CRITICAL CARE

COMMENTARY

Hypertension may be the most important component of hyperdynamic therapy in cerebral vasospasm

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See related research by Dankbaar *et al*., http://ccforum.com/content/14/1/R23

Abstract

Although hyperdynamic therapy is an accepted method of treatment of patients with symptomatic cerebral vasospasm after aneurysmal subarachnoid hemorrhage, it remains unproven in large scale trials and controlled studies. Furthermore, methods of hyperdynamic therapy and specific endpoints vary widely. A systematic review of clinical trials of the various techniques of hyperdynamic therapy and their effects on cerebral blood flow found only 11 studies suitable for analysis. Although controlled trials are lacking, there is some evidence to suggest that hypertension is the most promising component of hyperdynamic therapy. These findings support a future randomized trial of induced hypertension in patients with symptomatic cerebral vasospasm.

In a previous issue of *Critical Care*, Dankbaar and colleagues [1] presented a systematic review of clinical studies of hyperdynamic therapy and its components on cerebral blood flow (CBF). Symptomatic cerebral vasospasm is defined as cerebral ischemia attributable to narrowing of intracranial arteries and loss of cerebral autoregulation, and afflicts some 20 to 25% of patients after rupture of an intracranial aneurysm [2,3]. The cornerstone of medical therapy for cerebral vasospasm is so-called hyperdynamic therapy. Also referred to as triple-H therapy, this strategy includes the use of hypertension, hypervolemia, and hemodilution to optimize cerebral perfusion. Introduced in the 1970s, this management strategy has become widely accepted as first-line treatment for symptomatic vasospasm and is probably used in one form or another in nearly all neurosurgical centers. Indeed, this author favors the use of induced hypertension and volume supplementation for primary treatment of symptomatic vasospasm, prior to endovascular treatment, and, anecdotally, has observed rapid neurological improvement - over the course of an hour or less - in such circumstances. This acceptance of hyperdynamic therapy has evolved despite a relatively modest amount of supportive clinical evidence. The recent American Heart Association Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage described hyperdynamic therapy only as 'one reasonable approach' for the treatment of symptomatic vasospasm (Class IIa treatment effect, level of evidence B) [4]. Hyperdynamic therapy, particularly hypervolemic therapy, also comes with a price in terms of complications (reported in up to 30% of cases [5,6]) and cost. Furthermore, it is not yet clear which components of hyperdynamic therapy are most important.

Dankbaar and colleagues [1] provide a systematic review of clinical studies of hyperdynamic therapy and its components on CBF. Why focus on CBF instead of neurological or overall clinical outcomes? An increase in cerebral perfusion is the mechanism by which hyperdynamic therapy is purported to exert its beneficial effect, and increases in CBF have been linked to clinical improvement in patients with symptomatic vasospasm [7]. Also, an assortment of quantitative CBF measurement techniques have appeared in the past two decades, permitting relatively precise and quantitative analyses of the effects of hyperdynamic therapy.

Dankbaar and coworkers found 11 studies; only one included a control group and the remaining studies compared CBF before and during treatment. Hypertension was associated with an increase in CBF in two of four studies examining hypertension alone, and one of two studies assessing triple-H therapy found an increase in CBF. Only one of seven studies of hypervolemia found a significant increase in CBF compared to baseline. Hemodilution did not change CBF. A meta-analysis of the

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results was not possible due to study heterogeneity. Complication rates were also difficult to assess because they were included in only five of the studies, although it is interesting that complication rates of zero were reported in two trials that included hypertension.

The findings of this study are not surprising, as induced hypertension makes the most sense on a theoretical and practical basis. A key feature of cerebral vasospasm is loss of autoregulation [8,9], resulting in passive dependence of cerebral perfusion on systemic blood pressure. When loss of autoregulation is combined with a reduction in capacitance vessel caliber, cerebral perfusion becomes even more dependent on systemic blood pressure. It seems logical then that raising blood pressure is the most direct way to enhance CBF.

In contrast, hypervolemia is problematic because fluid balance is a poor surrogate for circulating blood volume [10] and sustained volume expansion is difficult to maintain [11]. Hypervolemia also appears to be the component of hyperdynamic therapy most associated with complications, such as pulmonary edema, congestive heart failure, and cerebral edema [11,12]. Since hypovolemia can also be hazardous in this setting, by exacerbating cerebral ischemia [11], maintenance of a normovolemic state may be the most prudent strategy. Hemodilution is even more problematic because the optimal hematocrit in patients with cerebral vasospasm is not known, and hemodilution has been associated with worsening of cerebral ischemia in clinical practice [13].

In addition to suggesting that hypertension may be the most effective component of hyperdynamic therapy, this review also hints that hypertension may actually be the safest component of hyperdynamic therapy. Much remains to be discovered, however. A wide array of different options for hypertensive therapy exists; the clinician must choose a vasopressor (dobutamine, phenylephrine or dopamine), a method of assessment (systolic blood pressure, cerebral perfusion pressure, or pulmonary capillary wedge pressure), and a therapeutic goal. No technique of hypertensive therapy has yet been shown to be superior to others. This is fertile ground for a well controlled, randomized trial. Based on their analysis, Dankbaar and coworkers managed to estimate that only a total of 104 subjects would be necessary for a two-armed trial of hypertensive therapy in patients with symptomatic cerebral vasospasm. Such a trial would be feasible and quick to complete.

Abbreviations

CBF = cerebral blood flow.

Competing interests

The author declares that he has no competing interests.

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