Changes in Intracerebral Environment During Induction of Anesthesia

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ABSTRACT

Background: Although marked hemodynamic changes do not generally occur during induction of general anesthesia with intravenous anesthetics, the effects of such hemodynamic changes on the intracerebral environment are not well known. We used a near-infrared oxygenation monitor to compare the effects of two intravenous anesthetics on the intracerebral environment.

Material and Methods: We investigated the effects of propofol and thiopental in adult patients according to age and the presence or absence of hypertension. The patients were divided into four groups: propofol in adult patients (PF group), thiopental in adult patients (TP group), thiopental in elder patients (TPE group), and thiopental in elder patients with hypertension (TPEH group). We measured the noninvasive blood pressure, pulse rate, oxyhemoglobin (oxy-Hb) level, deoxyhemoglobin (deoxy-Hb) level, and total hemoglobin (total-Hb) level in all patients.

Results: The maximum oxy-Hb level occurred 2.5 min after spreading the larynx to spray with lidocaine in the PF, TP, and TPE groups (5.1 ± 3.0, 6.8 ± 2.8, and 7.1 ± 2.8 nmol/L, respectively). The minimum deoxy-Hb level occurred 2.5 min after spreading the larynx in the PF group (−1.9 ± 1.8 nmol/L), 2.5 min after intubation in the TP group (−2.6 ± 3.0 nmol/L), and immediately after intubation in the TPE and TPEH groups (−3.9 ± 2.9 and −1.9 ± 1.4 nmol/L, respectively). The maximum total-Hb level occurred 2.5 min after spreading the larynx in the PF group (1.9 ± 5.0 nmol/L), immediately after intubation in the TP group (2.3 ± 3.1 nmol/L), 2.5 min after spreading the larynx in the TPE group (3.7 ± 3.6 nmol/L), and 2.5 min after intubation in the TPEH group (6.7 ± 5.2 nmol/L).

Conclusion: Intravenous anesthetics and changes in blood pressure influence the intracerebral environment during induction of anesthesia.
Introduction

Cerebral autoregulation maintains a constant cerebral blood flow of 50 to 170 mmHg during changes in cerebral perfusion pressure and is a complex process with several mechanisms operating at different rates. There is a rapid dynamic response to changes in pressure pulsations, followed by a slow static response that controls cerebral blood flow in accordance with the new mean pressure that become established after the initial dynamics have settled.

Marked hemodynamic changes do not generally occur during induction of anesthesia. However, such changes may include hypotension following intravenous induction of anesthetics, typically the coadministration of thiopental, propofol, or opioids with volatile anesthetics such as sevoflurane. These drugs depress cerebral metabolism with consequent reductions in oxygen consumption, cerebral blood flow, and intracranial pressure. Conversely, hypertension occurs especially when the larynx is spread with a laryngoscope, facilitating cerebral metabolism. The effects of these hemodynamic changes, particularly hypotension and hypertension, on the intracerebral environment during induction of general anesthesia are not well known.

Near-infrared spectroscopy (NIRS) is a noninvasive monitor to measure the intracerebral environment and is capable of measuring changes in the concentration of intracerebral oxyhemoglobin (oxy-Hb), deoxyhemoglobin (deoxy-Hb), total hemoglobin (total-Hb), and cytochrome oxidase (cyt). We designed this study to compare the effects of propofol and thiopental on the intracerebral environment during induction of general anesthesia by NIRS measurement. The aim of the first part of this study was to compare the effects of propofol and thiopental in adult patients, and the aim of the second part was to compare the effects of thiopental according to age and the presence or absence of hypertension.

Materials and methods

This observational study was approved by the Committee on Clinical Investigation for Human Research at Iwate Medical University.

