The influence of arterial oxygenation on cerebral venous oxygen saturation during hyperventilation

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Cerebral venous oxygen desaturation may occur when hyperventilation is employed during neurosurgical procedures. In this study, we examined the effect of arterial hyperoxia (PaO_2 > 200 mmHg) on jugular bulb venous oxygen tension ($PjvO_2$), saturation ($SjvO_2$) and content ($CjvO_2$) in 12 patients undergoing anaesthesia for neurosurgical procedures. Under stable anaesthetic conditions, the inspired oxygen fraction (FIO_2) was varied to give four different levels of arterial oxygen tension (PaO_2 100–200, 201–300, 301–400, and >400 mmHg), at two levels of controlled hyperventilation ($PaCO_2$ 25 and 30 mmHg). In five patients, a transcranial Doppler probe was used to insonate the middle cerebral artery throughout the study period. Regression lines were constructed for each patient for the $PjvO_2$, $SjvO_2$ and the corresponding PaO_2 for both levels of $PaCO_2$ (all $PjvO_2$-PaO_2 and $SjvO_2$-PaO_2 regression lines $r^2 > 0.85$, $P < 0.0001$). From these lines we calculated the $PjvO_2$, $SjvO_2$ and $CjvO_2$ at PaO_2 of 100, 250 and 400 mmHg, at each level of $PaCO_2$ for each patient. At $PaCO_2$ of 25 mmHg, hyperoxaemia increased $PjvO_2$ (from 27.6 ± 1.1 mmHg at PaO_2 of 100 mmHg to 30.6 ± 1.4 and 33.6 ± 1.8 mmHg at PaO_2 of 250 and 400 mmHg respectively) and $SjvO_2$ (from 54 ± 3% at PaO_2 of 100 mmHg to 60 ± 3 and 65 ± 3% at PaO_2 of 250 and 400 mmHg respectively, $P < 0.05$). Hyperoxaemia had a similar effect on $SjvO_2$ and $PjvO_2$ at a $PaCO_2$ of 30 mmHg. For a given PaO_2, the $PjvO_2$, $SjvO_2$ and $CjvO_2$ were lower at $PaCO_2$ of 25 mmHg than at a $PaCO_2$ of 30 mmHg ($P < 0.01$). The predicted $CjvO_2$ based on the increased PaO_2 and an unchanged cerebral metabolic rate for oxygen was also calculated and was no different from the measured $CjvO_2$ with hyperoxia. Middle cerebral artery flow velocity did not change with hyperoxia, but decreased with hypocapnia (48 ± 7 to 35 ± 4 $cm \cdot sec^{-1}$, $P < 0.01$). We conclude that hyperoxia during acute hyperventilation in the anaesthetized patient improves oxygen delivery to the cerebral circulation, as measured by a higher cerebral venous oxygen content and saturation. An increased PaO_2 should be considered for those patients in whom aggressive hyperventilation is contemplated.

La désaturation veineuse centrale peut survenir pendant l'hyperventilation réalisée au cours d'interventions neurochirurgicales. Nous avons étudié les répercussions de l'hyperoxémie (PaO_2 > 200 mmHg) sur la tension en oxygène du bulbe jugulaire ($PjvO_2$), sa saturation ($SjvO_2$) et son contenu ($CjvO_2$) chez 12 patients soumis à une anesthésie générale pour une intervention neurochirugicale. Sous des conditions stables d'anesthésie, la fraction en oxygène inspiré (FIO_2) a été variée pour produire quatre niveaux différents de tension artérielle en oxygène (PaO_2 100–200, 201–300, 301–400 et >400 mmHg) à deux niveaux d'hyperventilation ($PaCO_2$ 25 et 30 mmHg). Une sonde de Döppler intracrânienne a été insérée à cinq patients pour explorer l'artère méningée moyenne. A chaque patient, nous avons construit des lignes de régression de la $PjvO_2$, de la $SjvO_2$ pour la PaO_2 correspondante, aux deux niveaux de $PaCO_2$ (toutes les lignes de régression $PjvO_2$-PaO_2 et $SjvO_2$-PaO_2 $r^2 > 0,85$, $P < 0,0001$). A partir de ces lignes, nous avons calculé chez chaque patient la $PjvO_2$, la $SjvO_2$ et le $CjvO_2$ aux PaO_2 de 100, 250 et 400 mmHg, pour chaque niveau de $PaCO_2$. A la $PaCO_2$ de 25 mmHg, l'hyperoxémie a augmenté la $PjvO_2$ (de 27,6 ± 1,1 mmHg pour une PaO_2 de 100 mmHg à 30 ± 1,4 et 33,6 ± 1,8 mmHg aux PaO_2 de 250 et 400 mmHg respectivement, $P < 0,05$). L'hyperoxémie a eu le même effet sur la $SjvO_2$ et la $PjvO_2$ à la $PaCO_2$ de 30 mmHg. Pour une PaO_2 donnée, la $PjvO_2$, la $SjvO_2$ et le $CjvO_2$ ont été plus bas à la $PaCO_2$ de 25 mmHg qu'à celle de 30 mmHg ($P <$

