CASE REPORT

Factor VIIa as an adjunct to standard haemorrhage control after blunt pelvic trauma

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Accepted 27 February 2005

Introduction

Recombinant activated factor VII (rFVIIa) was originally designed for the treatment of bleeding episodes in haemophilia patients who had inhibitors. It has since been used for other coagulopathic states such as thrombocytopenia and Von Willebrand’s disease, and in liver transplantation. More recently it has been used for severe bleeding in non coagulopathic patients.

Factor VIIa is thought to act only at the site of bleeding and not induce a systemic activation of coagulation although there has been recent evidence to the contrary. It has previously been argued that FVIIa should not be used in patients with sepsis, disseminated intravascular coagulation or extensive tissue damage due to the potential for excessive clot formation. There are however, case reports of FVIIa successfully treating life-threatening bleeding after trauma. Kenet reported a case of FVIIa controlling massive bleeding from a high velocity gunshot wound.

We report, what we believe was, at the time, the first case of FVIIa being used in the UK to, pre-emptively, enhance standard haemorrhage control after a pelvic fracture.

Case report

A 30-year-old man was brought by ambulance to the emergency department 34 min after a crush injury between a crane and a wall at a dockyard. On arrival, he was talking and alert with initial observations of heart rate 100 bpm, BP 130/70, respiratory rate 30 and oxygen saturations of 99%. A primary survey revealed tenderness over the pelvis and blood present at the external urethral meatus. On rectal examination there was a large laceration of the anterior rectal wall with fragments of bone palpable. A pelvis X-ray showed comminuted displaced bilateral superior and inferior pubic rami fractures and sacroiliac joint disruption on the left side.

The patient subsequently developed cardiovascular compromise, dropping his blood pressure to 100/50 (heart rate 110). In the first 3 h in hospital he received 4 l of crystalloid, 3 units of colloid and 6 units of packed cells. At 3 h the patient was taken...
to theatre for external fixation of his pelvis and a
defunctioning colostomy; on induction of anaesthesia he was given a single dose of activated recombinant factor VIIa, 7.2 mg (90 μg/kg). Bleeding in the pelvis was reported by the surgeons as significant at the beginning of the operation but had ceased by the end, three hours later. Haemoglobin fell from a pre-operative level of 11.9–7.9 l h into surgery. During the operation he was given 2.5 l of colloid and 3 units of packed cells. Other haematology parameters preoperatively showed an INR of 1.0, APTT 27, fibrinogen 2.63 and platelet count 257. Post-operatively his results were INR 1.2, APTT 43, fibrinogen 0.93 and platelets 60. During the 24 h period post operatively he received 5 units of cryoprecipitate, 1 unit of platelets and 3 units of packed cells. His clotting parameters returned to normal 3 days after the operation.

His complications in the post operative period were a bleeding duodenal ulcer requiring urgent endoscopic injection at day 25, localised pelvic infection which developed into osteomyelitis with a fistula still discharging at 18 months and temporary neuropathic leg pain. There were no clinical thrombotic events in the 18 months after the injury.

Discussion

Recombinant activated factor VII enhances haemostasis at the site of injury by becoming biologically active only after binding to local tissue factor (TF) exposed by injury. Haemostasis is then initiated by the tissue factor (TF)-FVIIa complex through activation of factors X and IX and finally activating prothrombin to thrombin.

The presence of tissue factor on atherosclerotic plaques, monocytes and some tumour cells implies a risk of thromboembolic complications such as myocardial infarction or stroke with the use of rFVIIa in some patients. There is, likewise, a theoretical risk in patients with blunt trauma with significant tissue injury resulting in massive tissue factor exposure. Martinowitz et al.7 reported a series of patients with massive haemorrhage, penetrating and blunt, given rFVIIa after which the bleeding stopped and their clotting parameters returned to normal. There were no clinical thromboembolic complications found in these patients.

Pelvic fractures of the AP compression type II or III are associated with severe haemorrhage in 28 and 53% cases8 with mortality rates up to 25%. Current treatment options include external fixation and/or embolization via angiography.

In our patient’s case it is quite possible that his bleeding would have stopped anyway after application of the external fixator. However, these injuries have a high mortality and the greater the blood loss that occurs (with concomitant replacement using blood products) the greater the potential for developing disseminated intravascular coagulopathy (DIC) or systemic inflammatory response syndrome (SIRS). An important role for rFVIIa might be as an adjunct, early after injury, to attenuate or prevent the cycle of haemorrhage leading to hypothermia, acidosis and coagulopathy which can lead to further haemorrhage, DIC, SIRS, multi-organ failure and death.

The optimum dose required is unknown. The short half life of 3 h suggests that multiple doses may be needed. Our patient received only one dose with apparent good effect. Recombinant FVIIa is being trialled on a named patient basis in a number of trauma centres around the world. A multi-centre, randomized controlled trial of rFVIIa in the treatment of bleeding in severely injured patients should be undertaken.

Contributors

DM performed a literature search and wrote the paper. BE helped with writing the paper. DH initiated the idea, reviewed the manuscript and acts as guarantor of the paper.

Reference