

Clinical Article

Effects of Iso- and Hypervolemic Hemodilution on Regional Cerebral Blood Flow and Oxygen Delivery for Patients with Vasospasm after Aneurysmal Subarachnoid Hemorrhage

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Summary

Background. Arterial vasospasm after subarachnoid hemorrhage may cause cerebral ischemia. Treatment with hemodilution, reducing blood viscosity, and hypervolemia, increasing cardiac performance and distenting the vasospastic artery, are clinically established methods to improve blood flow through the vasospastic arterial bed.

Method. Eight patients with transcranial Doppler verified vasospasm after subarachnoid hemorrhage were investigated with global (two-dimensional ¹³³Xenon) and regional (three-dimensional ⁹⁹mTe-HMPAO) cerebral blood flow (CBF) measurements, before and after 1/isovolemic and 2/hypervolemic hemodilution. Hematocrit was reduced to 0.28 from 0.36. Hypervolemia was achieved by increasing blood volume by 1100 ml.

Findings. Isovolemic hemodilution increased global cerebral blood flow from 52.25 ± 10.12 to 58.56 ± 11.73 ml · 100 g⁻¹ · min⁻¹ (p < 0.05), but after hypervolemic hemodilution CBF returned to 51.35 ± 11.34 ml · 100 g⁻¹ · min⁻¹. Global cerebral delivery rate of oxygen (CDRO₂) decreased from 7.94 ± 1.92 to 6.98 ± 1.66 ml · 100 g⁻¹ · min⁻¹ (p < 0.001) during isovolemic hemodilution and remained reduced, 6.77 ± 1.60 ml · 100 g⁻¹ · min⁻¹ (p < 0.001), after the hypervolemic hemodilution. As a test of the hemodilution effect on regional CDRO₂ an ischemic threshold was defined as the maximal amount of oxygen transported by a CBF of 10 ml · 100 g⁻¹ · min⁻¹ at a Hb 140 g/l which corresponds to a CDRO₂ of 1.83 ml · 100 g⁻¹ · min⁻¹. The brain volume with a CDRO₂ exceeding the ischemic threshold was 1300 ± 236 ml before intervention. After isovolemic hemodilution the non-ischemic brain volume was reduced to 1206 ± 341 (p < 0.003). After hypervolemic hemodilution the non-ischemic brain volume remained reduced at 1228 ± 347 ml (p < 0.05).

Interpretation. The present study of controlled isovolemic hemodilution demonstrated increased global CBF, but there was a pronounced reduction in oxygen delivery capacity. Both CBF and CDRO₂ remained decreased during further hypervolemic hemodilution. We conclude that hemodilution to hematocrit 0.28 is not beneficial for patients with cerebral vasospasm after SAH.

Keywords: Cerebral blood flow; cerebral oxygen delivery; hemodilution; subarachnoid hemorrhage; vasospasm.

Introduction

Cerebral arterial vasospasm is a severe complication of aneurysmal subarachnoid hemorrhage (SAH) with a peak during day 7–10 after the bleed [10, 13, 24, 26, 34, 40, 45, 51, 59]. Such delayed vasospasm may lead to cerebral ischemia causing persistent neurological symptoms and signs. A well accepted pharmacological tool for prophylaxis is the calcium antagonist nimodipine. Induced hypertension and hemodilution with the aim to improve cerebral blood flow (CBF) is also widely used [5, 15, 23, 31, 33, 35, 37, 38, 41, 43, 47, 49, 50]. Hemodilution may be created either isovolemic or hypervolemic with the intention of achieving decreased blood viscosity. Isovolemic hemodilution has been reported to be as efficient as hypervolemic hemodilution in counteracting the effect of vasospasm [25, 28, 57, 61], but the literature is not conclusive. The purpose of the present study was therefore to evaluate the effect of isovolemic hemodilution followed by hypervolemic hemodilution on CBF and cerebral delivery rate of oxygen (CDRO₂) in patients with
transcranial Doppler (TCD) verified vasospasm after aneurysmal SAH.

Methods and Patients

Eight patients who fulfilled the following criteria participated in the study, after verbal and written informed consent. The local ethics and isotope committees approved the study protocol.

Patient inclusion criteria:
1. SAH due to a ruptured aneurysm, b) surgery with clipping of the aneurysm, c) clinical condition according to Hunt & Hess grade I to III [21], d) cerebral vasospasm indicated by TCD mean flow velocity (mFV) > 120 cm/s in middle cerebral arteries (MCA), e) hematocrit (Hct) > 0.35, with normal serum albumin, electrolytes and osmosis, f) central venous pressure < 8 mmHg, g) nimodipine treatment was administered in standard dose through a central venous catheter, h) a cardiac index of 2.5–3.5 l/min/m², i) aminoglycoside formula (male blood volume = 0.6041 weight + 0.03219 and female blood volume = 0.6041 weight + 0.0308 weight + 0.1833) [39].

One male and seven females were included in the study. Mean age was 42 years (ratio 19–56 years). Mean TCD mFV in MCA was 165 cm/s (ratio 150–198 cm/s).

Experimental Procedures

Each of the three measurement days (on the last two both before and immediately after hemodilution) global CBF, TCD mFV and cardiac output (CO), blood samples for haematology, electrolytes, glucose, albumin, and fibrinogen were measured as well as arterial and venous blood gases. The patient’s arterial blood pressure, heart rate and pulse oximetry values were monitored continuously.

