Obstetrical and Pediatric Anesthesia

Desflurane increases cerebral blood flow velocity when used for rapid emergence from propofol anesthesia in children

[Le desflurane augmente la vitesse circulatoire cérébrale quand il est utilisé pour un réveil rapide après l'anesthésie au propofol chez des enfants]

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Purpose: Desflurane may be used to replace propofol at the end of anesthesia to facilitate rapid emergence. This study determined the effect of administering desflurane during emergence of anesthesia on middle cerebral artery blood flow velocity (Vmca) in children anesthetized with propofol.

Methods: Thirty healthy chilren aged one to six years scheduled for orchidopexy or hypospadias repair under general anesthesia were enrolled. Anesthesia was maintained with a propofol infusion targeting an estimated serum level of 3 $\mu g \cdot mL^{-1}$, remifentanil 0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and a caudal epidural block. Transcranial Doppler sonography was used to measure Vmca at five-minute intervals. In half the patients, propofol was substituted with desflurane 1 MAC, 30 min prior to the end of the surgical procedure. Once steady-state had been achieved recordings of Vmca, heart rate, and mean arterial pressure were resumed. Upon termination of the surgical procedure, the maintenance agent was discontinued and recordings continued at one-minute intervals during emergence of anesthesia.

Results: There were no demographic differences between the two groups. Vmca increased from 37.2 ± 3.1 $cm \cdot sec^{-1}$ to 57.7 ± 4.1 $cm \cdot sec^{-1}$ when propofol was changed to desflurane ($P < 0.01$). Upon emergence of anesthesia, Vmca decreased from 57.8 ± 4.2 $cm \cdot sec^{-1}$ to 37.8 ± 3.2 $cm \cdot sec^{-1}$ in the desflurane group ($P < 0.01$) but remained unchanged in the propofol group.

Conclusion: Desflurane is associated with an increase in cerebral blood flow velocity when used to facilitate rapid emergence following a propofol infusion in children. This may be of clinical significance in patients with intracranial pathology.

Objectif : *Le desflurane peut être utilisé pour remplacer le propofol à la fin de l'anesthésie et faciliter un réveil rapide. La présente étude voulait déterminer l'effet du desflurane, administré pendant le retour à la conscience, sur la vitesse circulatoire de l'artère cérébrale moyenne (Vacm) chez des enfants anesthésiés avec du propofol.*

Méthode : *Nous avons recruté 30 enfants sains, de un à six ans, devant subir une orchidopexie ou la réparation d'un hypospadias sous anesthésie générale. L'anesthésie a été maintenue avec une perfusion de propofol, visant un niveau sérique de 3 $\mu g \cdot mL^{-1}$, 0,2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ de rémifentanil et un bloc péridural caudal. L'échographie Doppler transcrânienne a servi à mesurer la Vacm à cinq minutes d'intervalle. Chez la moitié des patients, le propofol a été remplacé par 1 CAM de desflurane, 30 min avant la fin de l'opération. Une fois atteint l'état d'équilibre, l'enregistrement de la Vacm, la fréquence cardiaque et la tension artérielle moyenne est repris. À la fin de l'opération, le médicament de maintien de l'anesthésie est supprimé et les enregistrements se poursuivent à une minute d'intervalle pendant le réveil de l'anesthésie.*

Résultats : *Il n'y avait pas de différence démographique intergroupe. La Vacm a augmenté de 7,2 ± 3,1 $cm \cdot sec^{-1}$ à 57,7 ± 4,1 $cm \cdot sec^{-1}$ quand le propofol a été remplacé par le desflurane ($P < 0,01$). Au réveil, la Vacm, a diminué de 57,8 ± 4,2 $cm \cdot sec^{-1}$ à 37,8 ± 3,2 $cm \cdot sec^{-1}$ avec le desflurane ($P < 0,01$) mais n'a pas changé avec le propofol.*

Conclusion : *Le desflurane est associé à une augmentation de la vitesse circulatoire cérébrale quand il est utilisé pour faciliter un réveil rapide après une perfusion de propofol chez des enfants. Ce résultat peut avoir une portée clinique significative chez des patients atteints de pathologie intracrânienne.*

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RAPID emergence from anesthesia may be desirable in the neurosurgical setting. Desflurane may be used to replace propofol at the end of anesthesia to facilitate rapid recovery. The effect of propofol and desflurane on cerebral blood flow velocity (CBFV) during general anesthesia has been studied.[1–4] However, to date no studies have reported the effect of these agents during emergence from anesthesia in infants and children. Propofol has cerebral vasoconstrictive properties and appears to be ideal for neurosurgical procedures where control of intracranial pressure (ICP) is indicated.[1] Desflurane is a potent cerebral vasodilator and may contribute to increases in cerebral blood flow and volume.[2–4] This study was designed to test the null hypothesis that when propofol is replaced with desflurane for emergence from anesthesia in children, there is no effect on middle cerebral artery blood flow velocity (Vmca).

