Cerebral Blood Flow and Oxygen Metabolism During Mild Hypothermia in Patients with Subarachnoid Haemorrhage

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Summary

Cerebral blood flow and O2 metabolism during hypothermia (33–34°C) was evaluated in 5 patients with aneurysmal subarachnoid haemorrhage by positron emission tomography (PET). Their preoperative clinical condition was WFNS scale IV or V. The patients received surface cooling postoperatively, and were maintained in a hypothermic state during transfer for radiological examination. Positron emission tomography revealed a decrease in cerebral blood flow and O2 metabolic rate. Cerebral blood flow was 34.8 ± 15.1 ml/100ml/min and the O2 metabolic rate was 1.85 ± 0.61 ml/100ml/min in areas of the middle cerebral artery ipsilateral to the ruptured aneurysms, whereas these values were 30.8 ± 7.1 and 2.21 ± 0.45 ml/100ml/min, respectively, on the contralateral side. This represents a decrease of 37 ± 27% compared to normal cerebral blood flow and 52 ± 16% compared to normal O2 metabolic rate (p < 0.02) in the ipsilateral areas, and decreases of 44 ± 13% and 43 ± 12%, respectively, on the contralateral side. The present results reflected the luxury perfusion state in almost all cases and provide the first PET evidence of decreased cerebral blood flow and metabolic rate of O2 during hypothermia in humans.

Keywords: Hypothermia; cerebral aneurysm; subarachnoid haemorrhage; positron emission tomography.

Introduction

Since hypothermia was first introduced as a brain protective measure in the 1950’s [3], many experimental and clinical investigations have demonstrated the therapeutic potential of hypothermia in cerebral ischaemia [8, 19]. Based on histological evidence that lowering brain temperature by a few degrees significantly decreases ischaemic brain injury [4], clinical application of mild hypothermia has been widely anticipated. However, the therapeutic value in stroke patients has not yet been established.

We recently devised a hypothermia bed system for stroke patients [16], which contains all necessary equipment including a respirator, cooling unit, physiological monitors, and a storage battery. During mild hypothermic therapy (33–34°C), patient transfer and radiological examinations including positron emission tomography (PET) could be easily and safely performed [16]. The purpose of the present paper is to investigate cerebral blood flow and oxygen metabolism using PET in patients with severe subarachnoid haemorrhage (SAH).

Patients and Methods

Subjects

Mild hypothermia was indicated for aneurysmal SAH patients who satisfied the following criteria: time from haemorrhage to admission of less than 6 hours; age less than 70 years old; no past history of ischaemic heart disease, such as myocardial infarction or angina pectoris; level of consciousness upon admission of semi-comatose or worse, or stage IV or V according to the WFNS scale, the universal SAH grading scale recommended by the World Federation of Neurological Surgeons [7]; and spontaneous respiration. SAH was confirmed by computed tomography (CT). From June 1997 to June 1999, of 108 SAH patients admitted to our hospital, six (5.6%) satisfied the criteria for inclusion in the study and underwent hypothermic therapy. Their clinical data are listed in Table 1.

The patients underwent conventional or CT angiography to determine the location of the ruptured aneurysms. When written informed consent was obtained from the patient’s closest relative (spouse, or close family member), aneurysm surgery was performed as soon as possible. During surgery, hypothermia was induced using a cooling blanket (Medi-Therm®; Gaymer Industries, Inc., NY, USA) until the temperature measured in the urinary bladder reached about 35.0°C. Cerebrospinal fluid (CSF) was drained from the basal cisterns or the Sylvian fissure to control the intracranial pressure within the normal range following surgery. CSF drainage was also performed postoperatively during intermittent administration of urokinase to resolve subarachnoid blood. Hypothermia was maintained postoperatively in the intensive care unit. Following hypothermic therapy, hyperdynamic therapy in which dobutamine was
The patient was moved from the hypothermia bed to a standard bed. Bladder temperature was maintained at <38.0 °C using the Meditherm for 2 weeks following SAH.

**PET Measurement**

The method of PET measurement has been described previously [11]. Briefly, each subject inhaled C15O2 and 15O2 continuously for regional cerebral blood flow (rCBF), oxygen extraction fraction (rOEF), and cerebral metabolic rate of oxygen (rCMRO2) measurements. Then, C15O was inhaled for one minute to measure regional cerebral blood volume (rCBV). C15O emission scanning was started 3 minutes after C15O inhalation. The tomograph provided scans of 4.0 mm full width at half maximum (FWHM) in planar resolution and 4.3 mm FWHM in axial resolution at the center of the field of view. Thirty-one slices were obtained with a 3.1-mm slice spacing above and parallel to the orbitomeatal line. Radioactivity concentration, haemoglobin, and haematocrit were measured, and gas analysis was performed on arterial blood.

CT was also performed during PET study, allowing accurate identification of the anatomical structures of the brain. Regions of interest (ROIs) were circular with a 16 mm diameter. Similar to our previous study [14], we selected 6 ROIs for each subject, the superior temporal, middle temporal, and inferior frontal gyri on both sides. All these regions fall within the area of the middle cerebral artery (MCA).

**Statistical Analysis**

The % decrease in CBF and CMRO2 during hypothermia was calculated in comparison with normal mean values. The paired Student’s t-test was used to compare decreases in each ROI. A p value of <0.05 was considered to be significant. All values are given as mean ± SD.

**Results**

**Clinical Outcome**

Clinical outcome was evaluated using the Barthel index [20]. These data and follow-up times are listed in Table 1. Cases 1 and 2 had a good surgical outcome and were able to function and live independently, although they had hemiparesis and mild aphasia, respectively. Case 3 was partially dependent (mildly dis-