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Role of Transcranial Doppler in Optimizing Treatment of Cerebral Vasospasm in Subarachnoid Hemorrhage

Ribal S. Darwish, MD, Edward Ahn, MD, and Nana S. Amiridze, MD, PhD

This study was undertaken to evaluate the role of transcranial Doppler ultrasonography in arterial blood pressure management during hypervolemia/hypertension/hemodilution therapy in patients with vasospasm from subarachnoid hemorrhage and correlate this data with neurologic outcome. The study included 18 adult patients, Hunt and Hess grades III-IV. Complete neurologic assessment was performed. Transcranial Doppler indices were calculated by standard formulas. On the basis of our results, resistance area product can be used to estimate the optimal arterial blood pressure in hypervolemia/hypertension/hemodilution therapy. An increase in the cerebral blood flow index was associated with better performance on neurologic examination. Estimated cerebral perfusion pressure from transcranial Doppler data analysis showed poor correlation with cerebral perfusion pressure derived from direct measurement of intracranial pressure in patients with cerebral vasospasm ($\rho = 0.15; 95\% \text{ CI}, 0.11-0.39; P = .2590$).

Keywords: cerebral blood flow index; cerebral perfusion pressure; cerebral vasospasm; transcranial Doppler ultrasonography; triple-H therapy

Subarachnoid hemorrhage (SAH) is a major cause of morbidity and mortality. Twenty-five percent of individuals die within 24 hours of experiencing an SAH, and 40% to 60% of all patients with SAH will die within 1 month. Cerebral vasospasm, one complication of SAH, occurs in 20% to 40% of patients with SAH and can result in disability or death. Cerebral vasospasm is characterized by decreased cerebral blood flow (CBF), decreased cerebral perfusion, and increased intracranial pressure (ICP).

Initial cerebral vasoconstriction after SAH is easily induced in animal models but is rarely the direct cause of morbidity. Cerebral vasospasm of delayed onset is responsible for serious neurologic disability and may be refractory to treatment despite intensive medical management. Hypervolemia/hypertension/hemodilution (triple-H) therapy is the standard of care in patients with symptomatic cerebral vasospasm, although the optimal blood pressure has not been defined. In this study, we attempted to define the optimal arterial blood pressure based on transcranial Doppler (TCD), which is a widely used diagnostic method in neurosurgical intensive care units (ICUs) in patients with cerebral vasospasm.

We also attempted to define clinical metrics that might identify patients in whom further increases in blood pressure would not increase CBF and therefore would require intervention to vasodilate the spasm ed cerebral arteries.

Materials and Methods

Patients

The study was approved by our institutional Internal Review Board. This study included 18 adult patients (age range = 35-83 years; 10 women and 8 men) who were admitted to the neurosurgical ICU of our
665-bed urban tertiary facility over a 12-month period and who met the criteria based on SAH grade. Each patient was diagnosed with an SAH with a Hunt and Hess scale grade of III-IV and required an intraventricular catheter for the management of hydrocephalus. A total of 15 patients underwent craniotomy and clipping of aneurysms within 48 hours of rupture. Two patients underwent endovascular coiling, and in one of these patients angiography-negative SAH was diagnosed. Nimodipine (60 mg orally every 4 hours) was administered to all patients. Triple-H therapy was initiated after securing the aneurysms. Serum magnesium levels were maintained above 2.0 mg/dL, hyperthermia was treated, and rescue treatment with hypertonic saline (23.4%) was performed on 12 occasions.6 Two patients required endovascular intervention with intraarterial injection of verapamil. The ICP was maintained below 20 mm Hg. Patients were maintained with head elevation at 30° and were kept normothermic. Patients were managed according to our institution’s standard protocols for treatment of cerebral vasospasm. The TCD studies (Nicolet TC-88; Viasys Healthcare, Conshohocken, Pennsylvania) of intracranial arteries were acquired on admission and every 3 days for 21 days by a technologist.

Data Acquisition and Processing
As a part of standard clinical practice, arterial blood pressure was monitored directly from the radial artery using a standard pressure monitoring kit (Baxter Healthcare, Cardiovascular Group, Irvine, California). The ICP was measured using the intraventricular catheter ([IVC]; Codman, Irvine, California), as a part of the standard protocol. The IVC was clamped for 3 minutes before the ICP was recorded. A operator performed all TCD studies, and calculations were performed on the resulting measurements based on equations introduced by Aaslid et al7 and modified by Belfort et al8 as follows:

Cerebral perfusion pressure (CPP) = mean arterial pressure (MAP) − ICP

Estimated CPP = Velocity (V)mean × (MAP − diastolic blood pressure) / (Vmean − Vdiastolic)

Resistance area product (RAP) = MAP / Vmean

CBF index (CBFI) = CPP / RAP

Calculated values did not influence patient management. Neurologic examination was recorded at the time of TCD study, including Glasgow Coma Scale (GCS) score and motor strength. The GCS >12 and motor strength >3 were criteria for good outcomes, and GCS <8 and motor strength <3 were considered poor outcomes.

Fisher scale grading was based on initial computed tomography (CT) appearance and quantification of subarachnoid blood (grade 1: no or minimal subarachnoid blood visualized on CT; grade 2: broad diffusion of subarachnoid blood, no clots and no layers of blood >1 mm; grade 3: either localized blood clots in the subarachnoid space or layers of blood >1-mm thick; and grade 4: intraventricular and intracerebral blood present in the absence of significant subarachnoid blood). The diagnosis of cerebral vasospasm is established at our institution based on TCD criteria (TCD mean velocity >120 cm/s for the middle cerebral artery [MCA], 100 cm/s for the anterior cerebral artery, and MCA/internal carotid artery >3). Statistical analysis was performed using Analyse-it version 1.71 (Analyse-it Software, Ltd, Leeds, United Kingdom).

