nicardipine or esmolol doses and no desaturation was observed. Esmolol caused less surgical bleeding and more surgical satisfaction than nicardipine. The monitoring rSO2 with NIRS technology may be a valuable tool to assess the controlled hypotension on adult patients having tympanoplasty and tympanomastoidectomy surgery.

Statement of ethics

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board on 3th July, 2020 (approval number: 101)

Source of Finance

The authors declare that they have received no financial support for this study

Conflict of interest statement

The authors declare that they have no conflict of interest.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request. https://tez.yok.gov.tr/UlusalTezMerkezi/TezGoster?key=v7BkNnnepTnbhn8rNR77La_VD6-jPmtvIG0rNuBFypVXZTzHzCYL8bv3QE832R_a

References

1.Barak M, Yoav L, Abu el-Naaj I. Hypotensive Anesthesia versus Normotensive Anaesthesia during Maxillofacial Surgery: A review of the Literature. The scientific W Lindop MJ. Complications and morbidity of controlled hypotension. Br J Anaesth. 1975;47:799-803. https://doi.org/10.1155/2015/480728

2.Moreno DH, Cacione DG, Baptista-Silva JC. Controlled hypotension versus normotensive resuscitation strategy for people with ruptured abdominal aortic aneurysm. Cochrane Database Syst Rev 2018;6:CD011664.5. https://doi.org/10.1002/14651858.CD011664.pub3

3.Upadhyay SP, Samant U, Tellicherry SS, Mallik S, Saikia PP, Mallick PN. Controlled hypotension in modern anaesthesia: a review and update. International Journal of Biological & Pharmaceutical Research 2015;6:532-42.

4.Degoute CS. Controlled hypotension: a guide to drug choice. Drugs. 2007;67:1053-76. https://doi.org/10.2165/00003495-200767070-00007

5.Testa LD, Tobias JD. Pharmacologic Drugs for Controlled Hypotension. J of Clin Anesthesia. 1995;7:326-37. https://doi.org/10.1016/0952-8180(95)00010-f

6. Cantarella G, Camera GL, Di Marco P, Grasso DC, Lanzafame B. Controlled hypotension during middle ear surgery: hemodynamic effect of remifentanil vs nitroglyserin. Ann Ital Chir. 2018;89:283-6.

7.Alkan A, Honca M, Alkan A, Gülec H, Horasanlı E. The efficacy of esmolol, remifentanil and nitroglycerin in controlled hypotension for functional endoscopic sinus surgery. Braz J Otorhinolaryngol. 2021;87:255-9. https://doi.org/10.1016/j.bjorl.2019.08.008

8.Toivonen J, Virtanen H, Kaukinen S. Deliberate hypotension induced by labetalol with halothane, enflurane or isoflurane for middle-ear surgery. Acta Anaesthesiol Scan.1989;33;283-9. https://doi.org/10.1111/j.1399-6576.1989.tb02909.x

9.Pilli G, Güzeldemir ME, Bayhan N. Esmolol for hypotensive anesthesia in middle ear surgery. Acta Anaesthesiol Belg. 1996;47:85-91.

10. 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. https://doi.org/10.1007/BF03019809

11.Komatsu R, Turan AM, Orhan-Sungur M, McGuire J, Radke OC, Apfel CC. Remifentanil for general anaesthesia: a systematic review. Anaesthesia. 2007;62:1266-80. https://doi.org/10.1111/j.1365-2044.2007.05221.x

12.Poveda-Jaramillo R, Monaco F, Zangrillo A, Landoni G. Ultra-Short-Acting β-Blockers (Esmolol and Landiolol) in the Perioperative Period and in Critically Ill Patients. J Cardiothorac Vasc Anesth. 2018;32(3):1415-25. https://doi.org/10.1053/j.jvca.2017.11.039

13.Kovac AL, McKinley C, Tebbe CJ, Williams C. Comparison of nicardipine versus placebo to control hemodynamic responses during emergence and extubation. J Cardiothorac Vasc Anesth. 2001;15(6):704-9. https://doi.org/10.1016/s1053-0770(01)70077-8

14.Gaab MR, Czech T, Korn A. Intracranial effects of nicardipine. Br J Clin Pharmacol. 1985;20 Suppl 1(Suppl 1):67S-74S. https://doi.org/10.1111/j.1365-2125.1985.tb05145.x

15.Apfel CC, Greim CA, Haubitz I, Goepfert C, Usadel J, Sefrin P et al. A risk score to predict the probability of postoperative vomiting in adults. Acta Anaesthesiol Scand. 1998;42:495-501. Https://doi.org/10.1111/j.1399-6576.1998.tb05157.x

