Original Article

Effects of Moderate Hyperventilation on Jugular Bulb Gases under Propofol or Isoflurane Anesthesia during Supratentorial Craniotomy

Lan Meng[1], Shu-Qin Li[1], Nan Ji[2], Fang Luo[1]

[1]Department of Anesthesiology and Pain Management, Beijing Tiantan Hospital, Capital Medical University, Beijing 100050, China
[2]Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing 100050, China

Abstract

Background: The optimal ventilated status under total intravenous or inhalation anesthesia in neurosurgical patients with a supratentorial tumor has not been ascertained. The purpose of this study was to intraoperatively compare the effects of moderate hyperventilation on the jugular bulb oxygen saturation (SjO_2), cerebral oxygen extraction ratio (O_2ER), mean arterial blood pressure (MAP), and heart rate (HR) in patients with a supratentorial tumor under different anesthetic regimens.

Methods: Twenty adult patients suffered from supratentorial tumors were randomly assigned to receive a propofol infusion followed by isoflurane anesthesia after a 30-min stabilization period or isoflurane followed by propofol. The patients were randomized to one of the following two treatment sequences: hyperventilation followed by normoventilation or normoventilation followed by hyperventilation during isoflurane or propofol anesthesia, respectively. The ventilation and end-tidal CO_2 tension were maintained at a constant level for 20 min. Radial arterial and jugular bulb catheters were inserted for the blood gas sampling. At the end of each study period, we measured the change in the arterial and jugular bulb blood gases.

Results: The mean value of the jugular bulb oxygen saturation (SjO_2) significantly decreased, and the oxygen extraction ratio (O_2ER) significantly increased under isoflurane or propofol anesthesia during hyperventilation compared with those during normoventilation (SjO_2: $t = –2.728$, $P = 0.011$ or $t = –3.504$, $P = 0.001$; O_2ER: $t = 2.484$, $P = 0.020$ or $t = 2.892$, $P = 0.009$). The SjO_2 significantly decreased, and the O_2ER significantly increased under propofol anesthesia compared with those values under isoflurane anesthesia during moderate hyperventilation (SjO_2: $t = –2.769$, $P = 0.012$; O_2ER: $t = 2.719$, $P = 0.013$). In the study, no significant changes in the SjO_2 and the O_2ER were observed under propofol compared with those values under isoflurane during normoventilation.

Conclusions: Our results suggest that the optimal ventilated status under propofol or isoflurane anesthesia in neurosurgical patients varies. Hyperventilation under propofol anesthesia should be cautiously performed in neurosurgery to maintain an improved balance between the cerebral oxygen supply and demand.

Key words: Hyperventilation; Isoflurane; Neuroanesthesia; Propofol

Introduction

Neurosurgical anesthesia should aim at providing brain relaxation. Mild-to-moderate hyperventilation because of the perceived advantage of brain relaxation and a lack of apparent serious deleterious effects has normally been recommended in neuroanesthetic management.

Gelb *et al*.[1] recently observed that intraoperative hyperventilation improves the intraoperative status of the brain bulk, which was related to a decrease in intracranial pressure (ICP) in patients with supratentorial brain tumors. They proposed that the effect of hyperventilation on the brain bulk assessment or ICP was independent of the anesthetic used during craniotomy procedures.[1] Whether intraoperative hyperventilation influences jugular bulb gases under different anesthetic regimens during craniotomy procedures has not previously been studied.

Isoflurane, as other volatile anesthetics, are strong cerebral vasodilators that increase the cerebral blood flow (CBF) and ICP. In contrast, intravenous anesthetics, such as propofol, are cerebral vasoconstrictors and suppress cerebral metabolism and reduce CBF and ICP. These two commonly used anesthetics were associated with similar operative conditions in patients undergoing a craniotomy.[2] A reduction in the arterial carbon dioxide tension ($PaCO_2$) leads to a rapid reduction in CBF.[3] As one of the neuroanesthesia adjunct therapies, hyperventilation is as effective as cerebral fluid drainage.[4] Thus, we considered that the optimal ventilated status under inhalation anesthesia or intravenous anesthesia should be detected.

