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CLINICAL RESEARCH

Effect of anesthesia induction on cerebral tissue oxygen saturation in hypertensive patients: an observational study☆

Yasin Taşkaldıran *, Özlem Şen, Tuğba Aşkın, Süheyla Ünver

Anesthesiology and Reanimation, Health Sciences University Dr. Abdurrahman Yurtaslan Oncology Health Application and Research Center, Ankara, Turkey

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KEYWORDS
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Abstract
Objective: In hypertensive patients, the autoregulation curve shifts rightward, making these patients more sensitive than normotensive individuals to hypotension. Hypotension following the induction of anesthesia has been studied in normotensive patients to determine its effects on brain tissue oxygenation, but not enough studies have examined the effect of hypotension on brain oxygenation in hypertensive patients. The current study aimed to use near-infrared spectroscopy to evaluate brain tissue oxygen saturation after the induction of anesthesia in hypertensive patients, who may have impaired brain tissue oxygen saturation.
Methods: The study included a total of 200 patients aged > 18 years old with ASA I–III. Measurements were taken while the patient was breathing room air, after the induction of anesthesia, when the lash reflex had disappeared following the induction of anesthesia, after intubation, and in the 5th, 10th, and 15th minutes of surgery. The patients were divided into nonhypertensive and hypertensive groups.
Results: There was a significant difference in age between the groups (p = 0.000). No correlation was found between cerebral tissue oxygen saturation and age (r = 0.015, p = 0.596). Anesthesia induction was observed to decrease mean arterial blood pressure in both groups (p = 0.000). Given these changes, there was no significant difference in brain tissue oxygen saturation between the nonhypertensive and hypertensive groups (p > 0.05).
Conclusion: There was no difference between hypertensive and normotensive groups in terms of the change rates in cSO_2 values. However, there was a difference between the groups in terms of cSO_2 values.

☆ Study conducted at the ''Anesthesiology and Reanimation, Health Sciences University Dr. Abdurrahman Yurtaslan Oncology Health Application and Research Center''.

* Corresponding author.
E-mail: yasintaskaldiran@gmail.com (Y. Taşkaldıran).

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Introduction

During anesthesia induction, hypotension occurs and may affect the blood supply to the organs.[1] The cerebral autoregulation mechanism protects the blood supply from hypotension. When an individual's mean blood pressure is between 60 and 150 mmHg, cerebral blood flow remains constant.[2] However, when this autoregulation changes, hypotension may lead to a decrease in cerebral blood flow, which may then cause a decrease in cerebral oxygenation.[3] Cerebral oxygenation can be measured using a noninvasive method, the Near-Infrared Spectroscopy (NIRS). In hypertensive patients, there is a change in cerebral autoregulation, and this alteration causes the cerebral autoregulation curve to shift rightward.[4] Hypotension due to anesthesia induction has been studied in normotensive patients in terms of its effects on brain tissue oxygenation, but to the best of our knowledge, not enough studies have examined the effect of hypotension on brain oxygenation in hypertensive patients. The current study aimed to use NIRS to evaluate brain tissue oxygen saturation after the induction of anesthesia in hypertensive patients, who may have impaired brain tissue oxygen saturation.

Methods

Two hundred patients who were aged over 18 years old, with American Society of Anesthesiologists (ASA) status I–III, and scheduled to undergo elective general anesthesia, were prospectively enrolled in the study after ethics committee approval (local ethics committee number: 2017–12/6, trial registry nº ACTRN12618000506291) was obtained, and the patients signed informed consent forms. Patients who represented emergency cases, were pregnant, had unstable hemodynamics, had cerebrovascular disease, underwent cranial surgery, had known carotid disease or previous carotid surgery, were allergic to the drugs of interest in the current study, or did not want to participate were not included in the study. In addition, patients who had a blood pressure > 180/90 mmHg were also excluded.

