



Acute Coagulopathy After Reperfusion of the Liver Graft in Children Correction With Recombinant Activated Factor VII

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ABSTRACT

Background. Several studies have proven that massive blood loss increases postoperative morbidity and mortality in liver graft recipients. Since we have successfully corrected coagulopathy preoperatively using an intravenous (IV) bolus of recombinant activated factor VII (rFVIIa) in 2 patients with fulminant liver failure, we observed that there was rapid reversal of preexisting advanced coagulopathy in another 40 patients with high risk for intraoperative bleeding by this treatment immediately before transplantation. Recently to control hemostasis we have administered rFVIIa also to patients presenting with acute coagulopathy and nonsurgical bleeding after graft reperfusion as described herein.

Materials and Methods. We have used rFVIIa in 7 children presenting with severe coagulopathy and nonsurgical bleeding after liver graft reperfusion. The dosage of rFVIIa ranged between 37 and 148 mcg/kg. An antifibrinolytic agent (aprotinin, tranexamic acid) was administered simultaneously.

Results. APTT before rFVIIa was 86.10 to 183 seconds, (mean, 132.1 \pm 39.88), after the bolus of rFVIIa 49.4 to 206.1 (mean, 112.7 \pm 58.53), and at the end of surgery 71.70 to 180 (mean, 110.3 \pm 40.98). INR after reperfusion was 1.82 to 3.91 (mean, 2.56 \pm 0.67), 1.03 to 1.92 (mean, 1.54 \pm 0.35) after rFVIIa, and 1.74 to 5.58 (mean, 2.64 \pm 1.35) at the end of surgery. Before rFVIIa administration intraoperative blood transfusions after graft reperfusion were 900 to 4200 mL of red blood cells (RBC) (0.82–5.4 total blood volume) and after reperfusion 0 to 1800 mL of RBC (0–2.5 TBV). No postoperative vascular complications were observed.

Conclusions. A single dose of rFVIIa effectively reverses the severe coagulopathy developing after graft reperfusion, establishing effective hemostasis in liver transplant recipients without an increased risk of thrombotic complications.

IT IS WELL KNOWN that massive blood loss during liver transplantation has a negative influence on postoperative morbidity and mortality, particularly in children. Severe blood loss maybe caused by impaired coagulation and technical difficulties during liver transplantation, such as portal hypertension, adhesions after previous surgery, collateral circulation, portal vein hypoplasia. Most of the blood loss occurs during hepatectomy; however, in some patients graft reperfusion is followed by an acute coagulopathy that is aggravated by activated fibrinolysis.¹

Since 1997 we have used an intravenous (IV) bolus of 50 to 100 mcg/kg of recombinant activated factor VII (rFVIIa) at the start of liver transplantation (LTx) in 40 patients, who were at high risk for intraoperative bleeding. This rapid

correction of a preexisting advanced coagulopathy aimed to reduce the intraoperative blood loss and transfusion requirement. In some patients an additional bolus was administered either during hepatectomy depending on the coagulation parameters and a clinical assessment of bleeding and blood loss, and no later than 2 hours before reperfusion

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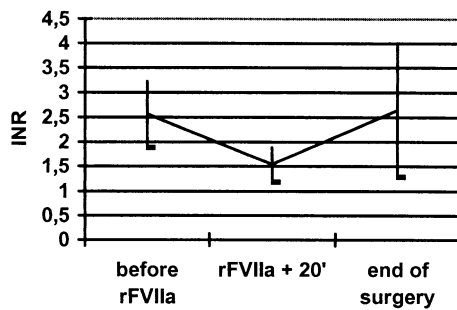


Fig 1. Intraoperative INR (■ - SD; — mean; +SD).

by vessel unclamping, due to fear of hypercoagulation and vascular thrombosis.² During the last 2 years 7 children with nonsurgical bleeding after liver graft reperfusion were administered rFVIIa in an effort to control a severe bleeding diathesis and achieve hemostasis. The aim of this study was to present our experience with rFVIIa for such indication.

