

The Cerebrovascular Response to Hypocapnia in Children Receiving Propofol

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Hypocapnia is used to treat acute increases in intracranial pressure during neurosurgery. Cerebrovascular reactivity to carbon dioxide (CCO₂R) is preserved above 35 mm Hg ETco₂ in children during propofol anesthesia; however, a plateau effect has been suggested below 35 mm Hg. To further delineate this phenomenon, we measured CCO₂R by transcranial Doppler (TCD) sonography over small increments in ETco₂ in 27 healthy children. Anesthesia comprised a standardized propofol infusion and a caudal epidural block. A TCD probe was placed to measure middle cerebral artery blood flow velocity (V_{mca}). ETco₂ was adjusted between 24 and 40 mm Hg at 1–2 mm

Hg increments using an exogenous source of CO₂. There was an exponential relationship between ETco₂ and V_{mca} above an ETco₂ value of 30 mm Hg ($r = 0.82$). However, V_{mca} did not change with ETco₂ less than 30 mm Hg ($r = 0.06$). There were no significant changes in heart rate or arterial blood pressure. We conclude that when contemplating methods to decrease brain volume and intracranial pressure, hyperventilation to ETco₂ values less than 30 mm Hg may not be necessary in children receiving propofol, as no further reduction in cerebral blood flow velocity will be achieved.

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Propofol is a suitable drug for neuroanesthesia in adult and pediatric patients undergoing neurosurgical procedures (1,2) because of its rapid clearance and distribution, resulting in rapid emergence from anesthesia (3). The increase in popularity of IV techniques for neuroanesthesia in children results from the potentially undesirable cerebral vasodilatory effects of the volatile anesthetics (4).

Carbon dioxide (CO₂) directly affects the cerebral circulation by dilating cerebral vessels and increasing cerebral blood flow (5). Hypocapnia is an important physiological variable used to manipulate intracranial pressure during neurosurgical procedures. Cerebrovascular reactivity to carbon dioxide (CCO₂R) is preserved above 35 mm Hg end-tidal CO₂ (ETco₂) in children during propofol anesthesia; however, a plateau effect has been suggested below 35 mm Hg (6). The level of hypocapnia for this plateau effect is not known. To further delineate this phenomenon, middle cerebral artery blood flow velocity (V_{mca}) was measured by transcranial Doppler (TCD) sonography over

small increments in ETco₂ in children anesthetized with propofol.

Methods

With Research Ethics Board approval and written parental consent, 27 unpremedicated children aged 1 to 6 yr, ASA I–II, undergoing urological surgery under general anesthesia were enrolled. Patients with cardiovascular or neurological disease, a history of premature birth, or contraindication to regional anesthesia were excluded. In each child an IV catheter was inserted after administration of 70% nitrous oxide; anesthesia was then induced with propofol 2.5 mg/kg, and tracheal intubation was facilitated with rocuronium 1.0 mg/kg. All subjects received a caudal epidural block with 1.0 mL/kg of 0.25% bupivacaine without epinephrine to block the cerebrovascular response to surgical stimulation. Surgery was allowed to commence 20 min after the caudal block had been performed and the block was assumed to be successful if on skin incision the heart rate (HR) and mean arterial blood pressure (MAP) did not increase more than 5% from baseline (immediately before skin incision). Based on a pharmacokinetic model (7), anesthesia was maintained with a propofol infusion of 15 mg · kg⁻¹ · h⁻¹ for the first 15 min, 13 mg · kg⁻¹ · h⁻¹ for the next 15 min, 11 mg · kg⁻¹ · h⁻¹ from 30 to 60 min, and 10 mg · kg⁻¹ · h⁻¹ for the next hour. This administration regimen was aimed at producing an estimated

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steady-state serum propofol concentration of 3 $\mu\text{g}/\text{mL}$. Using an Ayre's T-piece and intermittent positive pressure ventilation with 30% oxygen in air and zero end-expiratory pressure (Datex Ohmeda, Helsinki, Finland), ventilatory settings were adjusted to achieve a ETCO_2 of 24 mm Hg. Exogenous CO_2 was then introduced into the circuit and titrated to yield the desired ETCO_2 . A TCD probe (Neuroguard; Medasonics, Fremont, CA) was placed to measure V_{mca} at the M1 segment. V_{mca} was measured between 24 and 40 mm Hg ETCO_2 at increments of 1-2 mm Hg. After each change in ETCO_2 5 min were allowed for steady-state to be reached, at which time 3 measurements of V_{mca} , HR, and MAP were recorded at 1-min intervals. Airway pressures and respiratory rates were kept constant throughout the study. Body temperature was monitored rectally and maintained constant with a conductive water mattress and convective air warmer under the surgical drapes. The subjects were supine and horizontal throughout the study period.

Demographic and parametric data are expressed as mean \pm SD. The relationship between ETCO_2 and V_{mca} was determined using nonlinear regression analysis and the coefficient of correlation (r) was calculated. Within-group analysis of V_{mca} , HR, and MAP data was achieved with repeated measures analysis of variance and the Student-Newman-Keuls test for multiple comparisons. A $P < 0.05$ was accepted for significance.