We studied 32 patients with an American Society of Anesthesiologists physical status of I or II who were scheduled to undergo oral and maxillofacial surgery. The patients were divided into four groups: propofol in adult patients (PF group), thiopental in adult patients (TP group), thiopental in elder patients (TPE group), and thiopental in elder patients with hypertension (TPEH) (Table 1). All patients underwent intravenous administration of atropine sulfate (0.05 mg/kg) and midazolam (0.5 mg/kg) 30 min before admittance to the operating room. Measurements were made with the patients in the supine position. All patients breathed 100% oxygen with a mask for 5 min before induction, and fentanyl was administered in the operating room. The induction anesthetic was administered intravenously. After loss of verbal contact and the eyelash reflex, ventilation was gently assisted with an F circuit using a fresh gas flow of 6 L/min (100% oxygen). We monitored the noninvasive blood pressure (BP), pulse rate (PR), and blood oxygen saturation (SpO2) with a Life Scope 8® (Nihon Kohden, Tokyo, Japan) and changes in the oxy-Hb, deoxy-Hb, total-Hb, and cyt levels with a near-infrared oxygenation monitor (NIRO 500®; Hamamatsu Photonics, Hamamatsu, Japan). The NIRO sensor was placed on opposite sides of the forehead before starting the operation. The holder was secured to the forehead with tape. The NIRO measured the changes in parameters from a baseline that was set at zero at the start of measurement.

All parameters were continuously recorded using a PowerLab 4/25T data acquisition system (ADInstruments, Bella
Vista, Australia). Each parameter immediately before induction (control) was compared with that at induction, 2.5 min after induction, before spreading the larynx to spray with lidocaine, immediately after spreading the larynx, 2.5 min after spreading the larynx, immediately after intubation, 2.5 min after intubation, 5 min after intubation, and 10 min after intubation.

Values are presented as mean ± standard deviation. Intragroup comparisons were made using one-way analysis of variance for repeated measurements followed by Dunnett’s test for multiple comparisons. Differences were considered statistically significant at \( P < 0.05 \).

Results

The changes in invasive BP and PR are shown in Figure 1. In the PF, TP, and TPEH groups, the BP and PR increased immediately after spreading the larynx to spray with lidocaine and immediately after intubation. In the TPE group, the BP and PR exhibited significant differences between immediately before induction (control) and before spreading the larynx, 2.5 min after spreading the larynx, 5 min after intubation, and 10 min after intubation in the TPEH group. In the TPE group, the BP and PR increased from before spreading the larynx to immediately after intubation and decreased from 2.5 to 10 min after intubation; significant differences were observed between the control time point and 5 and 10 min after intubation (Fig. 1).

The maximum oxy-Hb level occurred 2.5 min after spreading the larynx in the PF, TP, and TPE groups (5.1 ± 3.0, 6.8 ± 2.8, and 7.1 ± 2.8 nmol/L, respectively; \( n = 8 \) in each group). In the TPE group, there were significant differences in the oxy-Hb level between the control time point and immediately after spreading the larynx, 2.5 min after spreading the larynx, immediately after intubation, 2.5 min after intubation, 5 min after intubation, and 10 min after intubation. In the TPEH group, the maximum oxy-Hb level occurred 2.5 min after intubation (\( 10.4 ± 5.6 \text{ nmol/L} \) (\( n = 8 \))), and significant differences were observed between the control time point and immediately after intubation, 2.5 min after intubation, and 5 min after intubation (Fig. 2).

The minimum deoxy-Hb level in the PF group occurred 2.5 min after spreading the larynx (-1.9 ± 1.8 nmol/L (\( n = 8 \))), that in the TP group occurred 2.5 min after intubation (-2.6 ± 3.0 nmol/L (\( n = 8 \))), and that in the TPE and TPEH groups occurred immediately after intubation (-3.9 ± 2.9 nmol/L (\( n = 8 \)) and -1.9 ± 1.4 nmol/L (\( n = 8 \)), respectively). There were significant differences the deoxy-Hb level between the control time point and 2.5 min after intubation in the TP group; 2.5 min after spreading the larynx, immediately after intubation, and 2.5 min after intubation in the TPE group; and immediately after intubation in the TPEH group (Fig. 3).

The maximum total-Hb in the PF group occurred 2.5 min after spreading the larynx (1.9 ± 5.0 nmol/L (\( n = 8 \))), that in the TP group occurred immediately after intubation (2.3 ± 3.1 nmol/L (\( n = 8 \))), that in the TPE group occurred 2.5 min after spreading the larynx (3.7 ± 3.6 nmol/L (\( n = 8 \))), and that in the TPEH group occurred 2.5 min after intubation (6.7 ± 5.2 nmol/L (\( n = 8 \))). There were significant differences the total-Hb level between the control time point and immediately after intubation in the TPE group and 2.5 and 5 min after intubation in the TPEH group (Fig. 4).