Key words
ANAESTHESIA: neurosurgical;
BLOOD FLOW: velocity, cerebral;
EQUIPMENT: Doppler
MEASUREMENT TECHNIQUES: Doppler ultrasound;
MONITORING: oxygen, jugular venous;
OXYGEN: consumption, brain.

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Accepted for publication 11th June, 1994.

0,01). La $CjvO_2$ prédite lorsque la PaO_2 augmente et que le taux métabolique cérébral demeure inchangé a aussi été calculée et n'a pas été trouvée différente de la $CjvO_2$ mesurée en hyperoxémie. La vélocité du courant sanguin de l'artère cérébrale moyenne n'a pas changé avec l'hyperoxémie mais a diminué avec l'hypocarbie (de 48 ± 7 à 35 ± 4 cm · sec^{-1}, $P < 0,01$). Nous concluons que chez le sujet anesthésié, l'hyperoxie produite pendant une hyperventilation aiguë améliore l'apport en oxygène de la circulation cérébrale, comme l'ont montré l'augmentation du contenu veineux cérébral et de la saturation en oxygène. On doit envisager d'augmenter la PaO_2 des patients qu'il faut ventiler agressivement.

Acute hyperventilation decreases cerebral blood flow (CBF).[1,2] It causes electroencephalographic slowing consistent with cerebral ischaemia[3] and an increase in brain tissue and cerebrospinal fluid lactate concentrations,[4] that can be reversed with the administration of hyperbaric oxygen.[3,5] Despite this potentially undesirable effect on CBF, hyperventilation reduces cerebral blood volume and intracranial pressure (ICP), and may improve cerebral perfusion pressure (CPP) in some patients. Consequently, hyperventilation provides improved operating conditions and is frequently used during neurosurgical procedures. Intraoperative surgical requirements (reduction of brain bulk) may necessitate marked hyperventilation at the risk of causing cerebral ischaemia. It would be desirable if hyperventilation could be employed to provide improved operating conditions and/or reduce ICP without the accompanying reduction in oxygen delivery to the brain. Increasing the arterial oxygen tension and content may allow greater oxygen delivery to the brain during this vulnerable period. However, hyperoxygenation has been shown to cause cerebral vasoconstriction which may negate the potential improvement in oxygen delivery.[6] To clarify this interaction, we studied the effect of hyperoxia at two levels of $PaCO_2$ on the cerebral venous oxygen content in 12 patients undergoing anaesthesia for neurosurgery.

Methods

The study was approved by the University of Washington Human Subjects Review Committee. After obtaining written consent, 12 patients, ASA physical status 1 or 2, who were about to undergo craniotomies for various elective neurosurgical procedures (nine cerebral aneurysms and three intracranial tumours) were studied. With all routine monitors in place (ECG, arterial catheter, pulse oximetry), patients received a standardized anaesthetic consisting of *iv* midazolam 1–2 mg, thiopentone 3–5 mg · kg^{-1}, fentanyl bolus 3 μg · kg^{-1} followed by infusion 3 μg · kg^{-1} · hr^{-1} and vecuronium 0.1 mg · kg^{-1}. After the trachea was intubated, the lungs were mechanically ventilated to normocapnia with an air/oxygen mixture and anaesthesia was maintained with low dose isoflurane (end-tidal 0.5–1.0%). Using an aseptic technique described previously,[7] we inserted a 16-gauge, 13.3 cm retrograde jugular bulb catheter (Angiocath®, Becton and Dickinson) in all patients without complication. The catheter was inserted contralateral to the operative site and the position of the catheter was checked radiographically and was satisfactory in all patients studied (tip of the catheter was at the level of and just medial to the mastoid bone). In five patients, surgical conditions permitted the measurement of cerebral blood flow velocity from the middle cerebral artery (MCA) ipsilateral to the jugular venous bulb catheter throughout the study period. The MCA was insonated with a 2 MHz transcranial Doppler probe (Medasonics, Fremont, CA, USA) through the temporal window, using a technique previously described.[8] A low profile attachment was used to secure the probe in position so that the angle of insonation remained constant throughout the study. Doppler signals were identified and measured at 45–50 mmHg. The shift in frequency spectra of the Doppler signals converted into mean flow velocity (Vmca) were displayed on a video monitor. Flow velocities were recorded at end-expiration.