Results

Twenty-seven patients were studied, with an average age and weight of 3.1 ± 1.6 yr and 13.9 ± 3.1 kg, respectively. The caudal block was successful and TCD measurements were completed in all children.

There was an exponential relationship between ETCO_2 and V_{mca} above an ETCO_2 value of 30 mm Hg ($r = 0.82$) (Fig. 1). However, nonlinear regression analysis revealed that there was no relationship between V_{mca} and an ETCO_2 below 30 mm Hg ($r = 0.06$, Fig. 2). There were no significant changes in HR or MAP throughout the study period. There were no complications that resulted from this study.

Discussion

The main finding of this study was the loss of cerebrovascular CO_2 reactivity below a CO_2 level of 30 mm Hg in children anesthetized with propofol. This serves to more precisely define the decrease in CCO_2R below 35 mm Hg ETCO_2 identified in a previous pediatric study (6) (Fig. 3). The direct cerebral vasoconstrictive effects of propofol are likely responsible for this phenomenon, as propofol has been shown to reduce cerebral blood flow velocity (CBFV) in both adults (8) and children (9). Despite this, similar

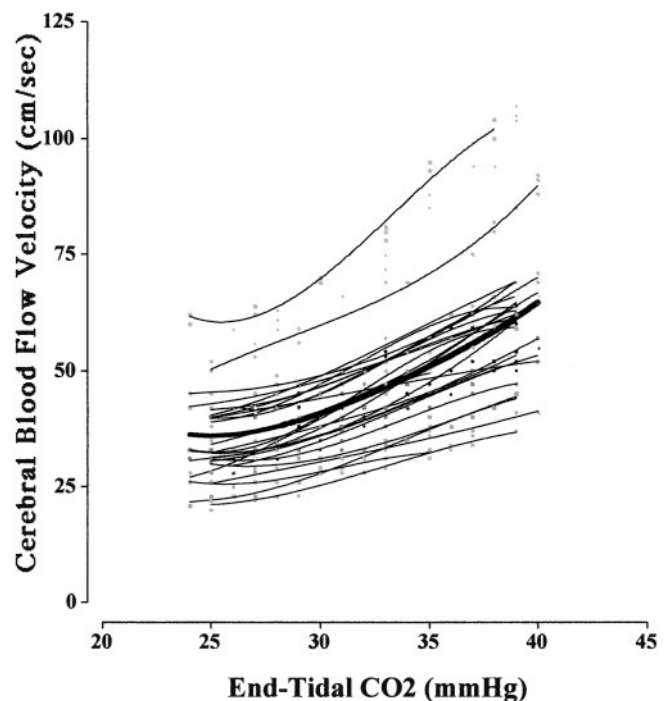


Figure 1. Changes in middle cerebral artery blood flow velocity (V_{mca}) between end-tidal CO_2 tensions of 24 and 40 mm Hg in children anesthetized with propofol. The heavy curve represents the line of best fit for all data points.

studies performed in adult patients have not reported this loss of CO_2 reactivity in the hypocapnic range (10,11).

CO_2 dilates cerebral arterioles, increasing both cerebral blood flow and volume (5). Manipulation of ETCO_2 is used in neuroanesthesia to reduce cerebral blood flow and therefore intracranial pressure in patients with reduced intracranial compliance. The results of this study suggest that hyperventilation to ETCO_2 levels below 30 mm Hg to reduce brain volume and intracranial pressure may not be necessary in children receiving propofol, as no further reduction in CBFV will be achieved.

A loss of cerebrovascular CO_2 reactivity at and above 50 mm Hg of ETCO_2 has been observed in pediatric studies using volatile anesthetics (12,13). This may be attributable to the inherent vasodilatory properties of volatile anesthetics. Although sevoflurane remains a popular neuroanesthetic, one study has demonstrated that CCO_2R may not be as well preserved between 45 and 55 mm Hg of ETCO_2 in children (13) (Fig. 3). A similar plateau phenomenon in CCO_2R has been seen with isoflurane and halothane (12). All volatile anesthetics are known to cause direct cerebral vasodilatation (4). This suggests that when volatile anesthetics are used in the presence of increasing ETCO_2 , a maximal degree of cerebral vasodilatation is achieved at an earlier stage. The effect of propofol on cerebrovascular CO_2 reactivity in children