Oral intake was stopped 8 hours before the operation. Patients were given fluids at 100 $mL.h^{-1}$ until the operation. Prior to the operation, 0.01 $mg.kg^{-1}$ intravenous (IV) midazolam premedication was administered. In the operating room, standard monitoring of the patients was performed, including electrocardiography, noninvasive blood pressure, capnography, and pulse oximetry. In addition, two NIRS sensors were placed on the frontal region of the patients. Cerebral tissue oxygen saturation (cSO_2) measurements were obtained using an INVOSTM 5100C (Medtronic, Minnesota, USA) cerebral/somatic oximeter. Preoxygenation was induced by asking the patient to take three deep breaths of 100% O_2 (total flow: 6 $L.min^{-1}$) prior to the induction of anesthesia. The induction of general anesthesia was performed using 2 $mg.kg^{-1}$ propofol, 0.7–0.9 $mg.kg^{-1}$rocuronium, 1 $mg.kg^{-1}$ lidocaine and 1 $\mu g.kg^{-1}$ fentanyl and was followed by endotracheal tube placement. There were no pharmacological interventions between anesthesia induction and tracheal intubation. Anesthetic management was ensured using 1 MAC of sevoflurane, 50% O_2 and N_2O. Volume-controlled ventilation was established with a tidal volume: 6 $mL.kg^{-1}$, PEEP: 5 mmHg, I/E: 1/2, and FiO_2: 40% at a frequency of 12 minutes. All patients' Mean Arterial Pressure (MAP), Heart Rate (HR), Peripheral Oxygen Saturation (SpO_2), End-Tidal Carbon Dioxide ($ETCO_2$) and bilateral cSO_2 were measured. The measurement times were as follows: T1 – First measurement in room air; T2 – After the induction of anesthesia; T3 – After orotracheal intubation; T4 – 5 minutes after induction; T5 – 10 minutes after induction; and T6 – 15 minutes after induction. During anesthesia induction and measurements, noxious stimuli were not applied to the patients, and only the cleaning and disinfection procedures were performed.

The patients were divided into two groups. The Hypertensive Group (HT) included patients who were diagnosed with hypertension before surgery and received anti-hypertensive therapy. Hypertension was diagnosed by doctors who followed up the patients; in addition, the diagnosis was checked by health reports. The nonhypertensive group included patients not diagnosed with hypertension.

All data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 24.0 (SPSS Company, Chicago, IL, USA). The Kolmogorov-Smirnov test was used to determine normality of data distribution. Differences between mean values for normally distributed variables were compared by using the Student's *t*-test. For data without normal distribution, Mann Whitney *U* test was performed. Chi-Squared test and Fisher's Exact test were used for categorical data where appropriate. The relationships between the variables were evaluated with Pearson correlation tests. A p-value < 0.05 was considered statistically significant. It was estimated that including 200 patients (100 patients in each group) would provide a power of 94% (α = 0.05, d = 0,5).

Results

A total of 200 patients were evaluated. In terms of age, the patients in the hypertensive group were older. No correlation was found between age and cSO_2 (cSO_2, Right: r = 0.015, p = 0.596; cSO_2, Left: r = 0.022, p = 0.448). There were no differences between the groups in terms of sex (Table 1). The mean length of time to a diagnosis was 8.0 (± 5.8) years. For hypertensive patients, the mean length of time the patients had taken anti-hypertensive drugs prior to surgery was 5.6 (± 2.3) hours. In the hypertension group, 42% of the patients used a single medication, and 58% used double medication (Table 2). After the induction of anesthesia, the mean arterial blood pressure decreased, but it then increased after intubation (p = 0.000). After anesthesia induction, the SpO_2 levels of the patients increased to more than 98%. End-Tidal CO_2 levels did not differ between the groups (p > 0.05) (Figure 1). The differences in MAP and cSO_2 measurements at T2 and T1 were evaluated for all patients. A weak correlation was detected between the MAP and cSO_2 levels (r = 0.287, p = 0.000) (Figure 2). After induction of anesthesia, MAP decreased from 113.1 (±14.5) mmHg to 85.3 (±18.1) mmHg in hypertensive group and from 109.6 (±15.3) mmHg to 87.5 (±17.6) mmHg in nonhypertensive group. The decreased rate of MAP in both groups was over 20%.