Under stable anaesthetic and surgical conditions, and at least 30 min after mannitol administration, the patients' lungs were hyperventilated to a $PaCO_2$ of 25 mmHg (±1). A 15-min period of stabilization was allowed at that $PaCO_2$. The FiO_2 was then varied to achieve four levels of PaO_2: 100–200, 201–300, 301–400 and >400 mmHg. After a further 15 min stabilization at each PaO_2 level, arterial and jugular venous blood gases were drawn (at a rate of <2 ml · min^{-1}) and Vmca (in five patients) was recorded at each level of PaO_2. The $PaCO_2$ was then increased to 30 mmHg (±1) and the same procedure repeated. The tidal volume and respiratory rate were altered in such a manner so as to maintain airway pressure constant, thus minimizing the effects on venous return and cardiac output. The study sequence was randomized so that half of the patients were studied at a $PaCO_2$ of 30 mmHg first and the other half were studied initially at a $PaCO_2$ of 25 mmHg. The blood samples were analyzed using an automated blood gas analyzer (Nova Biomedical 9, Waltham, MA, USA).

Regression lines were constructed for each patient for the $PjvO_2$, $SjvO_2$ and the corresponding PaO_2 for both levels of $PaCO_2$. From these lines we calculated the $PjvO_2$, $SjvO_2$, $CjvO_2$ and the arteriovenous oxygen content difference ($AVDO_2$) at PaO_2 of 100, 250, and 400 mmHg, at each level of $PaCO_2$ for each patient. The arterial and venous oxygen contents (CaO_2, $CjvO_2$) and $AVDO_2$ were calculated from the arterial PO_2 and sat-

uration, and jugular venous O_2 tension and saturation using the equation:

$$AVDO_2 = \text{arterial } O_2 \text{ content } (CaO_2) - \text{jugular venous } O_2 \text{ content } (CjvO_2)$$
$$= Hgb \times 1.39 \times SaO_2 + 0.003 \times PaO_2) - (Hgb \times 1.39 \times SjvO_2 + 0.003 \times PjvO_2).$$

The data were analyzed using two-way analysis of variance for repeated measures. We considered a P value <0.05 statistically significant.

To assess the magnitude of cerebral vasoconstriction secondary to hyperoxygenation, which would result in a $CjvO_2$ value lower than expected based on the increase in oxygen delivery, we derived the predicted $CjvO_2$ and compared it with the measured $CjvO_2$. To do this, we considered PaO_2 of 100 mmHg to be normoxia, and calculated the corresponding $AVDO_2$. Assuming an unchanged cerebral metabolic rate (therefore an unchanged $ADVO_2$ if CBF remains constant), we then calculated the $CjvO_2$ at PaO_2 of 250 and 400 mmHg. Thus the predicted $CjvO_2$ at PaO_2 of 250 mmHg = CaO_2 at PaO_2 of 250 mmHg − $AVDO_2$ at PaO_2 of 100 mmHg and the predicted $CjvO_2$ at PaO_2 of 400 mmHg = CaO_2 at PaO_2 of 400 mmHg − $AVDO_2$ at PaO_2 of 100 mmHg. The predicted values were then compared with the measured values using paired t test.

Results

The patient data are shown in Table I.

There was no change in the patients' body temperature (36 ± 0.5°C), mean arterial pressure (75 ± 5 mmHg) or heart rate (75 ± 10 bpm) throughout the study. The $SjvO_2$ vs PaO_2 mean regression coefficients for patients at $PaCO_2$ of 25 and 30 mmHg were 0.035 ± 0.01% $mmHg^{-1}$, $0.85 < r^2 < 0.996$ ($P < 0.001$), and 0.038 ± 0.01% $mmHg^{-1}$, $0.840 < r^2 < 0.998$ ($P < 0.001$), respectively.