16.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. https://doi.org/10.1177/1089253207311685

17. Aldrete JA. Modifications to the postanesthesia score for use in ambulatory surgery. Journal of PeriAnesthesia Nursing. 1998;13:148-55. https://doi.org/10.1016/s1089-9472(98)80044-0

18.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. https://doi.org/10.1007/s10877-015-9768-6

19.Kol IO, Kaygusuz K, Yildirim A, Dogan M, Gursoy S, Yucel E et al. Controlled hypotension with desflurane combined with Esmolol or dexmedetomidine during tympanoplasty in adults: A double-blind, randomized, controlled trial. Curr Ther Res Clin Exp. 2009;70:197-208. https://doi.org/10.1016/j.curtheres.2009.06.001

20.Salman SA, Shebab HA. Esmolol hypotension maintains tissue perfusion during myomectomy judged by Masimo monitoring of regional cerebral oxygen saturation and pleth variability index Egyptian Journal of Anaesthesia. 2019;34:49-53. https://doi.org/10.1016/j.egja.2018.03.005

21.Shin S, Lee JW, Kim SH, Jung YS, Oh YJ. Heart rate variability dynamics during controlled hypotension with nicardipine, remifentanil and dexmedetomidine. Acta Anaesthesiol Scand. 2014;58:168-76. https://doi.org/10.1111/aas.12233

22.Ghosh A, Elwell C, Smith M. Review article: cerebral near-infrared spectroscopy in adults: a work in progress. Anesth Analg. 2012;115:1373-83. https://doi.org/10.1213/ANE.0b013e31826dd6a6

23.Murkin JM, Arango M. Near-infrared spectroscopy as an index of brain and tissue oxygenation. Br J Anaesth. 2009;103:3-13. https://doi.org/10.1093/bja/aep299

24.Toraman F, Erkek E, Güçlü P, Sayın J, Arıtürk C, Ökten EM. et al. Near İnfra Red Spektroskopisi (NIRS) Gerçekten Doku Saturasyonunu Ölçüyor mu? Acıbadem Üniversitesi Sağlık Bilimleri Dergisi. 2013;4:115-7.

25.Slater JP, Guarino T, Stack J, Vinod K, Bustami RT, Brown JM, et al. Cerebral oxygen desaturation predicts cognitive decline and longer hospital stay after cardiac surgery. Annals of Thoracic Surgery. 2009;87:36-44. https://doi.org/10.1016/j.athoracsur.2008.08.070

26.Rigamonti A, Scandroglio M, Minicucci F, Magrin S, Carozzo A, Casati A. A clinical evaluation of near- infrared cerebral oximetry in the awake patient to monitor cerebral perfusion during carotid endarterectomy. J Clin Anesth. 2005;17:426-30. https://doi.org/10.1016/j.jclinane.2004.09.007

27.Kim MB, Ward DS, Cartwright CR, Kolano J, Chlebowski S, Henson LC. Estimation of jugular venous O2 saturation from cerebral oximetry or arterial O2 saturation during isocapnic hypoxia. J Clin Monit Comput. 2000;16:191-9. https://doi.org/10.1023/a:1009940031063

28.Trafidło T, Gaszyński, T, Gaszyński W, Nowakowska Domagała, K. Intraoperative monitoring of cerebral NIRS oximetry leads to better postoperative cognitive performance: A pilot study. Int Journal of Surgery. 2015;16:23–30. https://doi.org/10.1016/j.ijsu.2015.02.009

29.Cox RM, Jamgochian GC, Nicholson K, Wong JC, Namdari S, Abboud JA. The effectiveness of cerebral oxygenation monitoring during arthroscopic shoulder surgery in the beach chair position: a randomized blinded study. J Shoulder Elbow Surg. 2018;27(4):692-700. https://doi.org/10.1016/j.jse.2017.11.004

30.Shear T, Tobias JD. Cerebral oxygenation monitoring using near infrared spectroscopy during controlled hypotension. Paediatr Anaesth. 2005;15:504-8. https://doi.org/10.1111/j.1460-9592.2005.01495.x

31.Al-Rawi PG. Near infrared spectroscopy in brain injury: today's perspective. Acta Neurochir Suppl. 2005;95:453-7. https://doi.org/10.1007/3-211-32318-x_93

32.Hersey SL, O'Dell NE, Lowe S, Rasmussen G, Tobias JD, Deshpande JK et al. Nicardipine versus nitroprusside for controlled hypotension during spinal surgery in adolescents. Anesth Analg. 1997;84:1239-44. https://doi.org/10.1097/00000539-199706000-00012