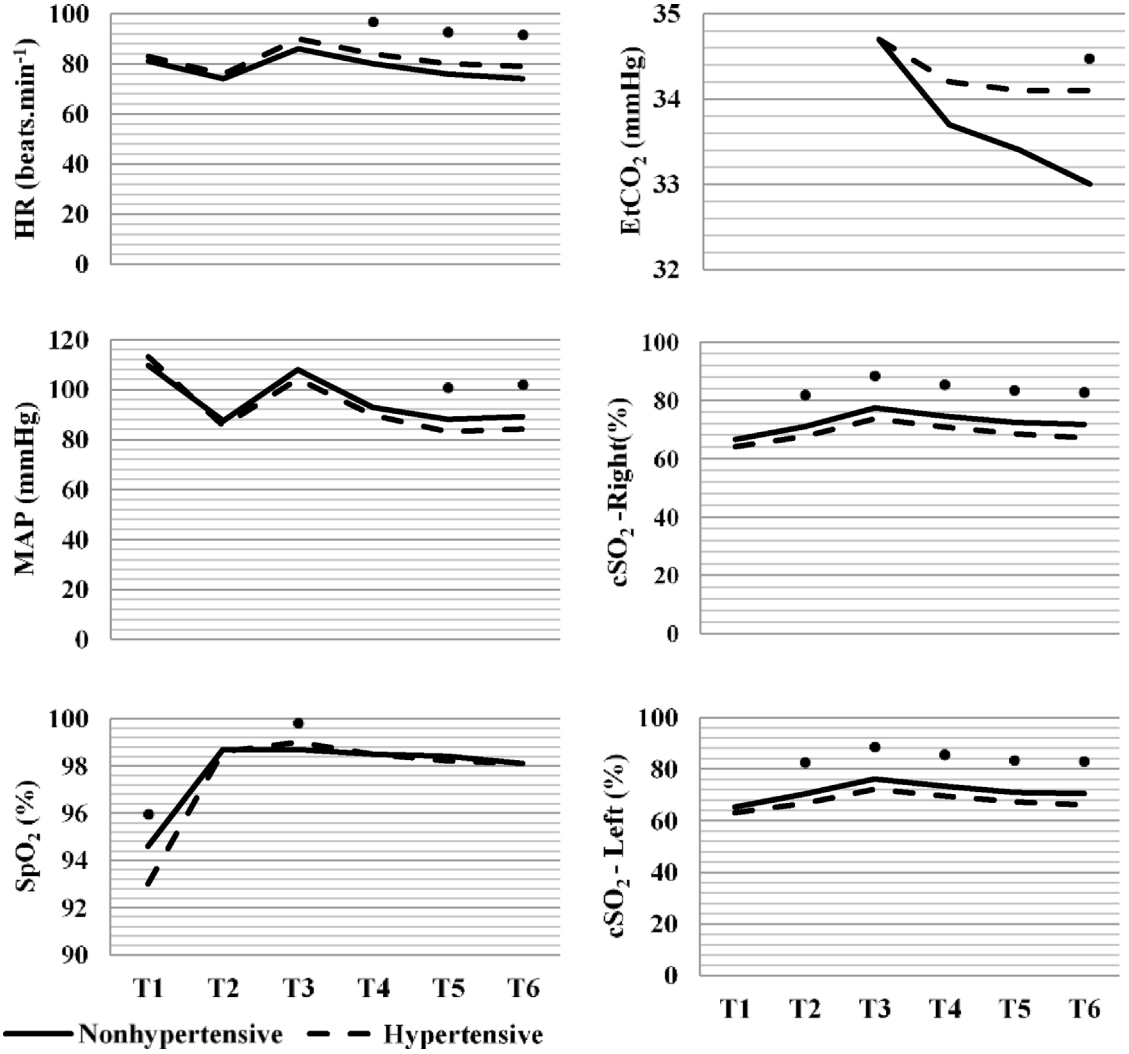

Figure 1 Vital signs: Comparison of nonhypertensive and hypertensive patients. (●) Comparison between the groups of nonhypertensive and hypertensive patients, $p < 0.05$; HR, Heart Rate; MAP, Mean Arterial Pressure; SpO_2, Peripheral Oxygen Saturation; $EtCO_2$, End-Tidal Carbon Dioxide; cSO_2, Cerebral Tissue Oxygen Saturation; T1, First measurement in room air; T2, After the induction of anesthesia; T3, After orotracheal intubation; T4, 5 min after induction; T5, 10 min after induction; T6, 15 min after induction.

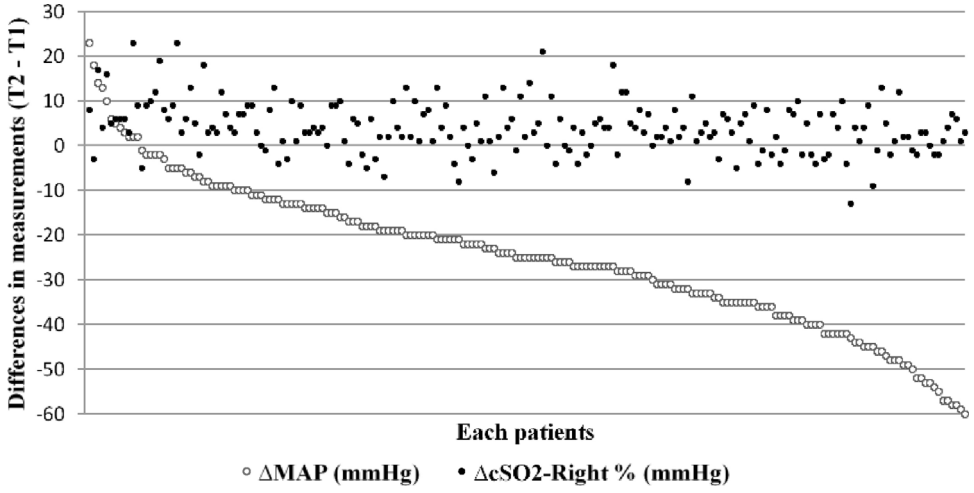

Figure 2 The differences between T2 and T1 among all 200 patients. MAP, Mean Arterial Pressure; cSO_2, Cerebral Tissue Oxygen Saturation.

