Hyperventilation and the brain – helpful or hazardous? (Did an Australian lead us astray with bad science?)

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Hyperventilation has been a common practice in neuroanesthesia since the 1960’s. However, a review of the literature suggests that hypocapnia was not initially deliberately introduced into practice to improve operating conditions but was perhaps an inadvertent by-product of muscle relaxation and thereby the need for intermittent positive pressure ventilation (IPPV). The first clinical report of its use in neurosurgery in the peer review literature came from Melbourne in 1957 and involved a review of “72 craniotomies and 28 spinal operations - far too small a number for statistical purposes.” The authors went on to draw the following conclusions: “It is, nevertheless, a strong clinical impression that we are obtaining better operating conditions with controlled respiration technique. After preliminary tentative trials, gradually the neurosurgeons were completely convinced and prefer this technique.” “It is impossible to say that this method is better than spontaneous respiration and equally good operating conditions are produced with perfect open circuit anaesthesia.” As blood gas or end-tidal gas sampling were not available it is in fact impossible to know if hyperventilation was indeed achieved and it is likely that the authors were simply referring to the use of mechanical ventilation.

Owing to the fact that good operating conditions were easily produced and the demonstrations that lowered PaCO₂ reduced ICP and with no clinical studies showing a poor outcome, hyperventilation became the standard of practice. By 1991, 83% of trauma centers surveyed reported prophylactic use of hyperventilation for patients with severe traumatic brain injury. However, there has been an
increasing number of laboratory and clinical trials demonstrating possible harmful effects of hyperventilation. Also, various interest groups have published recommendations against prolonged or excessive hyperventilation. Consequently there has been a recent reduction in its use in most clinical settings.

**Neurophysiology**

**Cerebral Blood Flow**

In normal subjects, the global cerebral blood flow (CBF) falls by 2 - 3% for each mmHg fall in PaCO$_2$ until about PaCO$_2$ of 20mmHg. More severe hypocapnia does not cause further reduction in flow. In healthy volunteers, sustained hyperventilation leads to a recovery of CBF to within 10% of baseline values in as little as four hours but the response rates may be different in the injured brain. Hyperventilation in the presence of volatile anaesthetic agents causes a greater reduction in CBF but from a higher initial flow owing to the vasodilatory effects of the anaesthetic. CBF, and its response to hypocapnia, are not affected by propofol, benzodiazepines or opioids.

**Cerebral Blood Volume**

The chief mechanism by which hypocapnia reduces ICP is by a reduction in cerebral blood volume (CBV). The baseline value for CBV is 3 – 4 ml.100g$^{-1}$ and hyperventilation reduces this by 0.05 ml.100g$^{-1}$.mmHg CO$_2$$^{-1}$. Over a four hour period of sustained hyperventilation CBV returns to the baseline value. The bulk of intracranial CBV is in the venous side of the circulation and only 15% is in the arterial tree. However it is the arteries that are predominantly responsive to CO$_2$ not the veins so that hyperventilation reduces CBV by constricting the arterial inflow which if excessive results in ischaemia.

**Cerebral Ischaemia**
In the normal brain, CBF remains greater than 20 ml.100g\(^{-1}\) even during extreme hypocapnia (PaCO\(_2\) = 10 mmHg). This is similar to the global CBF levels that cause slowing of the EEG. Severe hypocapnia does not reduce the cerebral metabolic rate or change the ATP and phosphocreatinine levels in the healthy brain but this is not always the case in the injured brain.

**Clinical Use of Hyperventilation**

*Cerebral Ischaemia*

Hyperventilation has a theoretical benefit in cerebral ischaemia because it is thought that by constricting resistance vessels in the normal areas of the brain, flow may be redirected towards ischaemic areas in which vessels do not respond to changes in carbon dioxide concentration. Early animal studies suggested that hyperventilation was beneficial after experimental focal cerebral ischaemia. However, despite a 10% increase in blood flow to ischaemic areas with hyperventilation in humans after a stroke, no outcome benefit has been shown. Further animal research has shown that hyperventilation after focal cerebral ischaemia actually exacerbates the reduction in high-energy compounds in the brain indicating a worsening of cerebral ischaemia.

