Evaluation Of Deliberate Mild Intraoperative Hypothermia In Craniotomy

Thesis

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From our study we conclude that although deliberate mild hypothermia during craniotomy is feasible, complete rewarming may be difficult to achieve with current methods. Inadvertent temperature decreases in the normothermic group were difficult to prevent. Redistribution hypothermia may be the cause of hypothermia during the first hour of general anesthesia; this can be minimized by active warming methods.

Patients undergoing craniotomy under mild hypothermia showed significantly higher jugular venous oxygen tension and jugular venous oxygen saturation levels and significantly lower jugular venous carbon dioxide tension, arterio-venous oxygen content difference and cerebral oxygen extraction ratio than normothermic patients suggesting decreased cerebral metabolism in the hypothermic group and hence possibly retarding energy depletion, reducing intracellular acidosis and reducing the extent of neurological damage. Therefore, hypothermia may exert a significant neuroprotective effect even in mild degrees (34.5°C).

Our study suggests that mild hypothermia does not appear to enhance the risk of coagulopathy. The measured coagulation variables (platelet count, PT, PTT) remained within normal ranges. This indicates that short term mild hypothermia has only minor effects in anesthetized humans. Limitations to this conclusion are: the laboratory assessment of coagulation

function under hypothermia is limited because temperature standardized coagulation assays at 37°C may not accurately reflect the magnitude of clotting dysfunction under hypothermic conditions. Therefore, further studies measuring bleeding time, clotting time and thrombelastography are recommended.

Patients in the hypothermia group exhibited significantly higher CRP levels after rewarming, which may suggest ongoing or persistent inflammatory activity. Further studies must be performed to determine the cause of the observed difference in the time courses for CRP levels and white blood counts to elucidate the role of hypothermia.

Patients undergoing craniotomy under mild hypothermic conditions demonstrate low serum potassium levels than normothermic patients which may be due to increased urinary excretion through hypothermia-induced polyuria. Prophylactic potassium supplementation should be considered, and electrolytes should be monitored regularly in all patients who undergo deliberate hypothermia.

Careful temperature manipulation during craniotomy should allow maximal neurological benefit with minimal detriment to systemic physiology.

The idea that the evolution of acute brain injury can be reversed either by reducing cerebral metabolic rate or arresting metabolic pathways that determine irreversibility is one of the central concepts of acute neuroprotection. Induction of hypothermia has for many years been an attractive means of achieving this, particularly in the absence of any widely practicable and proven pharmacological treatment. No data exists on neurosurgical procedures, but it seems obvious that hypothermia will not protect against a variety of iatrogenic events, including excision of an eloquent area of the brain. Of greatest relevance, however, to the use of mild hypothermia in the neurosurgical patient were three almost simultaneous reports in 1993 **(Clifton et al., 1993; Marion et al., 1993; Shiozaki et al., 1993)**. All three studies were only preliminary trials because of small sample size. Nevertheless, either a clear benefit or a trend towards benefit was observed in patients being rendered mildly hypothermic in the acute phase after head injury. Fortunately, as far as it is known, the risk associated with use of mild hypothermia is small. In a recent poll taken from members of the Society of Neurosurgical Anesthesia and Critical Care **(Craen et al., 1994)**, 40% of clinicians practiced induced hypothermia in patients undergoing surgery for cerebral aneurysm.

Several questions regarding the method of cooling and monitoring of core temperature arise. During craniotomy, for example, the brain is differentially exposed to ambient temperature. Despite core normothermia, some regions of the brain may undergo substantial cooling whereas other regions will not. As it is difficult to define exactly which regions are at greatest risk (that is, tissue under a retractor compared with tissue distal to a cerebral artery potentially undergoing occlusion) it is virtually impossible to use core temperature to accurately define ideal conditions for specific tissue at risk. Some work has been done to relate brain temperature to core temperature but most data is derived from the cardiopulmonary bypass literature. For example, in 1995, **Stone and coworkers** directly measured cortical surface temperature during cooling and rewarming for circulatory arrest in cerebral aneurysm surgery. Temperature from other measurement sites (e.g. nasopharynx, tympanic membrane) often varied by 0.5-2°C from brain temperature during various stages of cooling and rewarming **(Rumana et al., 1998; Schwab et al., 1998b)**. Although such differences might be negligible during profound hypothermia, when mild hypothermia is in question, such errors constitute the full therapeutic range. Other studies have examined the effects of various methods of cooling on the brain temperatures of patients in intensive care units. Results revealed

a close correlation between systemic and brain temperature with a mean difference of 0.41°C **(Gupta et al., 2002)**. Therefore, direct brain temperature measurement is more accurate.

