Positive Fluid Balance Is Associated With Poor Outcomes in Subarachnoid Hemorrhage

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Background: Strict maintenance of normovolemia is standard of care in the treatment of aneurysmal subarachnoid hemorrhage (aSAH), and induced hypervolemia is often used to treat delayed cerebral ischemia from vasospasm. We tested the hypothesis that positive fluid balance could adversely affect clinical outcomes in aSAH. *Methods:* We reviewed 288 patients with aSAH admitted to the Neuroscience Intensive Care Unit (NICU) from October 2001 to June 2011. We collected data on fluid balance during NICU stay, clinical and radiographic evidence of vasospasm, cardiopulmonary complications, and functional outcomes by modified Rankin Scale (mRS) on follow-up (mean 8 ± 8 months). Poor functional outcome was defined as an mRS score 3-6. Associations of variables of interest with outcome were assessed using univariable and multivariable logistic regression. Propensity scores were estimated to account for imbalances between patients with positive versus negative fluid balance and were included in multivariable models. *Results:* Average net fluid balance during the NICU stay was greater in patients with poor functional outcome (3.52 ± 5.51 L versus −.02 ± 5.30 L in patients with good outcome; $P < .001$). On multivariate analysis, positive fluid balance ($P = .002$) was independently associated with poor functional outcome along with World Federation of Neurosurgical Societies grade ($P < .001$), transfusion ($P = .003$), maximum glucose ($P = .005$), and radiological evidence of cerebral infarction ($P = .008$). After regression adjustment with propensity scores, the association of positive fluid balance with poor functional outcome remained significant (odds ratio, 1.18; 95% confidence interval, 1.08-1.29; $P < .001$). *Conclusions:* Greater positive net fluid balance is independently associated with poorer functional outcome in patients with aSAH. **Key Words:** Subarachnoid hemorrhage—fluids—balance—prognosis—outcome.

Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) is a catastrophic illness that is associated with significant mortality.[1] Delayed cerebral ischemia (DCI) secondary to vasospasm may be present in more than 60% of patients and becomes symptomatic in 30%.[2] Patients with thick subarachnoid clot, younger age, poorer neurologic grade, and history of smoking are more likely to develop vasospasm.[3,4] Ischemic strokes secondary to vasospasm are a cause of major morbidity and mortality.[5]

Triple-H (hypertension, hemodilution, and hypervolemia) therapy for treatment of DCI has been shown to improve neurologic status and has gained wide

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acceptance over the past 30 years.[6-9] Yet, prophylactic hypervolemic therapy after aneurysm clipping did not improve cerebral blood flow or benefit clinical outcome compared with subjects with even fluid balance in a randomized controlled trial.[10] Although patients with even fluid balance and vasospasm have increased regional cerebral blood flow after normal saline boluses,[11] the benefits of increased brain tissue oxygenation with induced hypertension may be lost with the addition of volume expansion and hemodilution.[12] Current practice is to target for an even to slightly positive fluid balance,[13,14] but many advocate inducing a frankly positive fluid balance when symptomatic vasospasm occurs.[15-17]

In poor-grade aSAH patients, treatment with moderate hypertension in patients with an even fluid balance and hemodilution has been associated with improved cerebral oxygenation and fewer complications compared with hypervolemic or aggressive hypertensive therapy.[18] Meanwhile, there is some evidence that hypervolemic therapy could worsen cerebral edema[19] and cause or exacerbate systemic complications.[20,21]

A positive fluid balance has been associated with worse clinical presentation and poor functional outcomes at 3 months (modified Rankin Scale [mRS])[22,23] but has not been assessed during the critical period when patients are most likely to develop symptomatic vasospasm and in a patient population treated with a practice targeted to achieve an even fluid balance. We hypothesized that patients with positive fluid balances during their Neuroscience Intensive Care Unit (NICU) stay would be more likely to have poor functional outcomes.

Methods

Study Design and Patient Selection

This study was approved by the Mayo Clinic Institutional Review Board. We retrospectively reviewed the records of 307 patients with aSAH admitted to the NICU from October 2001 to June 2011. The study included consecutive patients 18 years or older admitted to the NICU at St. Mary's Hospital-Mayo Medical Center in Rochester, Minnesota. Data were collected from the Mayo Clinic Electronic Medical Record System. The diagnosis of SAH was established by head computed tomography or supported by evidence of xanthochromia on CSF examination. The presence of aneurysm was detected or confirmed by cerebral angiography. Patients without aSAH were excluded from the study.

Management Protocol

After diagnosis of aSAH, patients were monitored hemodynamically with arterial lines and/or central venous catheters. Isotonic or hypertonic intravenous fluids were administered with the goal of maintaining a net even fluid balance throughout the ICU stay. Adjustments of fluid administration to account for insensible losses occurred at the discretion of the treating clinicians. Albumin boluses (5% or 25%) were occasionally added at the discretion of the treating clinician, typically in cases of severe polyuria or symptomatic vasospasm, but they were not part of the standard care. Urinary catheters were placed routinely in all patients to ensure accurate monitoring of urinary output. In patients with suspected or documented DCI, hypertension was induced with vasopressors, often preceded by a .5-1 L fluid bolus. When these symptoms were refractory to induced hypertension, we pursued endovascular therapy. The rest of our management protocol has been previously described in detail.[24]

Data Collection

The data were retrospectively collected from the electronic medical record and comprised patient demographics, risk factors for aSAH, clinical evaluation, brain and vascular imaging, aneurysm size and location, neurosurgical treatment, presence of hydrocephalus, World Federation of Neurosurgical Societies (WFNS) and modified Fisher scores, net fluid balance during NICU stay, albumin use, administration of transfusions, presence and treatment of vasospasm, presence of DCI, radiographic evidence of cerebral infarction, radiographic evidence of pulmonary edema, ejection fraction determined by echocardiography, medical comorbidities, systemic complications, serum troponin, serum sodium and glucose, and functional outcomes as assessed by mRS in posthospital follow-up. Insensible losses were not incorporated into the determination of net fluid balance because of their inherent variability and lack of a reliable method for estimation.

Vasospasm was considered present when documented by transcranial Doppler ultrasound (TCD) (mean blood flow velocity >120 cm/s in the distal internal carotid arteries or in the anterior, middle, or posterior cerebral arteries; severe when velocities exceeded 200 cm/s) or by unequivocal arterial luminal narrowing on invasive or noninvasive angiography. Angiographic vasospasm was determined by catheter angiograms showing unequivocal reduction in luminal diameter and deemed severe when luminal narrowing was greater than 50%. Symptomatic vasospasm was defined by the presence of new neurologic deficits (global or focal) that could not be explained by another cause and occurred in the presence of documented vasospasm on TCD or angiography. DCI was defined by the presence of new and otherwise unexplained neurologic deficits (global or focal) regardless of whether vasospasm was documented. New cerebral infarctions were identified on computed tomography scans obtained when clinically indicated during the hospital stay. Acute lung injury and acute respiratory distress syndrome were defined by PaO_2/FiO_2 ratio of