Hyperoxia increased jugular venous oxygen tension, saturation and content, at both levels of $PaCO_2$ ($P < 0.05$) (Figures 1 and 2). For a given PaO_2, the $SjvO_2$, $PjvO_2$ and $CjvO_2$ were higher at a $PaCO_2$ of 30 mmHg than at a $PaCO_2$ of 25 mmHg ($P < 0.01$) (Tables II and III).

At a $PaCO_2$ of 25 mmHg, four patients at PaO_2 of 100 mmHg and two patients at PaO_2 of 250 mmHg had $SjvO_2 < 50\%$, but no patients at PaO_2 of 400 mmHg had $SjvO_2 < 50\%$. At a $PaCO_2$ of 30 mmHg, one patient at PaO_2 of 100 mmHg had $SjvO_2 < 50\%$ but no patient at PaO_2 of 250 and 400 mmHg had $SjvO_2 < 50\%$.

In the five patients monitored with the transcranial Doppler, Vmca did not change with hyperoxia at either level of $PaCO_2$. Cerebral blood flow velocity increased from 35 ± 4.0 $cm \cdot sec^{-1}$ at a $PaCO_2$ of 25 mmHg to 48 ± 7 $cm \cdot sec^{-1}$ at a $PaCO_2$ of 30 mmHg ($P < 0.01$) (Table II). The measured $CjvO_2$ at hyperoxic PaO_2 (PaO_2 250 and 400 mmHg) was not different from the predicted $CjvO_2$ (Table III).

TABLE I Patient data

Patient n = 12	*Mean, SD*
Age, yr	51, 12
Weight, kg	72, 7
Sex (M:F)	6:6
Haemoglobin $g \cdot dl^{-1}$	11.9, 1.2

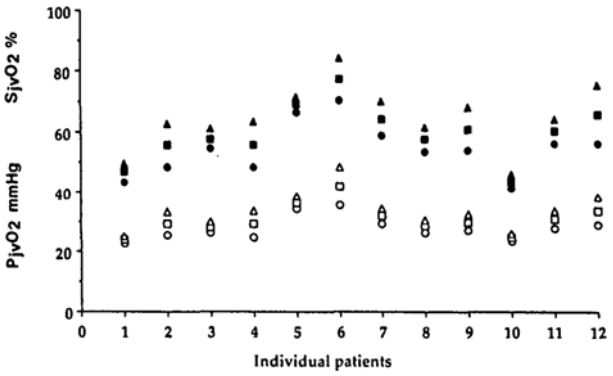

FIGURE 1 $SjvO_2$ and $PjvO_2$ at $PaCO_2$ of 25 mmHg. ●$SjvO_2$ at PaO_2 of 100 mmHg; ■$SjvO_2$ at PaO_2 of 250 mmHg; ▲$SjvO_2$ at PaO_2 of 400 mmHg; ○$PjvO_2$ at PaO_2 of 100 mmHg; □$PjvO_2$ at PaO_2 of 250 mmHg; △$PjvO_2$ at PaO_2 of 400 mmHg.

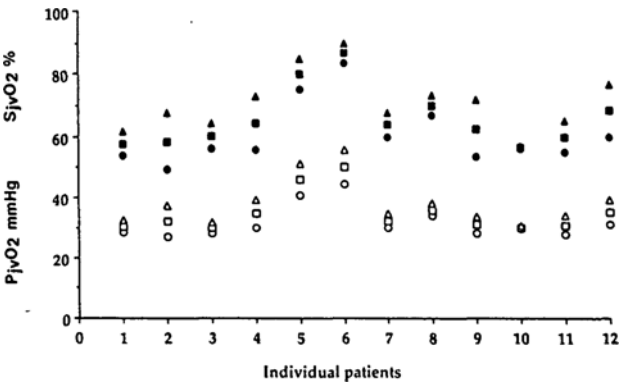

FIGURE 2 $SjvO_2$ and $PjvO_2$ at $PaCO_2$ of 30 mmHg. ●$SjvO_2$ at PaO_2 of 100 mmHg; ■$SjvO_2$ at PaO_2 of 250 mmHg; ▲$SjvO_2$ at PaO_2 of 400 mmHg; ○$PjvO_2$ at PaO_2 of 100 mmHg; □$PjvO_2$ at PaO_2 of 250 mmHg; △$PjvO_2$ at PaO_2 of 400 mmHg.