Table 1 Demographic information.

	Hypertensive (n = 100)	Nonhypertensive (n = 100)	p^a
Patients			
Age (years)	62.5 ± 9.4	49.0 ± 11.1	0.000[b]
Female/Male	76:24	73:27	0.626[c]
ASA (II/III)	60:40	88:12	0.000[c]
Surgery			
Abdominal surgery	46	40	
Modified radical mastectomy	35	39	
Total thyroidectomy	11	11	
Orthopedic surgery	8	5	

ASA, American Society of Anesthesiologists physical status.
[a] $p < 0.05$.
[b] Independent Samples *t*-test.
[c] Chi-square test.

Table 2 Hypertension drugs.

	Class of Drugs	Hypertensive (n = 100)
	CCB	20
Single Drug (42%)	ACE inhibitor	12
	Beta blocker	10
	ARB + Thiazide diuretic	37
Double Drugs	ACE Inhibitor + CCB	12
(58%)	ACE Inhibitor + Thiazide diuretic	6
	ARB + Beta blocker	3

ACE inhibitor, Angiotensin-Converting Enzyme Inhibitor; ARB, Angiotensin-2 Receptor Antagonist; CCB, Calcium Channel Blocker.

Table 3 Comparison of cSO_2 rates of change between the groups.

	Difference between times	Hypertensive (n = 100)	Nonhypertensive (n = 100)	p^a
	T2–T1	3.6 ± 6.5	4.5 ± 5.3	0.310
	T3–T2	6.0 ± 5.5	6.5 ± 4.9	0.553
cSO_2, Right (%)	T4–T3	−2.8 ± 4.9	−2.9 ± 4.0	0.874
	T5–T4	−2.4 ± 3.8	−2.0 ± 3.7	0.443
	T6–T5	−1.5 ± 3.3	−0.7 ± 2.7	0.075
	T2–T1	3.6 ± 5.7	4.9 ± 5.7	0.130
	T3–T2	5.4 ± 5.3	5.9 ± 5.3	0.525
cSO_2, Left (%)	T4–T3	−2.5 ± 4.8	−2.9 ± 4.8	0.577
	T5–T4	−2.2 ± 3.2	−2.3 ± 3.9	0.876
	T6–T5	−1.3 ± 3.8	−0.3 ± 3.3	0.051

cSO_2, Cerebral Tissue Oxygen Saturation; T1, First measurement in room air; T2, After the induction of anesthesia; T3, After orotracheal intubation; T4, 5-min after induction; T5, 10-min after induction; T6, 15-min after induction.
[a] $p < 0.05$, Independent Samples *t*-test.

The cSO_2 values were lower in hypertensive patients than in the nonhypertensive group ($p < 0.05$) (Figure 1). However, there were no differences between the groups in terms of the rate of cSO_2 change ($p > 0.05$) (Table 3).

Discussion

While the limits of cerebral autoregulation are generally known in healthy individuals, they remain vaguely understood in hypertension patients. Animal studies have shown that the autoregulation curve shifts rightward in hypertension. However, in those studies, the ranges for the limits of cerebral autoregulation were wide, and therefore how much the autoregulation curve shifts rightward is not clear.[5–7] This makes the prediction of the oxygen supply to the brain is affected after hypotension in patients with hypertension difficult. Therefore, instantaneous noninvasive methods that enable the prediction of supply to the brain can be useful in operations. For this purpose, it is believed that using NIRS to monitor patients during surgery can be informative regarding the autoregulation of the brain.[8]

However, frequent drops in blood pressure after the induction of anesthesia cause uncertainty regarding cerebral oxygenation. Moreover, drops in blood pressure are seen

more frequently in hypertensive patients than in normotensive patients.[9] In normotensive patients, when cerebral oxygenation was assessed upon a drop in blood pressure, it was found that cerebral oxygenation was maintained.[10,11] But the effect of hypotension on oxygenation after the induction of anesthesia in hypertensive patients is not known.

