Controversy: Does Prevention of Vasospasm in Subarachnoid Hemorrhage Improve Clinical Outcome?

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The first images of cerebral vasospasm were published in 1951. Although that report was followed by a debate regarding the role of angiographic narrowing in causing neurological deficits, the question seemed to be settled by Fisher in 1977 when he reported a strong relationship between angiographic vasospasm and delayed neurological deficits.

Simple explanations that are consistent with current thinking are usually quickly adopted and rapidly evolve into dogma. Dissenting voices are largely ignored except by a passionate few until the volume of evidence reaches critical mass. It seems that the results of the clazosentan trials have brought us to that point in our search for an intervention to prevent delayed cerebral ischemia after subarachnoid hemorrhage.

Over the decades, observations have suggested that there was not a one-to-one relationship between vasospasm and delayed ischemia. The acute injury from the hemorrhage itself and the subsequent intracranial circulatory arrest have been long recognized. It is widely accepted that ischemia can occur in the absence of vasospasm. Impaired vascular reactivity leads to impaired autoregulation and CO2 reactivity. Microthrombi may also contribute to cerebral ischemia. More recently, spreading cortical depression and inflammation have been added to the list.

At the conference the presenters were tasked with arguing the question, “Does Prevention of Vasospasm in SAH Improve Clinical Outcome?” They both present well-reasoned, cogent, and convincing arguments.

Hou and Zhang argue that only the most severe vessel narrowing would be sufficient by itself to reduce blood flow enough to cause ischemia. They cite animal and human studies that find discordance between vasospasm and neurological deficits. Finally, they point out all the alternative hypotheses with particular emphasis on the role of early injury. Although they do not argue that vasospasm has no role, they suggest it is relatively minor.

Macdonald focused on the question, “Is vasospasm an epiphenomenon or marker of other processes that cause poor outcome?” He argues no. In a review of the literature, he was unable to identify any study in animals where the intervention improved outcome without also reducing vasospasm. He provides several alternative explanations for the discordance found in clinical trials. Macdonald reminds us that rescue therapy is effective and could eliminate any signal of efficacy of a new treatment. In addition, outcome differences are very difficult to demonstrate using crude, usually dichotomized scales that were not developed for subarachnoid hemorrhage.

Although we may never have a definitive answer to the question posed, the debate has fostered the recognition that we must broaden our field of view and consider that delayed cerebral ischemia results from a complex interaction among multiple processes.

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References


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