An additional concern in the patient undergoing craniotomy is the practicality of cooling and rewarming in an interval of only several hours. One investigation **(Baker et al.,** 1994) has examined this practice and found that it is feasible to achieve core temperatures of approximately 34°C but that full rewarming to normothermia before emergence from anesthesia is unlikely. Factors known to affect cooling and rewarming include the morphometric characteristics of patients, the presence or absence of vasoconstriction, and the method of temperature management. Intraoperative thermoregulatory vasoconstriction thresholds may be influenced by the depth of anesthesia, age, and painful stimulation **(Washington et al.,** 1992; Kurz et al., 1993; Xiong et al., 1996). In our study, anesthesia and method of temperature management were standardized in both groups.

The results of our study suggest that patients undergoing craniotomy can be easily cooled to a body temperature approaching levels shown to offer cerebral protection (34-34.5°C) (Gupta et al., 2002) using a water blanket and circulating room air in a cool operating room. Active cooling was stopped at a temperature of 35°C, and patients continued to

drift downwards to a mean temperature of 34.1°C despite the initiation of active rewarming at a temperature of 34.5°C. Inadvertent temperature decreases in the normothermic group during skin incision, dural opening and dural closure were difficult to prevent. **Sessler and colleagues** have shown in 1991 that the decrease in core temperature after anesthetic induction is due primarily to redistribution of body heat to the periphery and not solely a result of increased environmental losses from anesthetic-induced vasodilation. In addition, isoflurane, halothane, fentanyl and N_2O anesthetics decrease the threshold temperatures at which compensatory peripheral vaso-constriction is initiated **(Sessler et al., 1988; 1989; Stoen and Sessler, 1990)**.

Rewarming occurs at variable rates with conventionally available devices, and an intraoperative return to normothermia is not always easy to achieve. At tracheal extubation, the temperature of the hypothermic group was (36.3°C± 0.55) despite the active measures of rewarming starting immediately after dural closure using the water blanket set at 40°C. It was surprising that complete rewarming could not be achieved. The use of convective heating devices, which are currently the most effective means of peripheral rewarming **(Lennon et al., 1990)**, may have made rewarming easier and can be continued in the postoperative period. Heated humidified inspired gases has little

effect on intraoperative temperature **(Hynson and Sessler,** 1992), and the administration of a limited amount of heated fluids would not add to warming appreciably. Studies are needed to determine if the administration of a vasodilator during rewarming would hasten the return to normothermia **(Inoue et al., 2001)**.

The monitoring of cerebral venous oxygen saturation is an integral part of multimodality monitoring following acute brain insult. The internal jugular veins drain virtually all of the blood from the brain. In most individuals the right lateral sinus is the larger of the two. It is unclear as to whether sufficient mixing of venous blood occurs to ensure that the oxygen saturation in the two sinuses is similar. Autopsy specimens have revealed that blood draining the subcortical areas tends to flow into the left lateral sinus while the cortical areas drain via the right **(Hatiboglu and Anil, 1992; Lam et al., 1996)**. Several small series have examined the relationship between side of catheter insertion and venous oxygen saturation **(Metz et al.,** 1998; Van den Brink et al., 1998). Most found similar saturations from both internal jugular veins, although it would appear that this might only be true in the case of diffuse cerebral injury **(Komiyama et al., 1999)**. It is likely however, in patients with focal disease i.e., stroke or unilateral hemorrhage, that there would be a greater difference between

the two sinuses **(Schell and Cole, 2000)**. The question therefore is: given that $SjVO_2$ is supposed to be representative of the global oxygen consumption by the brain, on which side should the catheter be inserted?

As the flow in the jugular veins is not the same, it would seem logical to insert the catheter into the vein with the greatest flow. There are several methods by which this can be accomplished. The first is purely functional where each jugular vein is compressed in turn and the catheter inserted into the vein with the largest rise in ICP following this maneuver **(Feldman and Robertson, 1997)**.The second uses the admission computer tomography scan to assess the jugular foramina and assumes that the larger must have the greater flow **(Stocchetti et al.,** 1994). The third uses ultrasound to visualize the dominant vein. None of these procedures has been studied in a controlled way and there is no evidence that the side of insertion is associated with better clinical outcome. Some advocate inserting the catheters into the side of injury but this is controversial **(Stocchetti et al., 1994)**.

During the early 1900's, the jugular bulb was pierced directly to obtain cerebral venous oxygen saturation. Later, permanent catheters were inserted high in the internal jugular vein. This allowed repetitive sampling of $SjVO_2$ without repeated needle punctures. More recently, fibreoptic technology

has allowed the development of in vivo spectrophotometric catheters. Recently, multimodal sensors can be inserted to the brain tissue to measure brain O_2, CO_2, pH and temperature **(Gupta et al., 2002)**.