MATERIALS AND METHODS

We have used rFVIIa in 7 children presenting with severe coagulopathy and significant nonsurgical bleeding developing soon after liver graft reperfusion. The dosage of rFVIIa ranged between 37 and 148 mcg/kg (mean, 68.43 \pm 38.83 mcg/kg). In 6 patients, 1 dose was administered, whereas 2 doses were given to 1 child (total dose, 146 mcg/kg). We retrospectively assessed coagulation parameters (APTT and INR), the number of blood transfusions before and after graft reperfusion, the incidence of postoperative re-laparotomies for bleeding, the occurrence of thrombotic complications, and the early survival of these patients.

RESULTS

All patients showed clinical improvement of hemostasis and control of bleeding immediately after delivery of a bolus of rFVIIa. Administration of rFVIIa was associated with rapid improvement of the INR from 1.82 to 3.91 (mean, 2.56 \pm 0.67) to 1.03 to 1.92 (mean, 1.54 \pm 0.35), although the APTT did not change, namely, 86.10 to 183 seconds (mean, 132.1 \pm 39.88), 49.4 to 206.1 (mean, 112.7 \pm 58.53 s). Before graft reperfusion intraoperative blood transfusion 900 to 4200 mL (mean, 2100 \pm mL) of red blood cells (RBC) namely 0.82–5.4 of total blood volume (TBV); (mean, 1.88 \pm 1.63) and after reperfusion and administration of rFVIIa this diminished significantly to 0 to 1800 mL RBC (mean, 728.6 \pm 667.6 mL) equal to 0 to 2.5 (mean, 0.7829 \pm 0.916) TBV. Although at the end of surgery the coagulation parameters again deteriorated, only 2 patients showed a recurrent mild bleeding diathesis, which was controlled with fresh frozen plasma (FFP) infusion (Fig 1 and Fig 2). On reoperation of 3 children on days 1 and 2 after Tx, only clots were observed; there was no active bleeding. No postoperative vascular thrombosis developed in any recipient. Two patients died due to multior-

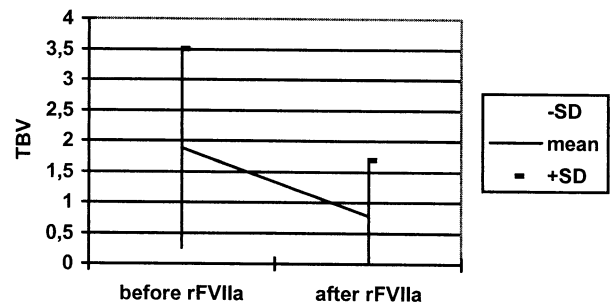


Fig 2. Intraoperative blood loss in relation to TBV.

gan failure and 5 survived during the posttransplantation hospitalization.

DISCUSSION

Reperfusion of a liver graft may be associated with an acute severe coagulopathy caused by several factors: progressive dilutional coagulopathy during hepatectomy, the anhepatic phase, and after influx of the preservation solution; heparin-like substances from donor hepatocytes; and release of tissue Plasminogen Activator (tPA) from the donor liver producing acute fibrinolysis.³ Clinically severe nonsurgical bleeding may further aggravate the coagulopathy. Administration of a bolus of rFVIIa in combination with an antifibrinolytic agents (aprotinin or tranexamic acid) seemed to produce immediate correction of the clinical and laboratory evidences coagulation, controlling bleeding diathesis with gradual improvement in the coagulation profile and hemodynamic stabilization without massive blood and FFP transfusions.^{4–6} In supraphysiological levels rFVIIa has been shown to initiate coagulation by formation of the FVII/tissue factor complex at the sites of injury with direct activation of factors IX and X on platelet surfaces, even when the normal coagulation pathway is impaired. We did observe neither an increased risk of thrombotic complications nor a recurrence of severe bleeding despite the requirement of 3 patients for early re-laparotomies. Based on our experience, we conclude that rFVIIa effectively reverses the severe coagulopathy developing after graft reperfusion, facilitating effective hemostasis in liver transplant recipients without an increased risk of thrombotic complications.

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