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Address for correspondence: Prof. Fang Luo, Department of Anesthesiology and Pain Management, Beijing Tiantan Hospital, Capital Medical University, Dongcheng District, Beijing 100050, China
E-Mail: 13611326978@163.com

We conducted a randomized trial to evaluate the efficacy of moderate hyperventilation in patients undergoing craniotomy for excision of supratentorial brain tumors during isoflurane or propofol anesthesia. Our hypothesis was that the optimal ventilated status under total intravenous (propofol) or inhalation (isoflurane) anesthesia in neurosurgical patients with a supratentorial tumor should potentially be different, under propofol anesthesia the $PaCO_2$ should be adjusted to a relatively higher level than that under isoflurane anesthesia. Thus, we measured the jugular bulb gases during propofol or isoflurane anesthesia in 20 patients undergoing a craniotomy for removal of a brain tumor and clarified the effects of hyperventilation on those variables. The purpose of this study was to intraoperatively compare the effects of moderate hyperventilation on the jugular bulb oxygen saturation (SjO_2), cerebral oxygen extraction ratio (O_2ER), mean arterial blood pressure (MAP), and heart rate (HR) in patients with a supratentorial tumor under different anesthetic regimens.

Methods

This study was approved by the Medical Ethics Committee of Beijing Tiantan Hospital affiliated to Capital Medical University (No. kylw-2012-001-02), and informed consent was obtained from the patients or their families.

Inclusion criteria

Aged 18–70 years, American Society of Anaesthesiologists I or II patients (both genders), body mass index of 20–24 kg/m^2 suffered from supratentorial tumors undergoing an elective craniotomy. Without comorbidities such as heart, lung, hepatic or renal disease, or acute inflammatory/infectious processes.

Exclusion criteria

Patients with abnormal results of blood routine test, hepatorenal function, blood coagulation function, electrocardiogram, or chest X-ray examination were excluded from this study.

The patients were fasted about 8 h, and the operations were performed under general anesthesia. Anesthesia was induced with 2 mg/kg of propofol and 4 μg/kg of fentanyl, and tracheal intubation was performed, facilitated with vecuronium at 100 μg/kg intravenously. Surgery was begun after insertion of a 22-gauze catheter in the radial arterial and a 16-gauze single lumen catheter (ES-04301, Arrow International, Inc., Germany) in the internal jugular venous (IJV) bulb. Before retrograde IJV cannulation, the length from the puncture point to the mastoid process was identified as the landmark of the IJV bulb. In all the patients in our study, the length was approximately 8–10 cm. The catheter in the radial arterial was connected to a disposable pressure transducer system (DPT-248A, Utah Medical Products Inc., USA) for the direct MAP measurement. Arterial and IJV bulb blood samples were obtained for blood gas analysis. The MAP, HR, inspired and end-expired isoflurane concentrations and end-tidal CO_2 tension ($P_{ET}CO_2$) were continuously monitored (Datex Cardiocap II and the Capivomac Ultima Instrument, Instrumentarium Co., Finland) was calibrated before each patient. A nasopharyngeal temperature probe was inserted, and the temperature was maintained at 36°C–37°C using water and air blankets during the surgical procedure.

After tracheal intubation, 20 adult patients were randomly maintained with propofol infusion at a rate of 8 $mg \cdot kg^{-1} \cdot h^{-1}$ followed by isoflurane at an end-tidal concentration of 0.9% after a 30-min stabilization period or vice versa. In addition, the patients were randomized to one of the following two treatment sequences: Hyperventilation (to increase tidal volume [10–12 ml/kg] and respiratory rate [12–15/min] properly to maintain the $PaCO_2 = 27 \pm 2$ mmHg) followed by normoventilation (to maintain the normal tidal volume [8–10 ml/kg] and respiratory rate [10–12/min] in order to reach $PaCO_2 = 37 \pm 2$ mmHg) or vice versa during isoflurane or propofol anesthesia, respectively.