The maximum cyt level in the PF and TP groups occurred 2.5 min after induction (0.8 ± 1.1 and 1.1 ± 1.4 nmol/L, respectively; \( n = 8 \) in each group), that in the TPE group occurred 2.5 min after induction (0.4 ± 0.9 nmol/L (\( n = 8 \))), and that in the TPEH group occurred 5 min after intubation.
(0.1 ± 1.2 nmol/L (n = 8)). There was no significant difference in the maximum cyt level among the four groups. The SpO₂ value was >99% at every time point in each group (Fig. 5).

Discussion

The present study highlights two important clinical issues. First, intravenous anesthetics influence the intracerebral environment during induction of anesthesia. Second, changes in BP influence the intracerebral environment.

Intravenous anesthetics influence the intracerebral environment during induction of anesthesia. When we compared changes in the intracerebral environment between the PF and TP groups, the time course of changes in the intracerebral environment differed between the two groups, especially the change in the oxy-Hb level. The oxy-Hb level in the PF group was stable until immediately after spreading the larynx to spray with lidocaine, rapidly increased 2.5 min after spreading the larynx, and then decreased. The oxy-Hb level in the TP group increased from induction to 2.5 min after spreading the larynx, then decreased. The deoxy-Hb level slowly decreased and then increased in both groups. The total-Hb in the PF group increased slightly 2.5 min after spreading the larynx, then decreased, while that in the TP group increased slightly, then decreased. The cyt level was stable in both groups. The change in the oxy-Hb level represents an index of changes in cerebral oxygenation, and the change in the total-Hb level represents an index of cerebral blood volume. It is possible that the changes in cerebral oxygenation did not occur immediately after administration of propofol (at induction), but occurred immediately after administration of thiopental (at induction); in other words, induction of general anesthesia with thiopental could influence the intracerebral oxygenation more than induction with propofol. In a previous study, the increase in the oxy-Hb level with propofol was lower than that with thiopental. In another study, the change in the oxy-Hb level was stable until 3 min after the start of anesthetic induction with propofol, but “increased 3 min after the start of anesthetic induction at with thiamylal”.

“Propofol reduced the cerebral blood flow via a decrease in the cerebral metabolic rate of oxygen”.

Our results are consistent with these previous reports and indicate that cerebral oxygenation increased by administration of propofol and thiopental. Next, when we compared the changes in the oxy-Hb level among the TP, TPE, and TPEH groups, the oxy-Hb levels in the TPE and TPEH groups were significantly higher than that in the TP group. It is possible that cerebral oxygenation was influenced by age or hypertension during induction of anesthesia with thiopental.

In all groups, we found that the oxy-Hb level increased, the deoxy-Hb level decreased, and the total-Hb level slightly increased during induction of general anesthesia. In general, these changes as shown by NIRS indicate a state of increased cerebral blood flow. The oxy-Hb level increases but the deoxy-Hb level decreases secondary to the hyperoxidation state that occurs by the avoidance of an increased oxygen consumption rate in tissues. These changes are suggested to have caused an increase in cerebral blood flow in the present study. The change in the total-Hb level represents an index of the cerebral blood volume if the hematocrit remains constant. Therefore, the change in the total-Hb level was proportional to the change in blood volume in this study. Our data indicate that the cerebral blood volume slightly increased because the total-Hb level slightly increased in all groups. In terms of other drugs that influence the intracerebral environment, one study showed that...
sevoflurane accelerated cerebral blood flow with nitric oxide but did not increase the cerebral blood volume\textsuperscript{13}. The effects of other drugs, including atropine sulfate, midazolam, fentanyl, and rocuronium bromide, remain unclear.

