Response to Letter Regarding Article, “Anticoagulants for Cerebral Venous Thrombosis: Harmful to Patients?”

My thanks to Dr Misra et al for the letter concerning my article. The authors reference the lopsided results of the old and flawed randomized controlled trial by Einhäupl et al without rebutting any of my extensive criticisms of the methodology and scoring of outcomes in this trial in my opinion piece.

Misra et al said about their own randomized controlled trial, “In our study comparing low-molecular-weight heparin versus unfractionated heparin in CVT, anticoagulation was suboptimal in 63.1% occasions despite full-dose heparin.” All 6 deaths occurred in their patients who had cerebral venous thrombosis (CVT)–related intracranial hemmorhages on presentation. Consequently, their statement implies that these 6 patients bled to death because they didn’t receive enough heparin. This makes no sense.

Regarding the Cerebral Venous Thrombosis Portuguese Collaborative Study Group (VENOPORT) study, Misra et al wrote, “…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.” Not so. The VENOPORT authors did not break down treatment of hospitalized patients by anticoagulation status. Below are some of the questions I posed to the VENOPORT authors by e-mail. Replies to these questions would have allowed me to determine how anticoagulated patients compared with nonanticoagulated patients:

1. How many of the 37 retrospective component patients who received anticoagulation received full-dose heparin?
2. Did any patients receive other anticoagulation (eg, vitamin K antagonists (VKAs), low-dose heparin)?
3. Of the patients who received full-dose heparin, how many died in the initial hospitalization?
4. Of the patients who received other forms of anticoagulation, how many died in the initial hospitalization?
5. Of the 14 patients who did not receive anticoagulation, how many died in the initial hospitalization?

Because the VENOPORT authors declined to answer my questions, all that can be said concerning their selectively reported data is that patients receiving anticoagulants (unknown drugs and unknown doses) had a much lower chance of presenting with intracranial hemorrhage (P=0.0009) or altered mental status (P=0.048). In 3 of the 9 deaths, the CVT was first diagnosed at autopsy, so it was disingenuous to report that anticoagulation correlated with recovery.

My article reported a higher rate of venous thrombosis recurrences in patients while receiving VKAs compared with while not receiving VKAs. Misra et al wrote that they would like to see venous thrombosis recurrence rates by pathogenesis of CVT. However, few CVT study authors reported venous thrombosis recurrences by CVT pathogenesis. It is unlikely that adjusting for pathogenesis of CVT would significantly change the higher rate of recurrences while taking VKAs (on VKAs: 0.33%/mo versus not on VKAs: 0.20%/mo; odds ratio, 1.60; 95% confidence interval, 1.06–2.42; P=0.0246).

Misra et al concluded, “We feel 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.”

The CVT authors, including Dr Misra, reported or divulged to me little data on covariates. However, their question could be answered with data from the International Study of Cerebral Sinus and Venous Thrombosis (ISCVT), the largest CVT observational study (n=624): full-dose heparin: 25 of 520 (4.8%) dead versus no full-dose heparin: 2 of 104 (1.9%); odds ratio, 2.6; 95% confidence interval, 0.60 to 11.1; P=0.29. Of the 2 patients not receiving heparin, one presented in coma and had multiple infarctions and the other had brain hemorrhage and infarction.

In conclusion, existing data on anticoagulation related to CVT show no benefit and likely harm.

Disclosures
None.

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References

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