Recombinant factor VIIa for life-threatening post-partum haemorrhage

Editor—We read with interest the article by Ahonen and colleagues. All patients in the case series sustained severe post-partum haemorrhage (PPH) and transfusion requirements were high. However, it is difficult to make assessments of the efficacy of recombinant factor VIIa (rFVIIa) from the data presented. As stated in the accompanying editorial, we need randomized controlled trials to determine whether rFVIIa is effective, but these studies are unlikely to be implemented in the setting of unanticipated PPH. However, the authors do have data available that could help demonstrate the efficacy of rFVIIa. In the 3 yr before the 16 month study period, there were 29 hysterectomies performed in the setting of PPH. The authors could compare the outcomes (transfusions, estimated blood loss, ICU length of stay, hospital length of stay) of those 29 cases with the five patients who required hysterectomies performed in the 16 month period when rFVIIa was available. A more extensive comparison could include all PPHs with blood losses >5 litres. Although this type of study is affected more by bias than a randomized controlled trial, there is an advantage to studying a case series before and after a change in practice. In this type of study, measured outcomes are from normal clinical care that is uninfluenced by study protocols.

In addition to studying the efficacy of rFVIIa, it would be worthwhile examining the cost effectiveness of this drug. This is a very expensive drug (a 4.8 mg vial currently costs ~$7100 in the USA). However, if rFVIIa can be shown to reduce the number of blood transfusions required and other therapeutic interventions, then its cost would be easier to justify.

When the cases from the report by Ahonen and colleagues are included with the others reported in the literature, rFVIIa has been used in 33 cases of severe obstetric haemorrhage, and post-partum haemorrhage was described in the majority. Proper dosing is difficult to determine because of the wide range of doses reported (mean total dose 149.6 μg kg$^{-1}$). Most case reports describing the use of rFVIIa for postoperative haemorrhage have shown a haemostatic effect with doses of 60–120 μg kg$^{-1}$ after a maximum of two doses. We recommend starting with a dose of 60 μg kg$^{-1}$ and, if necessary, escalating the dose until an adequate haemostatic effect is obtained.

Exactly what type of case will rFVIIa be useful in? There is not a clear pattern in the literature, but cases of bleeding refractory to standard therapy with blood replacement products and surgical management would be most appropriate. We emphasize that in situations of severe unanticipated PPH, surgical tamponade (using uterine packs, B Lynch brace suture, hydrostatic balloon catheters), correction of anaemia and abnormal coagulation (with red blood cells, fresh frozen plasma, platelets and cryoprecipitate), treatment of hypothermia and acidosis, invasive corrective measures (uterine artery embolization, uterine artery ligation) and the administration of pharmacological agents (uterotonics) are still the most important management strategies. However, it is possible that rFVIIa may reduce the number of hysterectomies performed in situations of severe obstetric haemorrhage refractory to other therapeutic interventions.

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Editor—we appreciate the comments of Drs Butwick and Riley on our case report about the use of rFVIIa in life-threatening PPH.1 During a 3 yr period, 29 women underwent hysterectomy at our institution because of life-threatening PPH. The 5 patients presented in our case series are included in this number. An additional 6 parturients underwent hysterectomy during the time period when rFVIIa was available but did not receive this medication because at that time we did not have guidelines for the use of rFVIIa. In 2003, we started to use rFVIIa in life-threatening PPH. With growing experience we started to use it to avoid hysterectomy. We believe that the patient series of 29 women undergoing a hysterectomy is biased that would be of no benefit in drawing any conclusions about the efficacy of rFVIIa.

We agree that rFVIIa is an expensive drug. At our institution, the cost of a mean single dose of rFVIIa is similar to that of an ICU treatment for 2 days. Only 3 of our 12 patients required ICU treatment, each for 1–2 days. Apart from one patient who was hospitalized for 5 weeks owing to an intra-abdominal infection, all other patients were discharged home in <14 days (mean 7 days).1 We therefore believe that in major uncontrolled bleeding, the use of rFVIIa may turn out to be cost-effective in avoiding massive transfusions of blood products and complications requiring ICU treatment.

We nowadays use a dose of 90–120 μg kg$^{-1}$ of rFVIIa.3 The effective dose of rFVIIa in the treatment of major PPH may depend on its mechanism of action, which remains to be established. We agree that surgery and/or medical management with effective transfusion therapy and uterotonic drugs is the cornerstone of the treatment of major PPH. However, the choice between additional interventions such as selective arterial embolization or the use of rFVIIa is not straightforward, and we strongly believe that all these manoeuvres should be available.

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