The patients were ventilated to achieve a stable $P_{ET}CO_2$. First, an arterial blood sample was obtained for the blood gas analysis. The $PaCO_2$ level was measured at 37°C and corrected to the patient's nasopharyngeal temperature. This finding was used to determine the difference between the arterial and end-tidal carbon dioxide tension. The lung ventilation was adjusted by the varying tidal volume and respiratory rate to achieve the desired $P_{ET}CO_2$. The $P_{ET}CO_2$ was maintained at a constant level for 20 min, which is sufficient time for stabilization of any vascular responses to the change in the $PaCO_2$.[5] The airway pressure was maintained at below 22 cmH_2O (1 cmH_2O=0.098 kPa). Positive end-expiratory pressure was not applied. At the end of each study period, the MAP, HR, hemoglobin (Hb), and the temperature were recorded, the arterial and IJV bulb blood samples were obtained and a blood gas analysis was performed (Compact 2, AVL Co., Switzerland), which were reported with the body temperature corrected to 37°C. The O_2ER were calculated according to Fick's formula as follows (arterial oxygen content [CaO_2]; jugular bulb oxygen content [CjO_2]; arterial oxygen saturation [SaO_2]; SjO_2; arterial oxygen tension [PaO_2]; jugular bulb oxygen tension [PjO_2]): $CaO_2 = 1.39 \times Hb \times SaO_2 + 0.003 \times PaO_2$, $CjO_2 = 1.39 \times Hb \times SjO_2 + 0.003 \times PjO_2$, $O_2ER = (1 - CjO_2)/CaO_2 \times 100\%$.

The sequence of the administration of isoflurane and propofol anesthesia and the sequence of hyperventilation and normoventilation studied here were randomized to eliminate any effect of time on the measurements.

Statistical analysis

The data are reported as the mean ± standard deviation (SD). The values were compared at each $PaCO_2$ during propofol or isoflurane anesthesia using a two-way repeated measures analysis of variance with Student's *t*-test and Newman–Keuls tests for the *post-hoc* comparisons. The differences corresponding to a *P* value of <0.05 were considered statistically significant.

Results

Twenty patients (12 male, 8 female; age range 21–59 years; weight range 53–87 kg) were included in this study. All the

patients underwent a selective craniotomy for a supratentorial tumor (14 gliomas and 6 meningiomas).

Table 1 shows the effects of moderate hyperventilation on the jugular bulb and arterial gases parameters during propofol or isoflurane anesthesia in patients undergoing a selective craniotomy for a supratentorial tumor. The mean $PaCO_2$ levels during hyperventilation under isoflurane or propofol anesthesia were 27.5 ± 2.3 mmHg and 26.9 ± 1.7 mmHg, respectively. The mean value of the SjO_2 significantly decreased, and the O_2ER significantly increased under isoflurane or propofol anesthesia during hyperventilation compared with those during normoventilation (SjO_2: t = –2.728, P = 0.011 or t = –3.504, P = 0.001; O_2ER: t = 2.484, P = 0.020 or t = 2.892, P = 0.009). The SjO_2 significantly decreased, and the O_2ER significantly increased under propofol anesthesia compared with those under isoflurane anesthesia during moderate hyperventilation (SjO_2: t = –2.769, P = 0.012; O_2ER: t = 2.719, P = 0.013). No significant changes in the SjO_2 and the O_2ER were observed under propofol anesthesia compared with the changes under isoflurane during normoventilation in the study.

Blood pressure showed a tendency of decrease from propofol anesthesia to isoflurane anesthesia, without significance. No significant HR changes were found in our study.

Discussion

Hyperventilation has been an integral part of neuroanesthesia for 50 years. Although more recent guidelines discourage the use of long-term hyperventilation in severe head injury patients, hyperventilation to some degree is typically used to facilitate intracranial surgery.[6] No previous study has included a formal evaluation of whether the optimal ventilated status is identical during volatile anesthesia or intravenous anesthesia in craniotomy. For a better understanding of ventilation management in neurosurgical anesthesia, the jugular bulb gases were measured under isoflurane anesthesia in comparison with the total intravenous anesthesia (TIVA) using propofol, during which patients were ventilated to maintain moderate hyperventilation followed by normoventilation or normoventilation followed by hyperventilation. Our null hypothesis was that because hyperventilation, which has been recommended for anesthetic management during craniotomy, decreases the CBF, the cerebral oxygen balance could deteriorate under propofol anesthesia, a cerebral vasoconstrictor, compared with that under isoflurane anesthesia, a cerebral vasodilator, during hyperventilation in neurosurgery.

