Chinese Journal of Traumatology 19 (2016) 54-55

Contents lists available at ScienceDirect

# Chinese Journal of Traumatology





# Uncontrolled haemorrhage in pelvic fractures—Can the inevitable be avoided?

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#### ARTICLE INFO

Article history: Received 6 January 2015 Received in revised form 6 May 2015 Accepted 21 August 2015 Available online 31 December 2015

*Keywords:* rFVIIa Uncontrolled haemorrhage Pelvic fracture

#### ABSTRACT

Pelvic fractures carry a considerable risk for morbidity and mortality. Half or more of the early deaths in these patients have been attributed directly to haemorrhage. The transfusional requirements are four times higher for open pelvic fractures compared with a similar group of closed pelvic fractures. The loss of the tamponade effect by disruption of the pelvic soft tissues and the energy imparted play a central role in this potentially life threatening situation. We reported a case of open pelvic fracture in which persistent haemorrhage was stopped by giving recombinant activated coagulation factor VIIa as our last resort.

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### Introduction

Uncontrolled haemorrhage is the major cause of death in trauma patient accounting for 40% of mortality.<sup>1</sup> This results in a state of acute coagulopathy that markedly increases the risk of morbidity and mortality.

In orthopaedic practice majority of mortality due to uncontrolled haemorrhage is because of pelvic fractures. Options available to control haemorrhage in pelvic fractures include external fixation, angiography and embolization etc. But when all these measures fail or are unavailable, there is no option but to frustratingly watch the precious life slipping away.

But now an option is available i.e. rFVIIa. It is recombinant activated coagulation factor VII. It stops bleeding fast by a site specific mechanism of action by acting on factor X. In large pharmacologic doses, rFVIIa can bypass several steps in the clotting cascade, interacting directly with the activated platelet to produce a thrombin burst and ultimately fibrin. By using it locally, haemostasis is achieved quickly, without any side effect which in turn decreases the need for transfusion and its complications.

Recently, there has been an increasing interest in the use of rFVIIa to treat bleeds in non-haemophiliac patients. Several case reports have suggested that this agent may be effective in treating non-haemophiliac patients with traumatic and other types of

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bleeds. Although its use is relatively new to trauma care, several authors have reported on the use of rFVIIa.  $^{2-6}$ 

### **Case report**

A 23-year-old male patient with the history of road traffic accident presented to our emergency ward in a state of shock. On examination patient was conscious with pulse rate of 120 beats per minute, blood pressure of 90/40 mmHg. Degloving injury on right side thigh and pelvis was noted on further examination. No pelvic compression test was done. Crepitus was noted on shifting of patient to operation theater (OT) for external fixator application. Abdomen was soft, non-tender with mild distension. Patient was resuscitated with central venous line, intravenous crystalloid and colloids. Radiographs were taken in the OT.

Patient was diagnosed as a case of open type C1 pelvic injury with extra peritoneal rupture of bladder and urethra on the OT table.

Anterior pelvic fixator was applied followed by suprapubic cystostomy, drain in retropubic space, debridement, and packing of cavity in OT under anaesthesia (Fig. 1a and b). These events took one hour and forty minutes from the time patient was received in emergency.

Patient was shifted to intensive care unit but continued to bleed in drains with no improvement in vitals even after twelve units of whole blood with four units of fresh frozen plasma and four units of platelets transfusion (another ten hours passed). After twelve hours of resuscitation with all the possible methods available with us at that time bleeding was not controlled. Then it was decided to try



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Peer review under responsibility of Daping Hospital and the Research Institute of Surgery of the Third Military Medical University.

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Fig. 1. A: Open pelvic injury; B: X-Ray showing pelvic fracture with external fixator.

rFVIIa based on some background knowledge of the treating orthopaedic surgeon for its use in wars to control massive haemorrhages.

Injection rFVIIa was administered at the dose of 100 mcg/kg i.e. 4.8 mg. Within one hour of administration blood pressure stabilised to 100/70 mmHg and bleeding reduced dramatically.

Patient had received a total of twelve units of blood before using rFVIIa within twelve hours and four units after the injection in three days.

#### Discussion

Traditionally recombinant factor VIIa has been used for haemophilia. Its use for treatment of trauma induced coagulopathy is relatively new with the first case reported in 1999 followed by anecdotal use reported by several authors.

Although the mechanism of action for levels of rFVIIa used in trauma is not fully elucidated at pharmacological level, it jumpstarts the defective coagulation process by bypassing several steps in clotting cascade, interacting directly with activated platelets to produce a thrombin burst and ultimately fibrin.

But there is a caveat to its use as it is a potent agent and theoretically predisposes a susceptible patient to thromboembolic complications such as stroke, myocardial infarction and deep vein thrombosis. That is the reason it is approved by Food and Drug Administration only for the treatment of haemophilia with all trauma uses being off label. Nevertheless there are several studies pertaining to use of rFVIIa for trauma although anecdotal and retrospective.

Martinowitz et al<sup>7</sup> noted that its use caused cessation of bleeding and decreased need for transfusions. They reported on the use of rFVIIa in 19 trauma patients, including patients from previous reports. Using one to three doses of rFVIIa, cessation of hemorrhage was documented in 79% of patients, transfusion requirements decreased and 13/19 (68%) patients survived. Review of animal studies confirmed the safety of drug in animal trials and suggested that rFVIIa is not associated with increased thromboembolic complications.

In 2004 Dutton et al.<sup>6</sup> reported reversal of coagulopathy. Coagulopathy was reversed in 61 out of 81 cases (75%), with 42% of patients surviving. In their series the indications for use of rFVIIa included acute post-traumatic haemorrhage, severe traumatic brain injury, septic coagulopathy, and factor deficiencies. In 2005 Boffard et al.<sup>8</sup> published the result of a two armed randomized placebo control, double blinded study to examine the effect of rFVIIA in trauma patients. The trial demonstrated that there was a statistically significant reduction in the need for transfusional requirement in blunt trauma group, whereas the penetrating trauma group showed no benefit. In addition the trial demonstrated the safety of rFVIIa.

In 2010 Hauser et al.<sup>9</sup> published the results of a large phase III randomised clinical trial called control trial evaluating safety and efficacy of rFVIIa. They concluded that rFVIIa reduced the use of blood products but did not affect mortality. Further they opined that the use of drug was safe to use.

In conclusion, adjunctive procoagulant agent such as rFVIIa should be used in any salvageable patient with massive uncontrolled bleeding who has not responded to conventional surgical measures and appropriate blood components in a case of severe pelvic trauma.

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