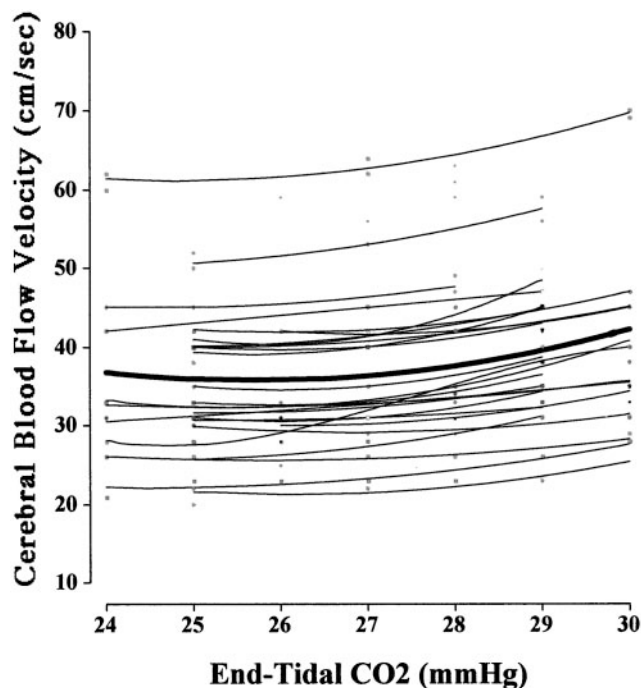


Figure 2. Changes in middle cerebral artery blood flow velocity (V_{mca}) between end-tidal CO₂ tensions of 24 and 30 mm Hg in children anesthetized with propofol. The heavy curve represents the line of best fit for all data points.

reported in this and previous studies seems to be the opposite (or mirror image) of that seen with sevoflurane (13) (Fig. 3).

Propofol seems to demonstrate many of the properties of a suitable anesthetic for adults undergoing neurosurgical procedures. Unlike volatile anesthetics, propofol has been shown to decrease both cerebral metabolism and blood flow (8). In addition, its rapid metabolic clearance provides for an early, predictable, and complete recovery, making propofol suitable for maintenance of anesthesia by continuous infusion (11). The propofol dosing regimen used in the present study was derived from published pharmacokinetic studies of propofol infusion data in children (14-17). A manual infusion regimen capable of maintaining an estimated steady-state blood concentration of 3 $\mu\text{g}/\text{mL}$ in children was used (7). This target concentration has been chosen in several adult studies (18-20), as the blood propofol concentration required to achieve sedation or anesthesia is very similar in both children and adults (21). Because of the significant pharmacokinetic and pharmacodynamic differences between children and adults, however, propofol doses and infusion rates required to achieve a certain target blood concentration are larger for pediatric patients (15,18).

Several physiological factors have been shown to alter CBFV, including cardiac output, surgical stimulation, body temperature, depth of anesthesia, and

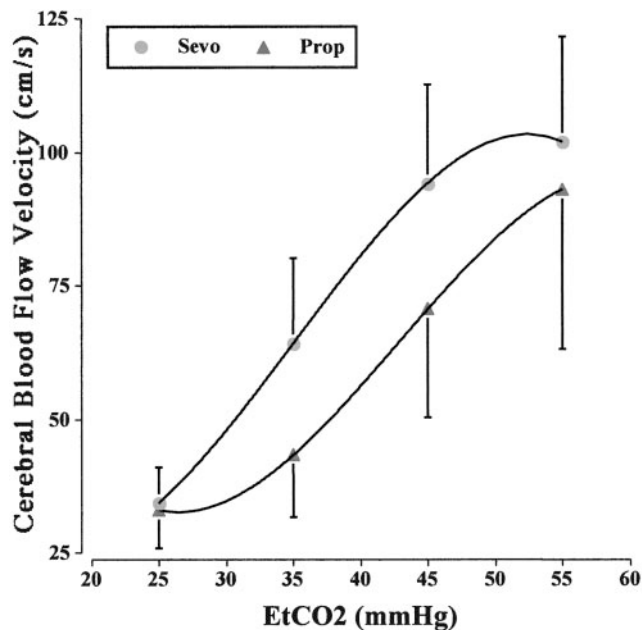


Figure 3. Changes in middle cerebral artery blood flow velocity (V_{mca}) at end-tidal CO₂ tensions of 25, 35, 45, and 55 mm Hg in children receiving propofol (Prop) or sevoflurane (Sevo) anesthesia. Data derived from references 7 and 14.

intrathoracic pressure (12). HR, MAP, and body temperature remained unchanged throughout the study period, and any cerebrovascular effects of surgical stimulation seemed to have been successfully eliminated by the caudal epidural block. Intrathoracic pressure was kept constant by maintaining the same ventilation variables throughout the study and adding an exogenous source of CO₂ to the breathing circuit to alter ETco₂. Cerebral blood flow responds rapidly to changes in Paco₂ and reaches a plateau within 2 minutes (22). In this study 5 minutes were allowed after each change in ETco₂ to achieve steady-state conditions within the brain.

The goal of hyperventilation in neuroanesthesia is to decrease cerebral blood flow and volume as well as intracranial pressure in susceptible patients. Relative changes in CBFV have been shown to correlate well with changes in cerebral blood flow (23,24), and TCD sonography is now widely used as a surrogate measure of cerebral blood flow (25). Inter- and inpatient variability in CBFV measurements can result from variations in initial Doppler probe positioning or changes in probe position during the course of a study. Thus to minimize these errors an experienced user fixed the Doppler probe to the subject's head using an established wheel frame (26).

In conclusion, the present study demonstrates that the decrease in CCO₂R in children anesthetized with propofol seems to occur below 30 mm Hg of ETco₂. This would suggest that when contemplating methods

to reduce brain volume and intracranial pressure, hyperventilation to ETco₂ levels below 30 mm Hg may not be necessary in children receiving propofol, as no further reduction in CBFV will be achieved.

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