After cardiac arrest hyperventilation has been shown to reduce jugular venous oxygen saturation and to increase lactate production. Thus clinical studies do not support the use of hyperventilation after focal or global ischaemic insults.

*Craniotomy*

Hyperventilation has long been considered an integral part of anaesthesia for intracranial surgery. Hyperventilation can overcome the increase in ICP & CBV associated with volatile anaesthetics and nitrous oxide. However a marked benefit has not been found with propofol which in its own right reduces ICP & CBV and there is (potential) concern because hyperventilation during TIVA has been associated with lowered jugular venous oxygen saturation.
A recent randomized trial we performed found that surgeons blinded to the CO₂ could not at initial assessment note a difference in operating condition by CO₂ level. However they could tell a change in CO₂ after they had made their initial assessment.

During craniotomy hyperventilation should not be a routine but should be guided by perioperative indicators of raised ICP and by the surgeons’ assessment of the brain at craniotomy. It should be noted that the latter two correlate poorly.

**Traumatic Brain Injury**

Patients with a significant head injury may benefit from hyperventilation by a reduction in CBV and ICP which may lead to an increase in CPP thus improving oxygen and nutrient delivery to the damaged brain. Cruz found that hyperventilation in selected head injury patients normalized both cerebral oxygen and glucose extraction. By contrast, a long term follow-up of patients after severe head injury by Muizelaar et al. found a greater incidence of neurological deficit in hyperventilated patients (PaCO₂ 25 mmHg) at 3 and 6 months. This latter study has greatly influenced clinical management despite its complex design and the fact that subsequent studies are not nearly as conclusive.

The adverse outcome is probably the result of a reduction in globa/regional CBF. One study found that severe hypocapnia (PaCO₂ of 21 mmHg) for 10 minutes caused a fall in tissue PO₂ and jugular bulb oximetry despite an increase in CPP and a fall in ICP. Robertson randomized 189 comatose patients to receive either a CBF-targeted management protocol (CPP > 70 mmHg) or an ICP-targeted protocol (hyperventilation to PaCO₂ 25–30 mmHg). Patients in the ICP-targeted group had a higher incidence, severity and duration of cerebral ischaemic events as measured by a SjvO₂ < 50%. However there was no difference in neurological outcome between the two groups. This may have been due to the increased risk of adult respiratory distress syndrome (ARDS) demonstrated in the CBF-targeted group,
who required more intravenous fluid and dopamine to maintain the high perfusion pressures. Conversely cerebral ischaemia is not a consistent finding in head injured patients treated with hyperventilation. Diringer et al. found no evidence of ischaemia, as measured by a fall in cerebral metabolic rate or an increase in oxygen extraction ratio, in 9 patients treated for 30 minutes with moderate hyperventilation (PaCO₂ of 30 mmHg).

No study has demonstrated improved patient morbidity or mortality due to the use of hyperventilation. For this reason the recommendations of the Brain Trauma Foundation include the avoidance of prolonged or severe (PaCO₂ < 25 mmHg) hyperventilation and also the avoidance of prophylactic use of even lesser degrees of hypocapnia. Where hyperventilation is to be used in the short-term management of acute neurological deterioration, it is recommended that a monitor of the adequacy of cerebral blood flow be used.

**Summary**

An examination of the evidence does not reveal a strong case for the use of hyperventilation in most neurosurgical scenarios. Indeed, there are numerous studies that indicate the potential for hypocapnia to be detrimental to the patient. If it is deemed necessary for acute control of raised ICP or brain bulge, mild degrees of hypocapnia (30 – 35 mmHg) are recommend. Where available, the use of monitors of cerebral ischaemia may be a further guide to the safe use of hyperventilation.

**References**