As one of the indexes of ischemia, the SjO_2 monitors the adequacy of cerebral perfusion, reflecting the ratio between the CBF and cerebral metabolism.[7] The balance between the cerebral oxygen supply and demand is a significant problem requiring unique attention. First, our results found that no significant changes in the SjO_2 and O_2ER were observed under propofol anesthesia compared with isoflurane during normoventilation in the study. Sato *et al*.[5] reported that little difference in cerebral metabolic rate of oxygen ($CMRO_2$) is hypothesized to exist between anesthesia by 0.9% isoflurane and by 8 $mg \cdot kg^{-1} \cdot h^{-1}$ propofol. Because the anesthetics used in our study was delivered at the above doses, $CMRO_2$ is hypothesized to be approximately identical in anesthesia by isoflurane or propofol in our study, and the results suggested that the balance between isoflurane and propofol under normoventilation showed no significant difference.

Second, our results demonstrated that the SjO_2 mean value significantly decreased and the O_2ER significantly increased during hyperventilation compared with those during normoventilation, regardless of whether isoflurane or propofol anesthesia was administered. Although hyperventilation might improve the operating condition, concern remains that hyperventilation might exacerbate a preexisting impairment of CBF and metabolism and lead to deterioration from cerebral ischemia in traumatic brain injury patients.[8] Chan *et al*.[9] reported that SjO_2 values of 40–45% were related to cerebral metabolic failure and secondary brain damage in patients suffering from brain injury. Coles *et al*.[10] suggested that a brief hyperventilation,

Table 1: Arterial and jugular bulb blood gases during isoflurane or propofol anesthesia at different $PaCO_2$ levels

Items	Isoflurane		Propofol	
	Hyperventialtion	Normoventilation	Hyperventialtion	Normoventilation
$PaCO_2$ (mmHg)	27.5 ± 2.3	37.3 ± 2.4†	26.9 ± 1.7	36.6 ± 2.1†
SjO_2 (%)	70.1 ± 7.7	78.3 ± 8.4*	58.9 ± 12.7‡	74.8 ± 12.6+
SaO_2 (%)	99.9 ± 0.1	99.9 ± 0.1	99.9 ± 0.1	99.9 ± 0.1
PjO_2 (mmHg)	38 ± 5	49 ± 12*	32 ± 6‡	46 ± 12†
PaO_2 (mmHg)	447 ± 77	461 ± 42	453 ± 67	476 ± 57
pHj	7.38 ± 0.04	7.33 ± 0.03	7.36 ± 0.04	7.33 ± 0.04
pHa	7.47 ± 0.05	7.39 ± 0.03†	7.46 ± 0.04	7.39 ± 0.03†
$PjCO_2$ (mmHg)	36.7 ± 3.3	45.0 ± 3.8†	36.5 ± 4.4	43.7 ± 4.6+
O_2ER (%)	34 ± 7	27 ± 8*	45 ± 12‡	31 ± 12†
Temperature (°C)	36.6 ± 0.3	36.5 ± 0.3	36.5 ± 0.3	36.3 ± 0.4

Values are mean ± SD for 20 patients. Values during normoventilation compared with those during hyperventialtion under propofol anesthesia or isoflurane, *P < 0.05; †P < 0.01. Values during propofol anesthesia compared with those under isoflurane, ‡P < 0.05. $PaCO_2$: Arterial carbon dioxide tension; SjO_2: Jugular bulb oxygen saturation; SaO_2: Arterial oxygen saturation; PjO_2: Jugular bulb oxygen tension; PaO_2: Arterial oxygen tension; pHj: Jugular bulb pH; pHa: Arterial pH; $PjCO_2$: Jugular bulb carbon dioxide tension; O_2ER: Oxygen extraction ratio; SD: Standard deviation.