Methods

With Research Ethics Board approval and written informed parental consent, 30 ASA I or II children aged one to six years scheduled for orchidopexy or hypospadias repair were enrolled. Patients with cardiovascular or neurological disease, a history of premature birth or contraindication to regional anesthesia were excluded. In each child, anesthesia was induced with sevoflurane in 100% oxygen. Standard anesthetic monitors were applied, an *iv* catheter was placed and propofol 2.5 $mg \cdot kg^{-1}$ was given. Rocuronium 1.0 $mg \cdot kg^{-1}$ was used to facilitate tracheal intubation. Intermittent positive pressure ventilation was instituted with 35% oxygen in air and sevoflurane was discontinued. Peak airway pressure was maintained constant at 15 cm H_2O with zero positive end-expiratory pressure and the ventilatory rate was adjusted to maintain an end-tidal CO_2 of 35 mmHg. Anesthesia was maintained with a propofol infusion regimen consisting of 15 $mg \cdot kg^{-1} \cdot hr^{-1}$ for the first 15 min, 13 $mg \cdot kg^{-1} \cdot hr^{-1}$ for the next 15 min, followed by 11 $mg \cdot kg^{-1} \cdot hr^{-1}$ for the next 30 min and 10 $mg \cdot kg^{-1} \cdot hr^{-1}$ thereafter. This was based on a pediatric pharmacokinetic model designed to target an estimated steady-state serum propofol concentration of 3 $\mu g \cdot mL^{-1}$.[5] Each patient also received a remifentanil 0.5 $\mu g \cdot kg^{-1}$ bolus followed by a 0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ infusion.[6]

Each child received a caudal epidural block with 1.0 $mL \cdot kg^{-1}$ of 0.25% bupivicaine without epinephrine in order to eliminate the cerebrovascular response to surgical stimulation. Surgery was allowed to commence 20 min after the caudal block was performed and the analgesic effect was assumed to be successful if, upon skin incision, the heart rate (HR) and mean arterial pressure (MAP) did not vary more than 5% from baseline. Fluid deficits secondary to fasting and ongoing losses were replaced with an initial bolus of lactated Ringer's solution 8 $mL \cdot kg^{-1}$ followed by a maintenance infusion of 10 $mL \cdot kg^{-1} \cdot hr^{-1}$. Further fluids were given as necessary to maintain normotension. A convective air warmer (Bair Hugger 500/OR, USA) and conductive heating mattress (Gaymar, New York, NY, USA) were used to maintain normothermia.

A transcranial Doppler probe (TCD; Neuroguard, Medasonics, Fremont, CA, USA) was placed to measure Vmca at the M1 segment using a 2-MHz emitted ultrasonic frequency. Simultaneous recordings of Vmca, HR, and MAP were taken at five-minute intervals throughout the study period. Patients were randomized using a computer generated random number table. In half the patients, propofol was substituted with desflurane, age-adjusted to 1 MAC, 30 min before the end of the surgical procedure (desflurane-substituted group). In the other half, the propofol infusion was continued (propofol group). Fifteen minutes were allowed to achieve steady-state and recordings of Vmca, HR, and MAP were resumed at five-minute intervals. Upon termination of the surgical procedure, the maintenance agent was discontinued and recordings continued at one-minute intervals for five minutes, during anesthetic emergence in both groups under remifentanil alone.

Statistical analysis

Demographics and data with parametric values are presented as mean ± SD. The number of patients needed to demonstrate a direct effect on Vmca during changes in anesthetic agent was calculated with the assumption that a 20% change would be clinically relevant. Based on a statistical power of 0.8, an $\alpha_2 = 0.05$ and a ß = 0.2, seven patients per group was suggested. The Student's unpaired t test, repeated measure ANOVA and Tukey-Kramer tests were used where appropriate. $P < 0.05$ was accepted as significant.

