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Prevention of delayed cerebral ischaemia after subarachnoid haemorrhage

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Physiological abnormalities are a worthwhile target

Delayed cerebral ischaemia (DCI) affects more than one quarter of patients between 3 and 14 days after the onset of their aneurysmal subarachnoid haemorrhage, and accounts for about one third of patients who are dead or dependent as a result of the haemorrhage. Despite the importance of DCI, little can be done to prevent it: only calcium antagonists are supported by good evidence, and the effectiveness of nimodipine is modest (20 patients need to be treated to prevent one poor outcome). Future hope is offered only by the window of opportunity between subarachnoid haemorrhage and DCI onset, and sufficient clinical research interest in finding further interventions for the prophylaxis and treatment of DCI.

In trying to discover whether potentially modifiable physiological abnormalities are a worthwhile target for intervention to prevent DCI, the paper by Naidech et al. (p 1340) explores the association between cerebral infarcts on computed tomograms of the brain after aneurysmal subarachnoid haemorrhage and a physiological derangement score at the time of admission to hospital (based on a patient’s oxygenation, acidosis, glycaemic control and blood pressure). In contrast with the study that originally derived the physiological derangement score, the present study is small and retrospective, with an over-representation of subarachnoid haemorrhages that were severe or located in the posterior circulation. Furthermore, the study used a radiological marker of DCI rather than clinically important outcome data after discharge from hospital. The authors strove to identify cerebral infarcts due to vasospasm, but multivariate analysis found only clinical severity of subarachnoid haemorrhage and physiological derangement score to be associated with cerebral infarcts. However, the size of the study sample precluded the inclusion of other known determinants of DCI (such as prolonged duration of unconsciousness at onset of subarachnoid haemorrhage), and its design did not allow an analysis of the influence of endovascular or surgical treatment.

The study by Naidech et al. provokes many questions. Might alternative scoring systems using additional variables be better at predicting poor clinical outcome? Might altered physiology

REFERENCES
simply be an epiphenomenon reflecting subarachnoid haemorrhage severity? Could physiological derangement at later stages of admission to hospital be even more influential (as is the case for hypomagnesaemia)? As vasospasm is neither necessary nor sufficient to account for DCI, retaining the focus on determinants of poor outcome and DCI is likely to be most beneficial for patients. There are many potential targets for prevention of DCI, including endothelial activation, cortical spreading depression, excitotoxicity mediated by raised intracellular calcium, apoptosis, nitric oxide depletion, free radical formation and mitochondrial dysfunction, many of which may be influenced by the physiological abnormalities in the patient.

For now, the correction of some physiological abnormalities (such as hypoxia, hypotension and hyperglycaemia) after aneurysmal subarachnoid haemorrhage seems to be clinical common sense, not least to try and mitigate the major effect on cardiorespiratory function after subarachnoid haemorrhage. This approach further reinforces the importance of multidisciplinary team management, including critical care. To investigate whether DCI could be prevented by more aggressive treatment of physiological derangements, would require large randomised controlled trials, in addition to the ongoing clinical trials of magnesium, simvastatin and clazosentan.

References