Authors' reply

Sir,

We appreciate the interest of the authors and thank them for their comments[1] regarding our article titled "Antifibrinolytics in Liver Surgery".[2]

We agree with the authors about their views regarding recombinant factor VIIa (rFVIIa). Because our topic of discussion was "Antifibrinolytics in Liver Surgery" and because rFVIIa is not an antifibrinolytic agent, we did not mention it.

However, there are a good number of evidences to prove the efficacy of rFVIIa beyond doubt to control severe bleeding that is refractory to other conventional therapy. But, in spite of different studies and reports including two large, well-conducted, randomized studies,[3,4] the definite conclusions on the use of rFVIIa during orthotopic liver transplantation (OLT) have yet to be drawn.[5] Prophylactic use of rFVIIa at the beginning of the OLT may reduce the perioperative transfusion requirements in a selected group of patients with prolonged PT and a high Model of End-stage Liver Disease (MELD) score.[6] But, this effect was not found to be very significant.[7] Four randomized controlled trials (RCTs) evaluating the prophylactic administration of rFVIIa during OLT[3,4,7,8] demonstrated no difference in mortality or thromboembolic adverse events except in one trial, which showed a reduction in RBC transfusion requirements (300 mL±133 in the rFVIIa group vs. 570 mL±111 in the control group; $P<0.017$).[7] Although rFVIIa is a very effective procoagulant, there is always a concern about hepatic artery thrombosis, which is a dreadful complication during OLT. Recently, Levi *et al.* studied a large and comprehensive cohort of persons in placebo-controlled trials of rFVIIa from 35 RCTs involving 4468 subjects and found that the rate of thromboembolic events among rFVIIa users was 11.1% (498 of 4468 subjects). They also observed that the rate of arterial thromboembolic events was higher among those who received rFVIIa than in those receiving placebo (5.5% vs. 3.2%), whereas the rate of venous thromboembolism was almost similar to placebo (5.3% vs. 5.7%).[9]

Consensus recommendations for the off-label use of rFVIIa were published by a multidisciplinary panel convened jointly by the Society for the Advancement of Blood Management and the University HealthSystem Consortium.[10] Rescue therapy with rFVIIa was deemed appropriate for patients with uncontrolled bleeding in the setting of cardiac, aortic, hepatic, or orthopaedic surgery if they failed to achieve haemostasis with significant clotting factor replacement (20 mL/kg or 6 units of fresh frozen plasma, 6 units of platelets twice for platelet counts less than 50,000, and/or 10 bags of cryoprecipitate twice when fibrinogen is low).[10,11]

Therefore, on the basis of the current literature, there is no evidence to support an extensive use of rFVIIa. It appears that there is a consensus that rFVIIa can be used with good results as a rescue therapy in extremely severe bleeding situations based on individual clinical conditions and patient risk/benefit profile.[12-15]

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