which decreases CBF, quickly increased the volume of severely hypoperfused cerebral tissue within the injured brain. The risk of intraoperative hyperventilation during a craniotomy has not been fully determined. Previous studies in neurosurgical patients have proposed that the SjO_2 decreased after hyperventilation and during mild hypothermia with up to 50% of patients having a SjO_2 <50%.[11] In our study, the patients underwent moderate hyperventilation, and the mean values of SjO_2 were 70.1% ±7.7% and 58.9% ±12.7% in the isoflurane and propofol groups, respectively. Because the oxygen consumption of the brain was constant, the decrease of the SjO_2 demonstrated the decrease of CBF globally from normal ventilation to hyperventilation.

Third, the SjO_2 significantly decreased, and the O_2ER significantly increased under propofol anesthesia compared with those levels under isoflurane anesthesia in cases in which the patients were hyperventilated. The results of our study suggested that the balance of the cerebral supply and demand under anesthesia by 0.9% isoflurane inhalation was better than that under anesthesia by 8 $mg \cdot kg^{-1} \cdot h^{-1}$ propofol administration under moderate hyperventilation. Recent evidence suggested that compared with inhalational anesthetics, propofol could deteriorate the cerebral oxygen balance which is more frequently related to lactic acidosis and hypertension in intracranial surgery.[12,13] Because propofol is hypothesized to suppress the cerebral metabolism and cause a decrease in the CBF if accompanied with hyperventilation, which decreases the CBF, the potential for causing the SjO_2 to fall below the critical threshold is greater than that for inhalational anesthetics. Although we did not find propofol-induced metabolic disturbances, our results suggested that the isoflurane group maintained a better balance of cerebral oxygen than that of the propofol group in the cases in which hyperventilation was performed. Although clinical and basic studies found that propofol was better than isoflurane in many respects,[14,15] concerns remain regarding the propofol-based regimen in neuroanesthesia.

Our results suggested that propofol, compared with isoflurane, could decrease the SjO_2 and increase the O_2ER only under hyperventilation, whereas under normoventilation, propofol could not further deteriorate the cerebral oxygen balance. The results are in agreement with a recent study, which found that hypocapnia caused by moderate hyperventilation in patients undergoing intravenous anesthesia significantly reduced SjO_2.[16]

Because propofol contracts and isoflurane dilates the cerebral vessels, the degree of hyperventilation in craniotomy should consider the anesthetic regimen. The SjO_2 under propofol anesthesia decreased 21%–58.9% ± 12.7%, whereas under isoflurane anesthesia, the SjO_2 decreased 10%–70.1% ± 7.7% from normoventilation to hyperventilation. According to our results, in the neurosurgery cases in which hyperventilation is performed under TIVA such as propofol, the SjO_2 should be adjusted to a relatively higher level than that under inhalation anesthesia to maintain an improved balance between the cerebral oxygen supply and demand. Although the outcome was not assessed in this article, the results of this study indicate that it is possible that hyperventilation under propofol anesthesia should be cautiously performed to maintain an improved balance between the cerebral oxygen supply and demand.

Based on this study, we suggest that the optimal ventilated status under total intravenous or inhalation anesthesia in neurosurgical patients should vary. Neurosurgery is typically performed under balanced anesthesia using volatile anesthetics and intravenous analgesics. Until now, the optimal $PaCO_2$ level administered in neurosurgery patients under isoflurane, propofol anesthesia or balance anesthesia has not been fully and clearly determined or standardized. Although an overall CBF decrease under propofol anesthesia with moderate hyperventilation was suggested by the decrease in the SjO_2, whether the blood flow might decrease in some areas is not clear. To verify these preliminary results, substantially more data are required. There were several other limitations, for example, we did not observe the clinical prognostic data in this study. Further researches should be performed to investigate the effect of different degree of hyperventilation under propofol or isoflurane anesthesia on patients' prognostic situations in the future.

In conclusion, the optimal ventilated status under propofol or isoflurane anesthesia in neurosurgical patients varies. Hyperventilation under propofol anesthesia should be cautiously performed in neurosurgery to maintain an improved balance between the cerebral oxygen supply and demand.

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