Response to Evidence-Basis for Anticoagulants for Cerebral Sinus Venous Thrombosis?

Response:

The aim of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) was to gather data on the clinical presentation, risk factors, and prognosis of patients with cerebral venous thrombosis (CVT). With the help of neurologists worldwide, these goals were achieved, and the ISCVT significantly improved our understanding of CVT. The ISCVT, however, was not designed to evaluate the efficacy of heparin for the treatment of CVT. Any attempts to draw conclusions on this topic based on data from the ISCVT, as Dr Cundiff does, may be flawed.

During the inclusion phase of the ISCVT, it was already standard practice for most neurologists to treat patients with heparin, as demonstrated by the fact that 83% of patients received this therapy. The minority of patients not treated with heparin are thus subject to all kinds of selection bias, and an unadjusted comparison between both groups yields meaningless data. The odds ratio Dr Cundiff calculated has, therefore, no value. An adjusted odds ratio is difficult to calculate because of the large number of potential (and unknown) confounders, the small number of patients not treated with heparin, and the small number of outcome events. Another fact rendering any comparison useless is that the majority of the 104 patients, who did not receive heparin in therapeutic dose, received other forms of anticoagulation. In fact, only 22% of these patients (n=23) received no anticoagulant treatment at all.

To evaluate the efficacy of heparin therapy in CVT, we should instead analyze the data from randomized trials, as we did in the Cochrane review, where we have presented a balanced and objective review of the available evidence. The meta-analysis showed an absolute risk reduction in death or dependency of 13% with a confidence interval of 30% to −3%. Notably, no new symptomatic intracranial hemorrhages occurred among anticoagulated patients, although 2 control patients had a diagnosis of probable pulmonary embolism (1 fatal). We concluded that the available evidence suggests that anticoagulation for CVT is safe and associated with a potentially important reduction in poor clinical outcome, which did not reach statistical significance.

It is true that improved imaging has led to the identification of milder cases and, as a result, an apparent increase in the incidence of CVT. There are, however, no clinical data that support Dr Cundiff’s hypothesis that these milder cases need not be treated with heparin. In fact, although these patients often have a better prognosis, they can still suffer from life-threatening complications, such as a pulmonary embolism or extension of the thrombus into cortical veins, leading to venous infarction. These complications can be avoided with anticoagulant therapy.

In conclusion, the available evidence from the small clinical trials, in combination with biological plausibility, and the vast clinical experience in expert centers all are in favor of heparin treatment for CVT, as recommended by international guidelines.5,6

Disclosures

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