Letters to Editor

Use of recombinant factor VIIa in orthotopic liver transplant

Sir,

This is with reference to the article by Makwana J, Paranjape S, Goswami J[1] "Antifibrinolytics in Liver Surgery", published in the Nov-Dec 2010 issue of the *Indian Journal of Anaesthesia*. I would like to congratulate the authors for a well-written review article.

Haemorrhage is a major problem in patients undergoing liver transplantation, necessitating high transfusion requirements. Although antifibrinolytic agents have been discussed by the authors, the use of recombinant factor VIIa (rFVIIa) in orthotopic liver transplant (OLT) also merits some discussion.

rFVIIa is considered to be the only true procoagulant drug available. rFVIIa actively enhances coagulation and stimulates fibrin formation in the presence of tissue factor. Although rFVIIa is approved by the US Food and Drug Administration (FDA) for haemophilia, a large number of case reports and studies have reported the use of rFVIIa in uncontrolled haemorrhage due to trauma or surgery. The data available seem to suggest a trend towards lower transfusion requirements.

The first clinical application of rFVIIa in adult cirrhotic patients undergoing OLT was reported by Hendriks *et al*.[2] In this pilot trial, six patients with Child B or C cirrhosis received a single dose of 80 μg/kg rFVIIa prior to the start of surgery. Compared with a group of matched historical controls, a significant reduction in median total red blood cell (RBC) transfusion requirements was observed in rFVIIa-treated patients, although one of the treated patients developed hepatic artery thrombosis. It was followed by two consecutive, large, randomized multicenter trials in liver transplant patients.[3,4] In the first multicenter trial, reported by Planinsic *et al*.,[3] 82 patients were randomized to receive placebo, 20, 40, or 80 μg/kg rFVIIa as a single dose at the start of the procedure. The decrease in perioperative RBC transfusion requirements observed in the pilot study could not be reproduced in the multicenter trial. There were no significant differences in thrombo-embolic complications among the four groups; however, they demonstrated that adequate plasma levels of rFVIIa were observed only during the first few hours of the operation.

In the second multicenter trial, reported by Lodge *et al*.,[4] 183 patients were randomized to receive placebo, 80, or 120 μg/kg of rFVIIa and the doses were repeated every 2 h during the operation until 30 min before graft reperfusion. In addition, an extra dose of rFVIIa was given at the end of surgery. Despite a more sustained shortening of the prothrombin time and longer duration of detectable plasma levels of rFVIIa during the operation, this trial again did not result in a significant reduction of RBC transfusion requirements in rFVIIa-treated patients compared to placebo. However, a small but significant percentage of rFVIIa-treated patients did not require any RBC transfusions.

Recently, Busani *et al*.,[5] reported a series of seven patients with persistent severe bleeding after application of a standard transfusion protocol. They administered a 90 microg/kg bolus of rFVIIa to be repeated if necessary after 3 h, and recorded the blood loss and the need for transfusions before and after the rFVIIa therapy. Blood losses and need for platelets significantly decreased after rFVIIa administration; a non-significant decrease in RBC and fresh frozen plasma transfusions also occurred. In six patients treatment with rFVIIa was effective; only one patient died because of haemorrhagic shock, and no thromboses were detected among the treated patients. The study suggested that in some challenging cases of massive bleeding rFVIIa should be considered as a useful option to control bleeding.

It can be concluded from these two large, well-conducted, randomized studies[3,4] that rFVIIa cannot be recommended as a universal prophylaxis to reduce transfusion requirements during OLT particularly considering the high cost of rFVIIa. However, a study by Busani *et al*.,[5] merits more work to define the possible role of rFVIIa as a therapeutic agent rather than as a prophylactic agent.

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Quick Response Code	Website: www.ijaweb.org
	DOI: 10.4103/0019-5049.82651