Effect of hypothermia on brain tissue oxygenation in patients with severe head injury

Editor—The interesting article on the effect of temperature on brain tissue partial pressure of oxygen appears to be methodologically flawed. A predictable, physically determined relationship between tissue \( P_{O_2} \) and temperature is shown that is expected from basic physical principles, and not from exacerbation of a pathophysiological process.

The aim of this observational study by Gupta and colleagues was to determine the effect of a reduction in brain parenchymal temperature on brain tissue \( P_{O_2} \). This is an important question to answer, and the investigators correctly measured brain temperature directly and did not infer it from body temperature measurements. The Paratrend 7 (Diametrics Medical, High Wycombe, UK) was used to measure both systemic arterial and brain tissue \( P_{O_2}, P_{CO_2}, \) pH and temperature. Patient clinical management was according to a standard cerebral perfusion pressure procedure, but hypothermia was induced if intracranial pressure became refractory to medical interventions.

In summary, the results show that brain tissue \( P_{O_2} \) decreased with temperature, as did brain \( P_{CO_2} \) and arterial \( P_{CO_2} \). Brain and arterial pH were not affected by a reduction in temperature and jugular venous saturation increased, with wide confidence intervals at the lowest temperatures. Arterial \( P_{O_2} \) increased by up to 2 kPa with temperature. No indication of \( F_{O_2} \) changes are given in the paper and an \( F_{O_2}/P_{O_2} \) ratio would have permitted more informed analysis.

To understand the results, the readers require information on how the Paratrend 7 processes the measured variables. This monitor measures its variables using the pH stat method, where \( pH, P_{CO_2} \) and \( P_{O_2} \) are measured at the local temperature and not corrected to 37°C (information on \( P_{CO_2} \) and pH analysis is given in the text; \( P_{O_2} \) processing information from Diametrics Medical, by personal communication). Charles’s Law states that, at a constant volume, the pressure of gas varies directly with absolute temperature. Therefore, a predictable, physically determined relationship, between brain tissue \( P_{O_2} \) and temperature is shown.

Conclusions that could be reached from this paper are therefore, that the predicted physical relationship between temperature and partial pressure are observed for \( P_{CO_2} \) and \( P_{O_2} \). This is further supported by the very small 95% confidence intervals, which, if attributable to a biological process, would be expected to show much greater variability. Such a pattern is seen in the jugular venous oxyhaemoglobin saturation data, as cerebral oxygen extraction is a biological process. Finally, using alpha stat processing, the opposite effect has been reported in 18 patients with severe traumatic brain injury who were treated with mild hypothermia within 24 h of injury. Mild hypothermia resulted in the mean (SD) brain tissue \( P_{O_2} \) increasing from 9.6 (6.8) mm Hg to 28.7 (8.8) mm Hg, and this change remained within this range for 3 days.

The changes reported in \( P_{CO_2} \) and \( P_{O_2} \) by Gupta and colleagues, at the lowest temperature range, could be attributable to changes in \( F_{O_2} \) and mechanical ventilation. These data, therefore, neither support nor refute the value of hypothermia after traumatic brain injury.

P. Andrews
Edinburgh, UK

Effect of hypothermia on brain tissue oxygenation in patients with severe head injury

Editor—Thank you for the opportunity to respond to the letter from Dr Andrews regarding our article. He highlights some important principles regarding brain tissue gas monitoring with hypothermia.

Dr Andrews is correct in his statement that the tissue sensor (Paratrend 7) measures at local temperature and not corrected to 37°C (alpha stat mechanism and not pH stat, contrary to that stated in his letter). Although it is not clear whether Dr Andrews is arguing in favour of the pH stat method, this would be counterintuitive, as it is more clinically relevant to have tissue measurements at actual brain temperature and not relative to a temperature of 37°C. In addition, studies have demonstrated that the alpha stat method of measurement applies more appropriately during hypothermia.

Dr Andrews is correct in his recount of Charles’s Law. However, if the findings in our study were a predictable response according to Charles’s Law as he suggested, then we should have seen a linear change in brain oxygen tension with temperature. This clearly is not the case. A non-linear decrease in brain tissue oxygen below 35°C is demonstrated in the results. Therefore these findings are unlikely to be attributable to Charles’s Law alone.

The observation that brain tissue oxygen tension decreases despite a rise in arterial oxygen content as temperature is reduced, further refutes Dr Andrews’ hypothesis that this is a predictable physical change.

Although no information regarding \( F_{O_2} \) was given in the manuscript, \( F_{O_2} \) was altered to maintain a target \( P_{O_2} \) according to our unit protocol. The \( P_{O_2} \) and brain tissue oxygen data is presented in the paper, and I fail to see how the \( F_{O_2} \) relationship has any useful bearing on the results.

Finally, Dr Andrews quotes a recent paper from the Chinese Journal of Traumatology, which demonstrated a rise in brain tissue oxygen tension after induced hypothermia, occurring 24 h after injury in pooled data from 18 patients with severe head injury. The temporal profile of an increase in tissue oxygen tension after 24 h has been documented in patients with severe head injury, because of well recognized changes in cerebral blood flow. The observation of the rise in tissue oxygen with hypothermia may therefore be attributable to predictable changes in pathophysiology within the first 24 h of injury, and not because of induced hypothermia. This would also explain the very low mean value of brain tissue oxygen found in the Chinese study within the first 24 h. We did not study patients within the first 24 h of injury, and tissue oxygen tension was higher in our patients before induction of hypothermia. It is also not clear from this paper as to whether the tissue oxygen results are controlled for cerebral perfusion pressure or \( P_{ACO_2} \), which was the case in our study. There are a number of other differences and shortfalls in the Chinese paper, and I therefore do not think that the results of the two studies are comparable.

Whilst we do not claim that our study should alter clinical practice as yet, we do suggest that our findings require further investigation to determine whether induced hypothermia should be targeted to a more limited temperature range. Whilst Dr Andrews raises some interesting questions regarding the methodology, I do not think that his conclusions are supported by the data presented in our paper.

A. K. Gupta
Cambridge, UK
what is happening clinically in vivo platelet aggregation. But it is probably a simplified approach of rates conditions, or pathways dependent on vWF, GPIb, GPIIb/IIIa. Platelet aggregation: either fibrinogen-dependent (under low shear rate conditions), or pathways dependent on vWF can bind to GPIb and GPIIb/IIIa. This distinction may be evaluated in this system, initial binding of von Willebrand factor (vWF) by GPIb followed by GPIIb/IIIa-dependent binding of fibrinogen is no longer efficient at mediating aggregation, whereas fibrinogen predominates over vWF in driving aggregation by epinephrine. The instrument determines the time required for initial binding of von Willebrand factor (vWF), is different from that of fibrinogen-mediated platelet aggregation. Nevertheless, we now know that the clinical process, and what is its clinical significance. His approach suggests that there are clear cut differences in the pathways of platelet-related haemostasis as whole blood flows under high shear rate conditions. Brieﬂy, the system consists of a disposable test cartridge in which citrated whole blood is aspirated through a capillary and the microscopic aperture cut in a membrane that had been designed to assess platelet function as demonstrated in patients with congenital afbrinogenemia. A®brinogenemia on hemorheology and platelet function interaction with the glycoprotein IIb/IIIa complex: its role in a®brinogenemia. platelet function analyser, PFA-100 system.

The authors presented the PFA

DOI: 10.1093/bja/aeg517