Discussion

The use of hyperventilation during neurosurgical procedures can result in cerebral venous oxygen desaturation (defined as jugular bulb venous oxygen saturations less

TABLE II The effect of hyperoxia at two levels of $PaCO_2$ on $SjvO_2$ and $PjvO_2$

	$PaCO_2 = 25$ mmHg			$PaCO_2 = 30$ mmHg		
PaO_2 mmHg	$SjvO_2$%* (n = 12)	$PjvO_2$ mmHg† (n = 12)	Vmca cm/sec‡ (n = 5)	$SjvO_2$%* (n = 12)	$PjvO_2$ mmHg† (n = 12)	Vmca cm/sec‡ (n = 5)
100	54 ± 3§	27.6 ± 1.1¶	35 ± 4	61 ± 3§	31.6 ± 1.6¶	48 ± 7
250	60 ± 3§	30.6 ± 1.4¶	35 ± 4	66 ± 3§	34.9 ± 1.9¶	48 ± 7
400	65 ± 3§	33.6 ± 1.8¶	35 ± 4	71 ± 3§	38.3 ± 2.2¶	48 ± 7

All values are mean ± SE.
*The difference between $SjvO_2$ at a $PaCO_2$ of 25 mmHg and $SjvO_2$ at a $PaCO_2$ of 30 mmHg is statistically significant at $P < 0.01$.
†The difference between $PjvO_2$ at $PaCO_2$ of 25 mmHg and $PjvO_2$ at $PaCO_2$ of 30 mmHg is statistically significant at $P < 0.01$.
‡The difference between CBFV at $PaCO_2$ of 25 mmHg and CBFV at $PaCO_2$ of 30 mmHg is statistically significant at $P < 0.01$.
§The difference between $SjvO_2$ at PaO_2 of 100, 250 and 400 mmHg is statistically significant at $P < 0.05$.
¶The difference between $PjvO_2$ at PaO_2 of 100, 250 and 400 mmHg is statistically significant at $P < 0.05$.

TABLE III The effect of hyperoxia at two levels of $PaCO_2$ on jugular venous oxygen content: predicted [$CjvO_2$ (p)] and measured [$CjvO_2$ (m)]

	$PaCO_2 = 25$ mmHg		$PaCO_2 = 30$ mmHg	
PaO_2 mmHg	$CjvO_2$ (m)* vol%	$CjvO_2$ (p)† vol%	$CjvO_2$ (m)* vol%	$CjvO_2$ (p)† Vol%
100	8.95 ± 0.48‡	8.95 ± 0.48‡	9.98 ± 0.53‡	9.98 ± 0.53‡
250	9.78 ± 0.45‡	9.73 ± 0.49‡	10.86 ± 0.50‡	10.76 ± 0.53‡
400	10.63 ± 0.47‡	10.18 ± 0.50‡	11.77 ± 0.54‡	11.22 ± 0.54‡

All values are mean ± SE.
*The difference between the measured $CjvO_2$ at $PaCO_2$ of 25 and $CjvO_2$ at $PaCO_2$ of 30 mmHg is statistically significant at $P < 0.05$.
†The difference between the predicted $CjvO_2$ at $PaCO_2$ of 25 and $CjvO_2$ at $PaCO_2$ of 30 mmHg is statistically significant at $P < 0.05$.
‡The difference between $CjvO_2$ at PaO_2 of 100, 250 and 400 mmHg is statistically significant at $P < 0.05$.

than 50%) in up to 40% of patients undergoing neurosurgery.[7] Although the clinical importance of this intraoperative desaturation remains unclear, at best it is indicative of increased extraction of oxygen with a decreased margin of safety, and at worst, indicative of limited oxygen supply with impending tissue hypoxia. Moreover, the use of hyperventilation in patients with severe head injury has been shown to cause cerebral oligaemia[9] which may lead to a worse neurological outcome.[10,11]

Despite this potential adverse effect, hyperventilation can reduce CBF, cerebral blood volume and intracranial pressure (ICP), and may improve cerebral perfusion pressure (CPP) in some patients. In addition, hyperventilation may provide improved operating conditions. Our study was designed to test the hypothesis that hyperoxia, by improving oxygen delivery, would improve the margin of safety during hyperventilation.