Results

The mean age of propofol and desflurane-substituted patients was 2.4 ± 1.3 yr and 2.3 ± 1.2 yr, and the mean weight was 13.1 ± 3.6 kg and 13.2 ± 3.5 kg, respectively. All patients were male. The caudal block was successful in all patients and TCD measurements were completed in all children. Vmca increased from 37.2 ± 3.1 $cm \cdot sec^{-1}$ to 57.7 ± 4.1 $cm \cdot sec^{-1}$ when propofol was changed to desflurane ($P < 0.01$; Figure, events 4–6). Upon anesthetic emergence, Vmca decreased from 57.8 ± 4.2 $cm \cdot sec^{-1}$ to 37.8 ± 3.2 $cm \cdot sec^{-1}$ in the desflurane group ($P < 0.01$) but

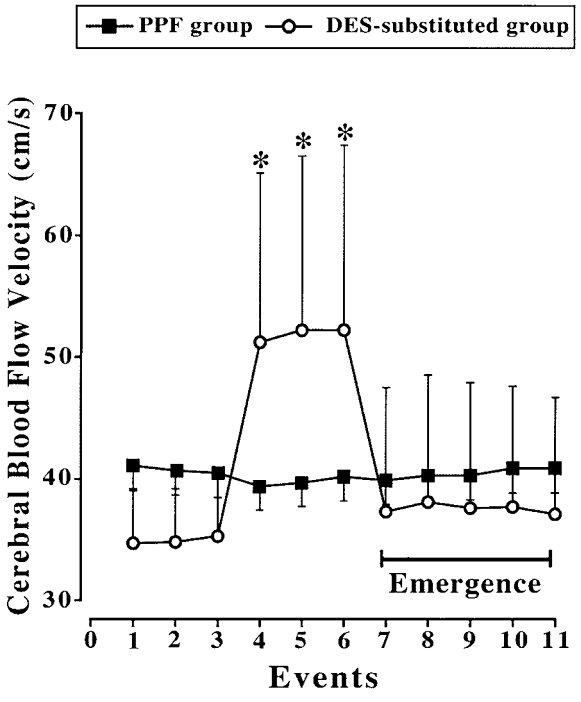

FIGURE Changes in middle cerebral artery blood flow velocity (Vmca) in the propofol (PPF) and the desflurane (DES)-substituted group intraoperatively and during emergence of anesthesia. Baseline measurements of Vmca during propofol maintenance for both groups are represented by events 1–3. Events 4, 5 and 6 correspond to the switch from propofol to desflurane in the DES-substituted group. Discontinuation of the anesthetic agent and emergence from anesthesia are represented by events 7–11. * $P <$ 0.01 compared to the PPF group.

TABLE Changes in heart rate and mean arterial pressure in the propofol (PPF) group and desflurane (DES)-substituted group, intraoperatively (intraop) and during emergence

	Heart rate (beats·min^{-1} ± SD)		*Mean arterial pressure (mmHg ± SD)*	
	Intraop	*Emergence*	*Intraop*	*Emergence*
PPF group	95.5 ± 11.1	97.1 ± 13.2	64.6 ± 11.6	60.1 ± 13.2
DES-substituted group	97.8 ± 10.9	96.9 ± 10.6	59.8 ± 12.5	60.3 ± 10.9

No significant differences between groups.

remained unchanged in the propofol group (Figure, events 7–11). MAP and HR did not change significantly during desflurane substitution or in either group during emergence (Table).

Discussion

To our knowledge, this is the first time that the effect of desflurane on CBFV has been studied on emergence of anesthesia. The current study demonstrates that desflurane is associated with a significant increase in CBFV when used to facilitate rapid emergence following a propofol infusion for maintenance of general anesthesia in healthy children. However, this transient increase in CBFV returns to baseline levels once desflurane is reduced below an end-tidal concentration of 0.2% during emergence of anesthesia. It remains to be determined how this technique will affect children with decreased intracranial compliance or a disrupted blood-brain barrier.

Propofol has been shown to decrease both cerebral metabolism and blood flow in adults.[7] Cerebrovascular reactivity to carbon dioxide is highly preserved under propofol anesthesia in children.[8] These properties make it an ideal anesthetic agent for children undergoing neurosurgical procedures. Due to significant pharmacokinetic and pharmacodynamic differences between children and adults however, propofol doses and infusion rates required to achieve a certain target blood concentration are higher for pediatric patients.[9,10] In addition, the context-sensitive half-life of propofol is longer in children than in adults, presumably due to altered compartment volumes of distribution.[9] This implies that recovery from a propofol infusion may be slower in children than in adults, which may limit its usefulness in prolonged neurosurgical procedures.

