remained unchanged. According to Rosner's model of vasodilation cascade, this episode of anemia and hyper-volemia could initiate such cascade by decreasing median arterial pressure. It also could explain the response to vasoconstriction therapies such as hyperventilation and mannitol.

Doctor Cruz also states that low cerebral extraction of oxygen (CEO) always reflects luxury perfusion. This may be true in his series of patients, but this is not a constant finding, as was demonstrated by Robertson, et al., in head-injury patients with infarction and by us in postoperative cardiovascular patients in whom low CEO correlated with ischemia/infarction and high jugular lactic acid levels.

There was no mention of the use of cooximetry for the measurement of oxygen saturation. If that was the case, the hemoglobin levels would be important to use the Siggard Andersen's nomogram, and it is more accurate to calculate CEO as \( \left( \frac{CaO_2}{CjO_2} \right) \), where \( CaO_2 \) is arterial oxygen content and \( CjO_2 \) is jugular oxygen content, calculated as \( Hb \times 1.34 \times SaO_2 + (0.003 \times pH) \).

In spite of these observations, arteriogenous measurements may be useful tools in the evaluation of patient status.

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References


The author implies that the widened cerebral arteriojugular venous difference of glucose before and after hyperventilation represents “normalization” of glucose extraction. This is not a reasonable conclusion because hyperventilation is associated with decreased cerebral blood flow (which was not measured).

If cerebral blood flow (CBF) were approximately normal to start (50 cc/100 g/min) then glucose extraction would be 2.75 mg/min/100 g of brain. If one assumes, as Dr. Cruz has in previous publications, that there is a reduction of 3% CBF/mm Hg PCO₂, then hyperventilation to 20 mm Hg would lower CBF to approximately 72 cc/100 g/min, yielding a glucose extraction of approximately 2.67 mg/min/100 g of brain based upon the arteriojugular venous differences presented by Dr. Cruz.

This figure is clearly not increased over the pre-hyperventilation value. It is also affected by some very optimistic assumptions including CO₂ reactivity remaining normal, adequate delivery of glucose under the baseline conditions, and baseline blood flow being normal. Hyperventilation may in fact reduce blood flow to very low levels and actually may decrease glucose extraction even further than suggested here.

Another view of these data is that hyperventilation has potentiated ischemia and it is the low blood flow that is leading to widened arteriojugular venous glucose rather than improvement in metabolism. One notes that intracranial pressure was actually higher in the hyperventilated patients as the CO₂ became lower. Why should this occur if hyperventilation were improving the overall metabolic condition of the brain?

There are many assumptions implicit in the author’s analysis but not addressed: 1) cerebral metabolic rate remains constant across this range of hyperventilation; 2) glycolysis remains fixed in terms of its aerobic/anaerobic ratio; 3) what is normal in an awake individual is “normal” or desirable for the comatose (regarding information on normal awake volunteers obtained approximately 50 years ago); and 4) the hemoglobin has remained constant over the 5 days of the studies. (The author’s estimate of cerebral extraction of oxygen also assumes that hemoglobin is a constant.) None of these assumptions across time is tenable.

The author provides information on cerebral perfusion pressure, but the patients are treated with the head elevated, and he does not state that he compensates for the difference between the intracranial pressure monitor and the arterial zero reference point. It is highly likely in his unit that the cerebral perfusion pressure values are far lower than he reports due to a lack of this correction (20–25 mm Hg or more in most patients).

Lastly, Dr. Cruz reports a 70% favorable outcome rate but in a very highly selected group of patients. Their average Glasgow Coma Scale score is 6, he has not included those who are “pending death,” and he has not included the patients with diffuse axonal injury (presumably defined as a very sick patient with a computerized tomography scan that shows some element of brain swelling and a few punctate hemorrhages). Many of these patients had Glasgow Coma Scale scores of 4 and 5. Although the author is free to relate the average length of stay to those reported by Rosner and Daughton, the latter publication refers to the entire spectrum of head-injured patients, without preselection. Given the relatively modest severity of injury in his patient group, we would have expected much better outcomes than reported, especially if “optimized hyperventilation” were truly salutary.

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Reference

TO THE EDITOR: “Optimized” hyperventilation therapy recently was proposed by Cruz as a method to improve the acute care of patients with severe traumatic brain injuries (TBI) (Cruz J: An additional therapeutic effect of adequate hyperventilation in severe acute brain trauma: normalization of cerebral glucose uptake. J Neurosurg 82
Cruz monitored arteriojugular venous glucose differences (AVD$_{Glu}$) during the first several days after a severe TBI in 33 patients and found that these values could be increased using aggressive hyperventilation (PaCO$_2$ of 21 ± 1.6 mm Hg). He concluded that aggressive hyperventilation can be used safely in the treatment of elevated intracranial pressure if it does not lead to abnormal differences in arteriojugular venous oxyhemoglobin saturation. He also suggested that hyperventilation may be used to restore “normal” arteriojugular venous oxyhemoglobin saturation differences and AVD$_{Glu}$ values.

