Neurosurgical forum

tients not selected by grade or age. J Neurosurg 97:250–259, 2002

RESPONSE: We are grateful for the interest of Drs. Ciappetta and Paolini in our article. The main question for a neurosurgeon who operates on a patient with a large intracerebral clot requiring urgent evacuation likely caused by a ruptured aneurysm is whether to perform angiography to establish if there is an underlying aneurysm prior to evacuation of the hematoma. In nearly all circumstances such patients in our institution are already paralyzed and ventilated. The time required for transfer from the district hospital to the regional neurosurgical unit. The time required to transfer a patient to the angiography suite from intensive care or the transferring ambulance can be minimized, and we would disagree that time required to coil an aneurysm in excess of that to obtain an angiogram is “several hours” for an experienced neurointerventional team. Indeed it is less than 30 minutes in most circumstances. The endovascular objective in these circumstances is not to achieve a perfect angiographic result but to secure the aneurysm from early rerupture while evacuating the clot or in the immediate postsurgical period. Prior to the angiogram and coiling we would in some circumstances place an external ventricular drain and/or an intracranial pressure monitor as the best way to monitor the status of a ventilated patient in these circumstances.

We agree that in terms of independent survival for this group of patients the results appear relatively good; however, we would emphasize that the numbers are small and thus comparison in these circumstances with other series must be circumspect. The overall results, however, are clearly worse than those reported for the management outcome in the International Subarachnoid Aneurysm Trial (ISAT) (30.5% dependent outcome for surgery; 23.5% for coiling). Despite all the limitations of this type of study we believe that for those centers with good available interventional treatment, this treatment strategy should be considered for patients in this dire clinical situation. We do not believe that it raises any ethical concerns as Ciappetta and Paolini suggest. Indeed in the light of the ISAT results, managing patients with acute aneurysmal SAH in centers without access to the endovascular coil treatment option does raise ethical concerns.

A. J. MOLYNEUX, M.D.
Oxford Radcliffe Hospitals
Oxford, United Kingdom

Etomidate, Transfusion, and Vasospasm

TO THE EDITOR: Two articles in the July issue of the Journal of Neurosurgery draw attention to the potential role of depletion or deficiency of nitric oxide in the occurrence of vasospasm after subarachnoid hemorrhage (SAH) (Fra-
confounding variables (OR 1.48, CI 0.83–2.63). Angiographic vasospasm was observed in 217 patients and, after adjusting for confounding variables, was more frequent among patients who received postoperative RBC transfusion (OR 1.68, CI 1.02–2.75). Among patients in whom angiographically confirmed vasospasm developed there was a tendency to have received more blood than in those with no vasospasm; however, a clear dose-dependent response was not observed.

Conclusions. Development of angiographically confirmed vasospasm after SAH is associated with postoperative RBC transfusion and worse outcome is associated with intraoperative RBC transfusion. Before blood is transfused, patients with SAH should be carefully assessed to determine if they are symptomatic because of anemia.

Those observations prompt us to draw attention to a “cerebral protection” practice (administering etomidate prior to temporary occlusion) that is still being used in the management of patients undergoing aneurysm clipping, in particular when temporary occlusion is used, and that may actually be deleterious. There are not only very few data to support the notion that it is actually a protective maneuver, but there is also reason to believe that it might actually be disadvantageous. Etomidate inhibits NO by two separate mechanisms. Etomidate is a carboxylated imidazole, and all of the compounds of that class are inhibitors of NO synthase. In addition, the preparation of etomidate that is available in North America produces some degree of hemolysis in humans (probably because of the propylene glycol vehicle) and thereby results in some free hemoglobin in the circulation. Free hemoglobin is an exceptionally effective scavenger of NO.

Shortly after the practice of administering etomidate as a cerebral protectant during aneurysm surgery was popularized, our group noted that there were few preclinical data to confirm etomidate’s protective efficacy. We undertook a series of investigations to provide that confirmation. In two investigations, using a model of severe forebrain ischemia in rodents, we did, in fact, demonstrate that etomidate provided modest histological protection in the hippocampus relative to other anesthetic agents. We next attempted to demonstrate protection in a laboratory model more analogous to the conditions that prevail during temporary vessel occlusion intraoperatively. Using a model of temporary middle cerebral artery occlusion in rats, however, we were not only unable to demonstrate a protective effect of etomidate but observed to our initial surprise a worsening of the area of histological injury relative to animals that received either isoflurane or thiopental during ischemia. We performed a fourth investigation to explore the hypothesis that the apparent adverse effect of etomidate was a function of inhibition of NO. In that investigation, the adverse effect of etomidate, relative to a halothane anesthetized control state, was no longer evident when both groups were pretreated with L-NAME to eliminate NO as a variable prior to the onset of ischemia. In an additional group, the adverse effect of etomidate was also not evident when there was simultaneous administration of etomidate and a large dose of L-arginine, suggesting that the inhibition of NO synthase by etomidate is competitive. Collectively, our investigations suggest that, in rodents, there is an adverse effect of etomidate in the setting of transient focal ischemia that is mediated by inhibition of NO. In addition, the inhibition of NO that we suspect would explain the reduction in brain tissue PO2 observed by Edelman, et al., in patients who received etomidate prior to temporary intraoperative cerebral vessel occlusion.

Our results certainly do not prove that etomidate is deleterious in patients who undergo temporary vessel occlusion. Our results, in conjunction with what is otherwise an absence of preclinical data to confirm the efficacy of etomidate as a protective substance, we think, should make clinicians circumspect about the use of etomidate for cerebral protection during aneurysm surgery. Whereas the practice of cerebral protection by etomidate is not as widespread as it may once have been, the results of the recently reported International Hypothermia in Aneurysm Surgery Trial included the information that etomidate was used during temporary occlusion in some patients included in the trial (personal communication, Michael M. Todd, Principal Investigator).

JOHN C. DRUMMOND, M.D., F.R.C.P.C. 
University of California, San Diego 
Veterans Administration Medical Center 
San Diego, California

PIYUSH M. PATEL, M.D., F.R.C.P.C.
University of California, San Diego 
Veterans Administration Medical Center 
San Diego, California

References


In this study, based on a retrospective review of prospectively collected data, the authors conclude that angio-