Comment to "Antithrombin III administration for portal vein thrombosis in patients with liver disease

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Letter to the Editor

Comment to "Antithrombin III administration for portal vein thrombosis in patients with liver disease: A randomized double-blind controlled trial"

Dear Editor,

We read with great interest the paper by Hidaka and colleagues who randomized patients with mild to moderate cirrhosis (Child–Pugh score <11) with a recently diagnosed portal vein thrombosis (PVT) and an antithrombin (AT) plasma level <70% between treatment with placebo or AT concentrate for a maximum of 15 days.[1] Although thrombus resolution in the short term was substantially improved in the AT arm, we think that the authors' conclusion that AT "should be considered an essential therapy for PVT in patients with liver disease" is premature.

Previous studies showed that thrombus resolution requires prolonged anticoagulant therapy (5–7 months).[2,3] Also, in patients who showed no recanalization after 6 months of anticoagulant therapy, total portal vein recanalization was reported after another 6 months of therapy.[4] Notably, spontaneous recanalization of PVT is reported in up to 40% of cases.[8–10] Based on these data, the rationale for giving a short course of AT supplementation is unclear. Hidaka *et al.*'s data actually suggest AT concentrate to lead to almost instantaneous thrombolysis, which is a mechanism that in our opinion lacks biological plausibility.

Patients with compensated cirrhosis are in a fragile hemostatic balance due to a concomitant decline in pro- and anticoagulant factors.[5] This fragile balance will be disrupted by administration of AT concentrate, which likely increases bleeding risk. We therefore disagree with the authors' statement that selective supplementation of AT is not associated with a bleeding risk.

As cirrhosis is a chronic condition, the risk of recurrent PVT after successful recanalization with a short-term course of AT concentrate may be high.

Nowadays, despite the lack of consensus on the type of anticoagulant, dose, and treatment duration, the majority of patients with PVT are given anticoagulants.[6,7] We feel Hidaka's study should have included a comparator arm of a conventional anticoagulant to better appreciate mechanisms underlying the rapid effect of AT concentrate. Based on literature, conventional anticoagulants are likely to decrease coagulation activation and increase fibrin breakdown, but are not expected to result in thrombus resolution in just 5–15 days.

As the risk of PVT increases with the severity of the cirrhosis,[8] Hidaka's study, with Child–Pugh <11 patients only, did not study the vast majority of cirrhotic PVT patients. Notably, Hidaka's study included 104 patients from 55 hospitals over a period of 1.5 years, which indicates the group is likely highly selected.

If short-term AT supplementation really is as beneficial as it appears from Hidaka's data, AT concentrate might also benefit PVT patients with AT >70%.

Finally, we would like to outline that, at present, it is still unclear whether treatment of PVT is (always) indicated because several factors need to be considered, namely, site of the thrombus, severity of the liver disease, comorbidities, and whether the patients is a liver transplant candidate.[6]

In aggregate, further studies with a less selected patient population, longer follow-up, and additional studies on mechanism of action are required before AT concentrate can be considered essential in the management of PVT.

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