Before Hemodilution. On day one the patient’s regional CBF distribution was measured.

Isovolemic Hemodilution. On day two, venesecion and simultaneous intravenous infusion of dextran 70 (Macrodex®, Pharmacia & Upjohn) and albumin 4% (Pharmacia & Upjohn) in equal volumes was made. The Hct value before hemodilution was used to calculate the blood volume (L) needed to be replaced by dextran and albumin to achieve the intended Hct level (0.28) from the Bourke and Smith equation:

\[ \text{L} = \text{V} \times (\ln(\text{Hct}_{\text{initial}} - \text{ln(\text{Hct}_{\text{asired}})})) \]

The estimated blood volume (V) was calculated using Nalders formula (male blood volume = 0.3669 * weight + 0.03219 * weight + 0.6041 and female blood volume = 0.3561 * weight + 0.0308 * weight + 0.1833) [39].

Approximately 60 minutes after hemodilution the regional CBF distribution was measured.

Hypervolemic Hemodilution. On day three, all patients were given autotransfusion with the blood that had been withdrawn the previous day. In addition to the blood transfusion, dextran and albumin 4% in equal parts were infused.

The additional volume was calculated using the formula: (withdrawn blood volume day 1) * (Hct before venesection)/(Hct after hemodilution).

Approximately 60 minutes after hemodilution the regional CBF distribution was measured.

Experimental Parameters

Transcranial Doppler Ultrasound. Normal mFV in the MCA has been defined as 62 ± 12 cm/s. TCD reliably detects a substantial narrowing, i.e. vasospasm, with the highest reliability for MCA. A mFV exceeding 120 cm/s is considered to indicate significant vasospasm [1, 2, 8, 9, 17, 27, 29, 48]. All TCD measurements were conducted daily before and after the hemodilution procedure by a 2 MHz transducer (EME TC-64 Eden Medical Electronics). Permanent recordings were documented on a Video Graphic Printer for later analysis (Sony VP 850).

Global CBF. The global CBF level was measured by an intravenous injection of 0.3 Gbq (10 mCi) 133Xenon, followed by an injection of 20 ml isotonic saline solution. The scintillation detectors were placed over the mouth and over the parieto-temporal region, recording input, uptake and clearance of the tracer by a Novo Cerebrograph 10a (Simonsen Medical A/S) CBF recorder. The sampling time was 11 minutes, but the global CBF is expressed as initial slope index (ISI) as it represent the blood flow of all tissue recorded, but is highly dominated by the grey matter blood flow and very little influenced by extracebral components [44].

Since the measured global CBF value is directly proportional to the 133Xenon solubility in blood, which has a linear correlation to the Hct value, a correction for the difference in Hct from the reference value of 0.32 was necessary.

The 133Xenon solubility was calculated from a linear equation based on Ostwald’s solubility coefficients [7]:

Solubility of Xenon in red cell plasma suspensions = solubility coefficient for plasma + (solubility coefficient for red blood cells – solubility coefficient for plasma) + Hct.

The measured global CBF was thus corrected for Hct level by the formula:

\[ \text{CBF}_{\text{corrected}} = \frac{\text{CBF}_{\text{measured}} \times (0.1503/0.0939 \times (1 + \text{Hct} \times (2.886 - 1)))}. \]

CDRO2. CDRO2 was calculated using the formula:

\[ \text{CBF}_{\text{corrected}} \times \text{hemoglobin (Hb)} \times O_2 \text{ saturation} \times 1.31. \]

The constant 1.31 represents the oxygen carrying capacity of 1 g Hb [62].

CVR. The cerebral vascular resistance (CVR) was calculated as:

\[ \text{mean arterial blood pressure/ CBF}_{\text{corrected}} \]

Regional CBF Distribution. Three-dimensional measurements of regional CBF distribution were made with intravenous injection of 0.9 Gbq (15 mCi) 99mTc-HMPAO (Ceretec®) and recording for 30 minutes with a SPECT camera (CERASPECT, Digital Scintigraphics Inc.). The tracer is lipid soluble when injected and distributed proportionally to the CBF. In the brain cells the carrier molecule HMPAO converts into a water-soluble form, which is not able to cross the cell membrane. Therefore the 99mTc remains intracellular, proportionally to the CBF level, with a half-life of about 6 hours [19, 20].

The three-dimensional distribution of 99mTc-HMPAO in the brain was recorded in 21 contiguous five millimeter thick slices, parallel to the orbito-meatal (OM) line, with the lowest slice located two centimetres below the OM line.

Regional CDRO2 Distribution. The global CBF level was measured with detectors aimed at the parieto-temporal regions. By relating the CBF value from the less affected hemisphere to the same region of the three-dimensional CBF distribution, the corresponding regional CBF (rCBF) level could be calculated in all areas of the brain. Furthermore, regional CDRO2 could be calculated from the rCBF.

An ischemic threshold was defined as the maximal amount of oxygen transported by a CBF of 10 ml*100 g⁻¹ * min⁻¹ at a Hb 140 g/l which corresponds to a CDRO2 of 1.83 ml*100 g⁻¹ * min⁻¹. The brain volume with perfusion levels above the ischemic threshold level was measured before and after iso- and hypervolemic hemodilution.

Cardiac Output. Hewlett-Packard Sonos 500 with 2.25 MHz transducer was used to evaluate the CO. CO was calculated as the