The second clinical issue highlighted by our study is that changes in BP influence the intracerebral environment. When the BP markedly increased after spreading the larynx, the oxy-Hb level increased in all groups, but most significantly in the TPEH group. The increase in cerebral blood flow was caused by tracheal intubation because cerebral hemodynamic changes may occur due to several events, such as anesthetic induction, intubation, and extubation\textsuperscript{9}. In one study, “the oxy-Hb level significantly increased secondary to an increase in cerebral blood flow with tracheal extubation”\textsuperscript{9}. Cerebral blood flow increases in response to noxious tracheal stimuli in patients with tracheal intubation because of a stimulated increase in muscle afferent activity\textsuperscript{14}. When the larynx is spread with a laryngoscope during induction, the BP markedly increases, which in turn increases the cerebral blood pressure. Among the four groups in this study, the TPEH group exhibited the greatest increase in the oxy-Hb level because the change in the BP was greatest. In other words, hemodynamic changes secondary to spreading of the larynx attenuate the cerebral blood flow, and this is more pronounced in elderly patients with hypertension. Therefore, it is prudent to maintain the BP within a safe range during induction of general anesthesia with intravenous anesthetics, especially thiopental, in elderly patients, particularly those with hypertension.

Our study has several limitations. First, this was not an observational study of the effect of only propofol or thiopental on the intracerebral environment. Several intravenous anesthetics affect the intracerebral environment during induction of general anesthesia, including atropine sulfate, midazolam, fentanyl, rocuronium bromide, and sevoflurane; the effects of these drugs will need to be elucidated in future studies. Second, the sample size was small (\(n = 32\)), and the number of patients may not have been sufficient to determine statistical significance. However, we believe that the data provide accurate and reliable information on intracerebral environmental changes influenced by intravenous anesthetics or changes in BP. Third, we only studied induction of anesthesia with thiopental in elderly patients and elderly patients with hypertension.

Conclusion

Intravenous anesthetics and changes in BP influence the intracerebral environment during induction of anesthesia. Our study suggests that intracerebral oxygenation is more strongly influenced by thiopental than propofol during induction of general anesthesia. Our findings also imply that induction of anesthesia with thiopental or propofol increases the cerebral blood flow and that the resultant hemodynamic changes attenuate the cerebral blood flow; this phenomenon is more pronounced in elderly patients with hypertension. Changes in BP must be controlled to prevent excessively high or low levels during induction of general anesthesia with intravenous anesthetics, especially thiopental, in elderly patients, particularly those with hypertension.

Acknowledgment

Non.

Competing Interests

The authors declare that they have no competing interests.
References


### Table 1: Demographic data

<table>
<thead>
<tr>
<th>Group</th>
<th>PF</th>
<th>TP</th>
<th>TPE</th>
<th>TPEH</th>
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<tr>
<td>Patients (n)</td>
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<td>8</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Age (years)</td>
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<td>35.4 ± 3.7</td>
<td>70.9 ± 1.8</td>
<td>75.3 ± 9.0</td>
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<tr>
<td>Weight (kg)</td>
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<td>62.8 ± 2.3</td>
<td>52.8 ± 2.3</td>
<td>54.7 ± 11.0</td>
</tr>
<tr>
<td>Sex (male:female)</td>
<td>2:6</td>
<td>5:3</td>
<td>5:3</td>
<td>4:4</td>
</tr>
<tr>
<td>Induction dose (mg/kg)</td>
<td>1.8 ± 0.1</td>
<td>4.5 ± 0.1</td>
<td>3.7 ± 0.3</td>
<td>2.8 ± 0.9</td>
</tr>
<tr>
<td>Fentanyl dose (µg/kg)</td>
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<td>0.9 ± 0.2</td>
<td>0.9 ± 0.1</td>
<td>0.7 ± 0.2</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation.

PF, propofol in adult patients; TP, thiopental in adult patients; TPE, thiopental in elder patients; TPEH, thiopental in elder patients with hypertension.

