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CORRESPONDENCE

Hyperoxia-induced brain ischemia: the Strawman comes up short

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To the Editor,

Dr. Mutch and colleagues hypothesized that intraoperative partial pressure of carbon dioxide ($PaCO_2$) may be a predictor of postoperative delirium due to ischemia induced by hypocapnia-induced cerebral vasoconstriction.[1] Support for this hypothesis was later provided by a retrospective analysis of 89 patients, in whom low end-tidal intraoperative $PaCO_2$ was a predictor of delirium after surgery.[2] Indeed, there is a credible rationale for this, as hypocapnia can reduce cerebral blood flow (CBF) to the point where there is loss of consciousness. Thus, it is plausible that regional cerebral hypoperfusion during anesthesia could cause brain dysfunction, which could then lead to postoperative delirium. Dr. Mutch's letter suggested that hyperoxia may also play a role, by further reducing CBF. Unlike the earlier hypothesis, this one requires further justification.

There is no evidence that addition of hyperoxemia to either normocapnia or hypocapnia augments brain tissue hypoxia. While hyperoxia is well-known to reduce CBF by depletion of nitric oxide through generation of reactive oxygen species,[3] there is no evidence that it limits oxygen delivery or uptake, even in the presence of hypocapnia. On the contrary, a large body of evidence in both animals and humans is consistent with arterial hyperoxemia inducing a parallel rise in indices of brain oxygenation.[3,4] Measurements of jugular vein blood oxygen levels, a surrogate of overall brain oxygenation, show an increase when 100% oxygen is administered.[4] Although direct brain tissue PO_2 is only measured in humans if there is a medical reason to implant an electrode, in a study of patients with traumatic brain injury, increasing inspired oxygen fraction from 0.35 to 1.0 for six hours led to both an increase in brain tissue oxygen and a decrease in brain lactate.[4] Supplemental oxygen administration under various clinical circumstances is accompanied by a rise in brain PO_2. In his review, Johnston reports that brain tissue oxygen normally has a linear relationship to arterial PO_2.[4]

Is it possible that reduced flow could result in inadequate uptake of another nutrient molecule, such as glucose? This is unlikely, since whole brain glucose utilization is typically 18–60 $\mu M \cdot 100\ g^{-1} \cdot min^{-1}$ (ranging from white to grey matter). Over the same range of tissues CBF varies from 30 to 110 $mL \cdot 100 g^{-1} \cdot min^{-1}$, thus glucose delivery (assuming a normal blood glucose concentration of 130 $mg \cdot dL^{-1}$ (7 $mM.L^{-1}$) is 200–770 $\mu M \cdot 100\ g^{-1} \cdot min^{-1}$.[5] Therefore if blood flow were to limit glucose utilization it would have to be reduced by a factor of 10–12, considerably beyond any reduction due to hyperoxia.

Dr. Mutch and colleagues have proposed an interesting idea, but before avoiding hyperoxemia, either a plausible mechanism or outcome data are needed.

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This letter is accompanied by a reply. Please see Can J Anesth 2021; this issue.

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