Propofol causes a decrease in cerebral blood flow.[12] This may affect brain oxygenation when combined with the hypotension that occurs following the induction of anesthesia.[3] However, propofol may preserve cerebral oxygenation due to the depression of cerebral electroencephalographic activity[13] and a decrease in the cerebral metabolic rate.[14] In addition, propofol is also effective in maintaining cerebral autoregulation[15] or masking the relationship between hypotension and cerebral oxygen saturation.[10]

The body's oxygen reserve also affects cerebral oxygenation. With preoxygenation, the SpO_2 levels of patients can be increased to more than 97%.[16] Because we used preoxygenation to increase our patient's SpO_2 levels from 93% to 98%, we might have contributed to the maintenance of cerebral oxygenation by increasing the oxygen reserve.

One of the factors that affects cerebral autoregulation is hypertension treatment, but there are differences among the efficacies of the drugs used in this treatment. For instance, it was found that angiotensin-converting enzyme inhibitors and beta-blockers have only little effect on cerebral blood flow and cerebral autoregulation.[17–19] There is not enough consensus regarding the effects of calcium channel antagonists on cerebral autoregulation and cerebral blood flow. Studies on baboons revealed that there was an increase in cerebral blood flow and no change in cerebral autoregulation,[20] while studies performed in rats showed that cerebral blood flow did not change and that the cerebral autoregulation curve shifted leftward.[21] Due to the differences and uncertainties among the efficacy of the drugs used in hypertension treatment, we did not group the patients according to the anti-hypertensive medication they were using. Nevertheless, it is known that despite the differences among these drugs, with treatment, the cerebral autoregulation curve of these patients verges on that of normotensives.[22,23] We believe that the rates of cerebral tissue oxygenation changes were similar between hypertensive and normotensive patients as a result of this improvement in autoregulation.

Normal cSO_2 levels can be between 55% and 80%, which is a wide range. Thus, it would be useful to monitor the rate of change in measured cSO_2 levels instead of checking whether the measured cSO_2 levels are within the normal range. In this regard, medical intervention is recommended if basal cSO_2 levels drop by 20% or 25% or if the measured levels are below 50%.[24–26] In our study, we found that both groups exhibited parallel cSO_2 changes, and their rates of change in cSO_2 levels were similar (Figure 1). Moreover, the graphs showed that there is a difference between the two groups in terms of cSO_2 levels; however, while this difference was not clinically significant, it was numerically clear. We believe that this is due to the difference in cerebral blood flow caused by hypertension. In a study on this subject, follow-up was performed in hypertensive patients who were treated for 9 years. These follow-ups showed that prefrontal blood flow was lower in hypertensive patients under treatment than in normotensive patients. It appears that hypertension treatment is useful for cerebral autoregulation but unable to prevent blood flow to different areas of the brain.[27]

While blood pressure is one of the important factors affecting cerebral blood flow, it is not the single determining factor for cerebral blood flow in patients whose cerebral autoregulation is maintained. In our study, the correlation between the rate of MAP change and the rate of cSO_2 change was weak. As shown in Figure 2, the changes in cSO_2 levels were not affected by the amount of decrease in MAP. End-organ injury might occur when MAP decreases below 80 mmHg for more than 10 minutes.[28] In our study, the mean MAP did not decrease below 80 mmHg by induction. This may have led to a weak relationship between MAP and cSO_2.

Another factor that affects brain metabolism is age. While aging affects brain metabolism, its effect on cerebral autoregulation is uncertain. Cerebral autoregulation has been shown to be similar between individuals between 50 and 75 years old and younger individuals. There is not enough information on the cerebral autoregulation of individuals over 75 years old.[29] In our study, the cSO_2 changes observed in the older hypertensive group and the normotensive group were found to be similar. Moreover, a weak correlation was detected between age and cSO_2 levels.

Limitations of this study include the observational nature of this study and the recruitment of patients undergoing elective surgery alone, which prevented an investigation of the effect of nonregulated hypertension. Another limitation was the noninvasiveness of the method used to monitor blood pressure. Since the mean MAP value in our study did not decrease below 80 mmHg, this was a limitation to evaluate to brain tissue oxygen saturation levels at lower blood pressure.

Summary

In conclusion, the results of the study demonstrated that hypotensive response to anesthesia induction did not make any difference in terms of the change rates in cSO_2 values in patients receiving antihypertensive therapy when comparing to normotensive patients. However, there was a difference between hypertensive and normotensive groups in terms of cSO_2 values.

Trial registry number

ACTRN12618000506291

Conflicts of interest

The authors declare no conflicts of interest.

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