Desflurane has pharmacokinetic properties that allow for rapid emergence which is often desirable in the neurosurgical setting. Infants anesthetized with desflurane demonstrated a faster recovery when compared to those anesthetized with isoflurane.[11] However, some of the potentially undesirable cerebrovascular properties of desflurane deserve mention. Cerebral blood pressure autoregulation is impaired at 1.0 MAC, and almost completely abolished at 1.5 MAC desflurane in adults.[2] Desflurane has been shown to cause a dose-dependent increase in Vmca and HR in children,[3] an effect which appears to be enhanced with the addition of nitrous oxide.[12] CBFV increases when propofol is replaced with desflurane for maintenance of anesthesia in pediatric patients.[13]

Factors known to alter CBFV include surgical stimulation, arterial carbon dioxide partial pressure, cardiac output, body temperature, and intrathoracic

pressure. End-tidal CO_2 and body temperature remained constant throughout the study period and the caudal epidural block seemed to eliminate the cerebrovascular response to surgical stimulation.

The absence of any significant change in HR or MAP at the time of desflurane substitution or during emergence of anesthesia in either group is likely due to the fact that remifentanil was used as part of a balanced anesthetic technique. Remifentanil has been shown to attenuate the somatic and hemodynamic responses in children at doses used in the current study.[6] A recent pediatric study has demonstrated that remifentanil 0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ does not alter CBFV.[14] The *iv* crystalloid administration regimen likely also contributed to the overall hemodynamic stability noted in the current study.

The transient sympathetic hyperactivity observed with desflurane in children is known to persist for up to nine minutes.[15] As such, physiologic variables were recorded no earlier than 15 min after desflurane substitution in order to eliminate this source of error and achieve steady-state concentrations.

The increase in variability of Vmca in the desflurane-substituted group needs to be addressed. Desflurane is known to cause cerebral vasodilatation, perhaps even more so than other volatile agents.[4,16] Physiologically, measurements of flow during vasodilatation would be expected to exhibit greater variability as compared to vasoconstriction, which has a more finite endpoint.

TCD sonography is a non-invasive and reproducible technique that has been validated as a surrogate measure of cerebral blood flow.[17] To reduce inter-patient variability in Vmca measurements, the TCD examination was performed by one of three experienced researchers. Fixing the TCD probe in place using an established frame reduced intra-patient variability.[18]

In conclusion, the current study demonstrates that desflurane is associated with an increase in CBFV when used to facilitate rapid emergence following a propofol infusion for maintenance of general anesthesia in children. However, this transient increase in CBFV returns to control levels once desflurane is reduced to subanesthetic concentrations during emergence. This should be taken into consideration when contemplating the administration of desflurane in the pediatric neurosurgical setting, particularly in those patients with decreased intracranial compliance.

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A Historical Note:

An anesthetic disaster

As a first year resident in a Toronto teaching hospital during a dry, cold January day in 1965, I became involved in an anesthetic disaster. The senior anesthesiologist was manually ventilating a patient having a hysterectomy using cyclopropane, which was highly explosive, for maintenance. Every effort was made to reduce electrical leakage and "static build-up" by avoiding cautery and electronic monitoring.

However, on that cold, dry day, a static charge was possibly created in the operating room (OR) in association with a leak in the anesthetic circuit. The result was a massive explosion in the OR which blew up the gas machine, created a blast injury to the patient's lungs and left the OR and its staff in complete confusion and disarray. As the resident on call, I rushed to the OR and was able to get another gas machine and ventilate the patient's lungs with O_2.

The OR was littered with broken glass, fragments of rubber tubing, and bits of metal, but no gas cylinders exploded. The OR staff had transient deafness, but were able to rapidly complete the surgical procedure. The patient continued to have vital signs, but was bleeding from the endotracheal tube as a result of the blast injury. I continued manual ventilation with O_2 as there was no mechanical ventilator available.

I transferred the patient to the intensive care unit (ICU) and continued ventilation with the aid of a Bird Mark VII pressure controlled ventilator. As the resident also on call for the ICU, I watched the patient deteriorate due to pulmonary hemorrhage and lack of lung tissue for gas exchange. There was no ECMO at that time and lung transplant had not even been thought of.

Historical incidents such as the one that I was involved in, should make us thankful that one of the great dangers to patients and OR personnel is now a thing of the past in modern anesthesia. The use of explosive agents such as ether and cyclopropane is no longer even considered due to the array of electrical equipment in the OR. Cyclopropane was a wonderful agent, but it explodes! A generation of anesthesiologists who began practice after 1965 will never see it used in Canada.

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