Kennealy *et al.*[12] have shown that, in dogs, hyperoxygenating the blood results in an increase in jugular venous bulb and brain tissue oxygen tension. However, others have shown reductions in CBF with hyperoxia in normocapnic piglets,[13] ponies,[14] infants[15] and adults.[16] This cerebral vasoconstriction may negate any potential beneficial effects of hyperoxia during hyperventilation. The effect of arterial hyperoxygenation on cerebral venous O_2 content in anaesthetized patients during acute hyperventilation has not been fully investigated and is the purpose of this study.

We chose two levels of $PaCO_2$, 25 mmHg and 30 mmHg, to assess whether hyperoxygenation improves $SjvO_2$ during moderate and marked hyperventilation. During hyperventilation to a $PaCO_2$ of 25 mmHg, four patients had $SjvO_2 < 50\%$ at PaO_2 of 100 mmHg and two patients had $SjvO_2 < 50$ at PaO_2 of 250 mmHg. At a $PaCO_2$ of 30 mmHg, only one patient had $SjvO_2 < 50\%$ and this was at a PaO_2 of 100 mmHg. There were no episodes of desaturation during hyperoxia at PaO_2 of 400 mmHg at either level of $PaCO_2$. Although not applicable to the patients in this study, episodes of cerebral venous desaturation ($SjvO_2 < 50\%$) have been shown to be common in patients with head injury even when receiving intensive care with advanced cardiovascular and intracranial monitoring. The observation that head-injured patients with cerebral venous desaturation had a higher mortality than those without such episodes highlights the potential benefit of detecting and treating such desaturation.[16] It would appear that the most important factor controlling cerebral blood flow (CBF) is

$PaCO_2$, as shown by the higher $SjvO_2$, $PjvO_2$ and $CjvO_2$ at the higher $PaCO_2$ of 30 mmHg ($P < 0.01$). Nonetheless, in the 12 patients studied, hyperoxygenation was beneficial in reducing the incidence of cerebral venous oxygen desaturation during hyperventilation. Hyperoxygenation improved $CjvO_2$ at both levels of $PaCO_2$ ($P < 0.05$). As the study was conducted during relatively steady-state anaesthetic and surgical conditions, this increase presumably reflects an increase in O_2 delivery.

Does normobaric hyperoxygenation produce cerebral vasoconstriction in hypocapnic patients? To answer this question, we derived the predicted $CjvO_2$ based on an unchanged CBF and an unchanged cerebral metabolic rate for oxygen ($CMRO_2$) and compared this to the actual measured $CjvO_2$. We considered PaO_2 of 100 mmHg to be normoxia, and calculated the corresponding $AVDO_2$. Assuming an unchanged $CMRO_2$ (therefore an unchanged $AVDO_2$ if CBF stays constant), we then calculated $CjvO_2$ at PaO_2 of 250 and 400 mmHg. We found the measured and the predicted $CjvO_2$ to be almost identical with hyperoxia during hypocapnia. This suggests that, during steady state anaesthesia, when $CMRO_2$ is presumed constant, there is no change in CBF when $PaCO_2$ is constant and PaO_2 is increased (Table III). Had there been any decrease in CBF with hyperoxia, the measured $CjvO_2$ would have been lower than the predicted value. The Vmca determination in the five patients with transcranial Doppler monitoring supports this contention and is in agreement with recently published data on Vmca and hyperoxia.[17,18] These findings indicate that the vasoconstrictive response to hyperoxia reported in other studies is abolished by hyperventilation, the anaesthetic conditions employed in this study, or both. It is likely that hypocapnia, even at $PaCO_2$ of 30 mmHg, results in cerebral vasoconstriction that exceeds any vasoconstrictive effect of normobaric hyperoxia.

We conclude that hyperoxia during acute hyperventilation in the anaesthetized patient improves oxygen delivery to the brain as measured by increased cerebral venous oxygen content and saturation. This increase is seen without any apparent change in CBF. Hyperoxia should be considered for those patients in whom hyperventilation is contemplated and cerebral ischaemia is considered a risk.

Acknowledgements

The authors greatly acknowledge Dr. H. Richard Winn for his permission to perform this study on his patients, and Karen Rutherford for secretarial assistance.

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