Results
A total of 146 TCD studies were performed. Vasospasm was detected in 38% of these studies, and Fisher grade 3 (8 patients) was associated with the highest incidence of vasospasm. Correlation between RAP, CBFI, and functional examination in the corresponding areas of blood supply was assessed using the Spearman rank correlation (ρ) for MCA, which was calculated to be −0.88 (95% CI, −0.93−−0.81; P < .001; Figure 1). Motor strength in the left arm correlated with increased CBFI (Figure 2). No correlation was found between CPP measured by TCD and direct measurement for the MCA (Figure 1) and ophthalmic arteries (Figure 3; bias = 19.3; ρ = 0.15; 95% CI, 0.11-0.39; P = .2590).

Statistical analysis of these data indicated that the CPP-derived formula from TCD cannot be used in the measurement of CPP in either spasmed or nonspasmed arteries (Figures 1 and 3). An optimal value for CBFI can be identified based on the RAP (1-1.5). Increased CBFI was associated with better performance on neurologic examination (arm motor strength) when CBFI was measured for the MCA indices. This suggests that RAP values might be used to identify an optimal target for arterial blood pressure in patients with cerebral vasospasm.
Discussion

The present study was designed primarily to validate that TCD can help in determining the optimal arterial blood pressure during triple-H therapy. The main finding was that an optimal value of RAP can be calculated and is associated with optimal CBF.

Cerebral vasospasm is suspected (1) when there is a deterioration of neurological status 3 to 14 days after SAH, including insidious onset of confusion, disorientation, or decline in the level of consciousness, as well as focal deficits that may fluctuate in severity; (2) when structural changes affecting neurologic worsening have been excluded by appropriate investigations, including diagnostic imaging; and (3) when (1) and (2) are noted in the absence of seizures and electrolyte abnormalities. Clinical diagnosis of vasospasm is confirmed using cerebral angiography and TCD ultrasonography.
The theoretical basis of this study rests on Hagen-Poiseuille's law, which describes the relationship of flow to pressure, radius, viscosity, and vessel length. Cross-sectional flow velocity is the ratio of flow to the cross-sectional area of the artery. Experimental models of laminar flow indicate a linear relationship between flow velocity and perfusion pressure. Under certain circumstances, such as cerebral vasospasm, turbulent flow develops. The significance of turbulent flow is that a substantial part of the driving energy is lost.

Under conditions of turbulent flow, flow velocity is not proportional to CPP but to the square root of CPP without changes in blood viscosity. An increase in CPP, then, will increase the flow velocity. In the absence of change in the vessel diameter, an increase in blood flow velocity will increase the flow. One question that we asked in this study was at what point the elevation of CPP becomes significantly significant to provide adequate flow and at what point further increases in the CPP will not increase the flow and will require intervention to increase the vessel diameter. In patients who are awake and in whom detailed neurologic examinations can be performed, triple-H therapy can be adjusted, based on changes observed in the examination (aphasia, motor strength, and so on). In patients with poor performance on neurologic examination, there is a need to objectively determine the optimal CPP. A significant increase in arterial blood pressure using pressors and inotropic support in triple-H therapy can cause significant myocardial morbidity, bowel ischemia, perfusion injury to the brain, and even intracranial hemorrhage.

The RAP reflects the ratio between the MAP and $V_{\text{mean}}$. Regional CBF is proportional to the $V_{\text{mean}}$ and CPP. We used these indices and correlated them with performance on neurologic examination at the time of the studies. We used MCA velocity and corresponding area of blood supply as a target for our investigation and found a RAP value between 1 and 1.5 to be associated with optimal CBF and with better performance on neurologic examination. Further increases in the RAP value neither improve the CBFI nor correspond to improved performance on neurologic examination.

In spasm ed arteries, CBF can be maintained through an increase in CPP or a decrease in the resistance to flow. Considering blood viscosity to be constant, an increase in CPP in the spasm ed artery will increase the flow. The treatment of cerebral vasospasm is based on this principle. Triple-H therapy is the standard of care in patients with symptomatic cerebral vasospasm. A number of other treatments attempt to improve the flow by decreasing cerebral vascular resistance. All our patients received nimodipine, a calcium channel blocker routinely used after SAH to prevent vasospasm, for 3 weeks after SAH. Refinements in interventional neuroradiology allowed direct angioplasty of the spasm ed artery and intraarterial injection of vasodilators.

The optimal approach to assess CBF in cerebral vasospasm is based on well-established diagnostic methods, including CT perfusion, magnetic resonance imaging perfusion-diffusion, xenon flow studies, and positron emission tomography (PET), which can provide accurate quantitative assessment of blood flow and determine corresponding arterial areas of blood supply. These approaches are limited by the requirement for a contrast agent or radiopharmaceutical (in CT and PET, respectively), by the “snapshot” nature of the findings, and by requirements for transportation, personnel, and associated costs. Regional methods for assessment of cerebral vasospasm are invasive, with risks of infection. Moreover, regional assessment may miss other areas of compromised blood flow.
Conclusion

On the basis of outcome data in our patients, a RAP of 1.0 to 1.5 was determined to be optimal and correlated well with optimal CBFI and with better performance on neurologic examination.

No correlation was found between CPP measured directly and that measured through TCD. We concluded that TCD cannot be considered a reliable approach for measuring CPP in patients with cerebral vasospasm. Despite continued controversy about its role in the evaluation and management of patients with cerebral vasospasm, TCD continues to be a diagnostic modality commonly used in ICUs, and knowledge of its limitations may help us identify the optimal use of this technology.16,17

References


