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### Editorial

## Carbon Dioxide – a Substance to be Manipulated with Care Dióxido de Carbono – una sustancia que debe manipularse con cuidado

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Hyperventilation has been a part of the management of neurosurgical patients for over half a century. A relationship between arterial carbon dioxide and cerebral blood flow (CBF) was already noted in 1936.<sup>1</sup> But it was not till 20 years later that this relationship entered more regular clinical practice. Lundberg, Lassen and then Gordon used and recommended its use in patients with elevated intracranial pressure after head trauma and Furness described its use in elective craniotomy.<sup>2-5</sup> In studies of that time, including the report by Furness, it is not clear whether the patients had a reduced carbon dioxide level and to what extent as arterial blood gases were not always measured. The benefits may therefore have been due to better airway management and oxygenation from intubation and ventilation compared to spontaneous ventilation. It's also apparent from the literature that the effects of hyperventilation were not consistent in every patients as some patients respond and others do not.<sup>6,7</sup> Despite this, hyperventilation became part of the standard management of patients with increased intracranial pressure having an elective operation or in the intensive care unit.

The mechanism by which hyperventilation reduces cerebral blood flow is well described in the extensive review in the current issue of the *Colombian Journal of Anesthesiology*.<sup>8</sup> By reducing perivascular pH, the cerebral arterioles, but not veins, constrict resulting in a reduction in cerebral blood flow. The vasoconstriction also results in a reduction in cerebral blood volume (CBV) and it this latter change that may reduce ICP. Every 1 mmHg reduction in PaCO<sub>2</sub> reduces CBF by 2-4% but only reduces CBV by 1%.

The enthusiasm for hyperventilation came to an abrupt end in 1991. Muizelaar et al reported a worse outcome 3 and 6 months after 5 days of hyperventilation.<sup>9</sup> 113 patients were randomized into 3 groups. There were two hyperventilated groups, one with THAM and one without. PaCO<sub>2</sub> was kept at 24-28mmHg. In the control group PaCO<sub>2</sub> was kept 30-35mmHg, which would also be considered hyperventilation today! The actual indication for hyperventilation may also be doubtful because only 14% of patients had ICP>20mmHg. Despite these shortcomings the study attracted a lot of attention and a re-examination of the use of hyperventilation in head trauma. Subsequent studies, all using surrogate outcomes such as jugular venous oxygen saturation or metabolic brain imaging, have confirmed that hyperventilation can adversely affect the measured parameter or increase the area of ischemic brain.<sup>10-12</sup> No other clinical outcome studies have been performed. All the studies have studied very short periods of hyperventilation eg<20 minutes so that one doesn't know whether collateral blood flow would improve flow over time. We attempted to address this in a rodent head trauma study where animals were randomized to 4 hours of hyperventilation or normocapnia and then recovered and studied for 21 days. We found that hyperventilation enhanced histological injury but there was no long-term neurocognitive effect.<sup>13</sup> This somewhat ambiguous outcome emphasizes the need to clearly decide what outcomes are important or potentially clinically relevant.

The use of hyperventilation during elective neurosurgery has followed the traumatic brain injury guidelines although the intracranial pathologies are very different. Elective lesions are usually focal and have grown over time compared to the

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sudden and diffuse nature of traumatic injury. Further once the skull is removed, intracranial pressure is atmospheric and the surgeon's assessment of operating conditions is the determinant of the need to reduce brain bulk. We performed a blinded randomized cross-over trial of hyperventilation in patients with supratentorial tumors and found that it did indeed improve operating conditions as assessed by the surgeons.<sup>7</sup> There is no study that meaningfully addresses the potential adverse outcomes from hyperventilation in elective neurosurgery. Such a study would likely require several thousand patients.

Much has been learned about hypocapnia and its potential to do harm through cerebral arterial vasoconstriction. The best way to think about hyperventilation is to consider it like a drug that may be helpful or harmful. It should be used, as advised by Solano ME et al,<sup>8</sup> with a clear indication and for as short a time as possible. Ideally one should monitor for the beneficial and the potential detrimental effects.

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## Conflict of interests

None declared.

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