Letter by Misra et al Regarding Article, “Anticoagulants for Cerebral Venous Thrombosis: Harmful to Patients?”

To the Editor:

We read with interest the article by Dr Cundiff in which he has highlighted the harmful effect of heparin and oral anticoagulant in cerebral venous thrombosis (CVT). CVT is more common in the developing countries because of high incidence of infection, pregnancy, puerperal complications, dehydration, and hot climate. We have concerns regarding grouping of the patients in the above study. The patients in the study by Nagaraja et al received low-dose heparin (2500 thrice daily) have been grouped with those who did not receive heparin. In this study on 150 patients with CVT, 73 received heparin and 77 did not. Even the low-dose heparin was effective in reducing death (8 versus 18; P<0.001) and resulting in complete recovery (34 versus 14; P<0.001) compared with no heparin group. It is conventional to compare the treatment with placebo/no treatment group rather than with low-dose therapy. It will be better to analyze the patients with CVT receiving anticoagulants versus no anticoagulants/placebo. In a randomized, blinded, placebo-controlled study, 10 patients each received heparin and placebo. At 3 months in the heparin group, 8 patients had complete recovery and 2 had mild neurological deficit, whereas in the placebo group, only 1 had complete recovery, 3 had neurological deficit, and 3 died which resulted in termination of the trial.

The therapeutic level of anticoagulation is more important than the dose of anticoagulant. In our study comparing low-molecular-weight heparin versus unfractionated heparin in CVT, anticoagulation was suboptimal in 63.1% occasions despite full-dose heparin. Low-molecular-weight heparin has been reported to be effective both in deep vein thrombosis and CVT when compared with unfractionated heparin.

Mortality in CVT is not only dependent on the sinus thrombosis per se, but also related to brain edema, herniation, hemorrhage, infections, and comorbidities. Hemorrhagic parenchymal lesion in CVT increases death. In a study on 220 patients with CVT, presence of hemorrhagic lesion resulted in death in 32% compared with 12% in nonhemorrhagic lesion. The author has quoted Cerebral Venous Thrombosis Portuguese Collaborative Study Group (VENOPORT) study to highlight the inefficacy of anticoagulant. In this study, the patients with hemorrhagic lesion had similar outcome to those without hemorrhagic lesion despite a greater chance of death. This result could as well suggest the benefit of anticoagulation even in the patients with hemorrhagic lesions.

The author has reported high recurrence of CVT in the patients receiving anticoagulants compared with those without anticoagulants (0.3% versus 0.2% per month). The recurrence of CVT may depend on the underlying cause. Has the author analyzed the underlying causes of CVT? Are the underlying causes different in the group with and without recurrent CVT? The patients with prothrombotic conditions such as antiphospholipid antibody syndrome, factor V Leiden mutation, paroxysmal nocturnal hemoglobinuria, and malignancy are prone for recurrent venous thrombosis.

Those who treat the patients with CVT are impressed by the temporal relationship between anticoagulation and clinical improvement. If the anticoagulation is suboptimal, the patient reports worsening of headache and features of raised intracranial pressure. CVT is a manifestation of diverse causes, many of which need prolonged anticoagulation. The duration and degree of anticoagulation depend on the underlying cause. CVT has low mortality (<5%) and rare sequel if diagnosed and treated early. We think that the data in the article by Cundiff should be reanalyzed in reference to heparin versus no heparin and mortality should be adjusted for covariates.

Disclosures

None.

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References

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Stroke. 2014;45:e110; originally published online April 17, 2014;
doi: 10.1161/STROKEAHA.114.005410

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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