In fact, the only conclusion supported by this study is that the AVD$_{Glu}$ can be manipulated by changing the PaCO$_2$. Because of significant limitations in the methods used in this study, the data do not support the author’s implications that aggressive hyperventilation therapy is safe or that such therapy will not cause regional ischemia. Jugular venous sampling, the primary method used to describe cerebral physiology, is insensitive to regional areas of ischemia that hyperventilation can cause. Thus, the resulting data pertain only to the global effects of hyperventilation. Cruz’s conclusions and implicit recommendations for the treatment of severe TBI could be adopted safely only if cerebral metabolism and blood flow were regionally homogeneous after a TBI and if unilateral jugular venous samples were reliably representative of global metabolites. However, most studies of cerebral blood flow (CBF) and metabolism indicate that there are significant regional differences in both.$^{2,4,5}$ Local variations in CBF are particularly common surrounding contusions or underlying subdural hematomas. Additionally, in the only available report on simultaneous right and left internal jugular vein monitoring, 15 of the 32 patients had side-to-side differences in oxyhemoglobin saturation of greater than 15%.$^6$ Thus, the “normal” values for jugular venous oxygen saturation and AVD$_{Glu}$ that Cruz obtained using aggressive hyperventilation likely represent averages of regions with decreased and increased values, or they may not even accurately reflect global cerebral metabolism.

Cruz concluded that “optimized” hyperventilation normalized glucose uptake and aerobic metabolism, but he did not present the additional physiological information necessary for such a liberal interpretation. Cerebral glucose uptake was not and cannot be measured without determining CBF at the same time AVD$_{Glu}$ is measured. A determination of the degree of aerobic versus anaerobic metabolism also requires measurement of the oxygen and glucose utilization or lactate production, and these data also were not presented.

A primary finding of this study was that AVD$_{Glu}$ levels were below the lower limits of normal in patients treated with mild hyperventilation (PaCO$_2$ of 36 ± 5.2 mm Hg) and that more aggressive hyperventilation (PaCO$_2$ of 21 ± 1.6 and 26.5 ± 4.4 mm Hg) brought these levels into the normal range. Cruz used levels of 6.5 to 13 mg% as the normal range for AVD$_{Glu}$ based on a report of normal values by Gibbs, et al.$^1$ In fact, the normal range reported by Gibbs, et al., in that article was 5 to 13 mg%. If 5 mg% is used as the lower limit of normal, the mean AVD$_{Glu}$ values for the group that was not hyperventilated were also in the normal range, rather than “significantly below normal” as described.

The use of mean values to analyze AVD$_{Glu}$ data in a small group of patients with a severe head injury is of questionable scientific validity. The large standard errors found in this study (larger than the mean value in some cases) probably reflect the variability in the types of brain injuries suffered by patients with similar Glasgow Coma Scale scores. Conclusions regarding efficacy based on changes in these mean values disregard a substantial proportion of patients whose AVD$_{Glu}$ levels may have risen or fallen outside the normal range with the use of hyperventilation.

To support his methods of acute management for TBI, the author reported 6-month clinical outcomes that appear to be much better than outcomes reported by others. However, significant differences in the types of patients studied confound comparisons with other series. For example, the patients in the study by Cruz were not consecutive but selected to exclude those with a Glasgow Coma Scale score of 3, a pure diffuse axonal injury, prolonged hypotension, prolonged hypoxia, initially unmanageable intracranial hypertension, or computerized tomography findings of more than a 1.5-cm midline shift.

Because of these methodological shortcomings, the data presented in this paper do not support the conclusion that hyperventilation improves cerebral glucose metabolism. After reading this paper we are concerned that some clinicians will use prophylactic hyperventilation in the belief that they are improving cerebral metabolism. But only one prospective, randomized study has measured the clinical effects of aggressive prophylactic hyperventilation, and that study found that outcomes were worse in the hyperventilated group (PaCO$_2$ of 25 mm Hg) than in those maintained relatively normocapnic (PaCO$_2$ of 35 mm Hg) for the first 5 days after injury.$^3$ For some patients, the use of hyperventilation therapy is necessary to control elevated intracranial pressure. However, during the first 1 or 2 days after injury, when CBF is critically low, clinicians should be very conservative with the use of this therapy, which is likely to reduce CBF even further.

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