![Graph showing changes in arterial blood pressure](image)

**Fig. 1**: Changes in arterial blood pressure in extraoral regions.

(a) Immediately before induction (control), (b) induction, (c) 2.5 min after induction, (d) before spreading the larynx to spray with lidocaine, (e) immediately after spreading the larynx, (f) 2.5 min after spreading the larynx, (g) immediately after intubation, (h) 2.5 min after intubation, (i) 5 min after intubation, and (j) 10 min after intubation.
The blood pressure and pulse rate significantly increased immediately after spreading the larynx and immediately after intubation in the adult propofol, adult thiopental, and hypertensive elder thiopental groups and immediately after intubation in the elder thiopental group. There were significant differences in the blood pressure and pulse rate immediately before induction (control) and before spreading the larynx, 2.5 min after spreading the larynx, 5 min after intubation, and 10 min after intubation in the hypertensive elder thiopental group. In the elder thiopental group, the blood pressure and pulse rate increased from before spreading the larynx to immediately after intubation and decreased from 2.5 min after intubation to 10 min after intubation; significant differences were observed between the control time point and 5 and 10 min after intubation.

(a) Immediately before induction (control), (b) induction, (c) 2.5 min after induction, (d) before spreading the larynx to spray with lidocaine, (e) immediately after spreading the larynx, (f) 2.5 min after spreading the larynx, (g) immediately after intubation, (h) 2.5 min after intubation, (i) 5 min after intubation, and (j) 10 min after intubation.

The maximum oxyhemoglobin level occurred 2.5 min after spreading the larynx in the adult propofol, adult thiopental, and elder thiopental groups. The elder thiopental group exhibited significant differences in the oxyhemoglobin level between the control time point and immediately after spreading the larynx, 2.5 min after spreading the larynx, immediately after intubation, 2.5 min after intubation, 5
min after intubation, and 10 min after intubation. The maximum oxyhemoglobin level in the elder thiopental group occurred 2.5 min after intubation; significant differences were observed between the control time point and immediately after intubation, 2.5 min after intubation, and 5 min after intubation.

(a) Immediately before induction (control), (b) induction, (c) 2.5 min after induction, (d) before spreading the larynx to spray with lidocaine, (e) immediately after spreading the larynx, (f) 2.5 min after spreading the larynx, (g) immediately after intubation, (h) 2.5 min after intubation, (i) 5 min after intubation, and (j) 10 min after intubation.

The minimum deoxyhemoglobin level occurred 2.5 min after spreading the larynx to spray with lidocaine in the adult propofol group, 2.5 min after intubation in the adult thiopental group, and immediately after intubation in the elder thiopental and hypertensive elder thiopental groups. There were significant differences in the deoxyhemoglobin level between the control time point and 2.5 min after intubation in the adult thiopental group; 2.5 min after spreading the larynx, immediately after intubation, and 2.5 min after intubation in the elder thiopental group; and immediately after intubation in the hypertensive elder thiopental group.

Fig. 3: Changes in intracerebral deoxyhemoglobin level.
(a) Immediately before induction (control), (b) induction, (c) 2.5 min after induction, (d) before spreading the larynx to spray with lidocaine, (e) immediately after spreading the larynx, (f) 2.5 min after spreading the larynx, (g) immediately after intubation, (h) 2.5 min after intubation, (i) 5 min after intubation, and (j) 10 min after intubation.

The maximum total hemoglobin level occurred 2.5 min after spreading the larynx in the adult propofol group, immediately after intubation in the adult thiopental group, 2.5 min after spreading the larynx in the elder thiopental group, and 2.5 min after intubation in the hypertensive elder thiopental group. There were significant differences in the total hemoglobin level between the control time point and immediately after intubation in the elder thiopental group and 2.5 and 5 min after intubation in the hypertensive elder thiopental group.

Fig. 4: Changes in intracerebral total hemoglobin level.
Fig. 5: Changes in intracerebral cytochrome oxidase level.

(a) Immediately before induction (control), (b) induction, (c) 2.5 min after induction, (d) before spreading the larynx to spray with lidocaine, (e) immediately after spreading the larynx, (f) 2.5 min after spreading the larynx, (g) immediately after intubation, (h) 2.5 min after intubation, (i) 5 min after intubation, and (j) 10 min after intubation.

The maximum cytochrome oxidase level occurred 2.5 min after induction in the adult propofol and adult thiopental groups, 2.5 min after induction in the elder thiopental group, and 5 min after intubation in the hypertensive elder thiopental group. There were no significant differences among the four groups.