In our study we cannulated the right jugular vein (the side of dominant drainage) in the cephalad direction, either distally between the heads of the sternocleidomastoid or more proximally, at the level of the cricoid ring. The catheter is then pushed retrograde to the jugular bulb (in order to limit the contamination from extra cerebral blood) and the exact position is confirmed using x-ray. As continuous jugular venous oximetry was not available, frequent sampling of blood (from both arterial and jugular catheters) was done during skin incision, dural opening, dural closure and end of surgery.

Our study showed very little change in arterial pH, PO_2 and PCO_2 with temperature. The same results were obtained by **Inoue and colleagues**, in 2001, **Gupta and colleagues** in 2002 and **Kawano et al.** in 2004. Because the solubility of oxygen and carbon dioxide in blood or extracelluar fluid is an inverse function of temperature, the capacity of the fluid to contain gas molecules in solution increases at lower temperatures. In this study, α-stat method (pH and CO_2 measurement corrected to 37°C) was chosen because it has been shown to better preserve cerebral autoregulation, is associated with a better

neuropsychologic outcome after cardiopulmonary bypass procedures, and is more commonly used in clinical practice **(Goldsack and Berridge, 1996; Patel et al., 1996)**. If the alternative *p*H-stat method (which corrects for the actual temperature of the patient) was used, decreased pH and increased intracranial blood volume may have been found **(Tasker et al., 1999)**.

In our study there was no significant change in $PaCO_2$ as the ventilator settings were adjusted to maintain an end-tidal CO_2 of 34-36 mmHg. Arterial oxygen tension appeared to be insignificantly higher during mild hypothermia which may be due to the leftward shift of the oxygen dissociation curve associated with hypothermia. This enhances the affinity of oxygen to hemoglobin, causing reduced oxygen release and thereby reducing the availability of oxygen to diffuse into cells **(Bacher et al., 1998)**. The small changes in arterial pH with hypothermia indicate that ischemic acidosis was not occurring.

The results obtained in the present study show that jugular venous oxygen tension and oxygen saturation are significantly higher during mild hypothermia (34.2±2.3 and 69.4±6.2 respectively) than during normothermia (31.7±2.5 and 65.3±6.4 respectively) with p values: <0.001 and 0.015 respectively. These results are similar to those reached by **Cook et al., 1994; Croughwell et al., 1997; Okano et al., 2000** and

Gupta et al., 2002. The increase in $Sjvo_2$ observed below 37°C is most likely the result of cerebral metabolic suppression resulting in a reduction in oxygen extraction by cerebral tissue. On the other hand **Sato and coworkers** observed in 2000 that $Sjvo_2$ were significantly lower in the hypothermic group than in normothermic group ($55.2 \pm 6.6\%$ vs 60.9 ± 6.6, $p < 0.05$) in patients undergoing clipping of cerebral aneurysm.

Jugular bulb venous oxygen saturation is an established method of measuring global cerebral oxygenation. The limitations of $Sjvo_2$ monitoring are well recognized. Continuous monitoring has a number of technical difficulties, whereas intermittent sampling gives a "snapshot" of the state of cerebral oxygenation **(Stocchetti et al., 1994)**.

One of the major limitations of this technique is that regional changes in cerebral oxygenation may not be detected unless the changes are large enough to affect the global measurements. It is accepted that regional variations in brain temperature occur as a result of the heterogeneous nature of cerebral blood flow and metabolism. Changes in brain temperature will therefore affect both global and regional brain oxygenation. Thus, the regional variations of brain oxygenation arising from changes in brain temperature may not be detected by jugular bulb venous oxygen saturation or even continuous monitor of jugular venous saturation. Tissue sensors, however,

have been shown to be a more sensitive measure of regional oxygenation compared to $Sjvo_2$, and will therefore be more likely to detect these regional changes **(Ritter et al., 1996; Souter and Andrews, 1996; Howard et al., 1999; Schell and Cole, 2000)**.

A second limiting factor concerns the possibility of extracerebral contamination. If blood is sampled at a site within 2 cm of the jugular bulb and at a rate of < 2 mL/min there is negligible (approximately 3%) extracerebral contamination. A related concern is the observation that, as CBF decreases, the relative extracerebral contribution to a $SjVO_2$ reading increases **(Jakobsen and Enevoldsen, 1989; Matta and Lam, 1997)**.

In awake healthy humans, $SjVO_2$ ranges between 55-75% (mean 62%). $SjVO_2$ reflects the balance between brain oxygen supply and demand and indicates whether CBF is sufficient to satisfy the oxygen demands of the brain. Values of $SjVO_2$<50% indicate cerebral hypoperfusion, and readings <40% are associated with global cerebral ischemia **(Gopinath et al.,** 1996).

Correct interpretation of increased $SjVO_2$ requires confirmation that the catheter tip is at the jugular bulb. Reduced $CMRO_2$ (e.g., hypothermia, sedatives), increased CBF, pathologic arterial-venous communications, and brain death may result in increased $SjVO_2$ **(De Deyne et al., 1998)**.