The efficacy of recombinant activated factor VII in severe trauma

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CRD summary
The review found that there was no evidence that use of recombinant activated factor VII had a significant effect on mortality rates among patients with severe trauma and that more research was required. Although the review was limited by failure to provide relevant details of review processes, the authors' cautious conclusions appear well founded.

Authors' objectives
To evaluate the efficacy and safety of recombinant activated factor VII (rFVIIa) for treating adults with severe trauma.

Searching
MEDLINE, EMBASE, The Cochrane Library, Emergency Medical Abstracts, BestBETS and ClinicalTrials.gov were searched from inception to September 2008. Search terms were reported. Reference lists of relevant studies and systematic reviews were checked and the manufacturers of rFVIIa were consulted. It was unclear whether the search was limited by publication or language status.

Study selection
Randomised placebo-controlled trials (RCTs) of therapeutic use of any dose of rFVIIa (in addition to standard care) to treat severe trauma in non-haemophiliac adults in an out-of-hospital or emergency department setting were eligible for inclusion. Studies were required to report mortality (primary review outcome), neurological status, delayed surgical intervention and/or adverse effects (secondary outcomes). Severe trauma was defined as multisystem trauma not amenable to urgent surgery and that needed large volumes of fluid resuscitation or blood products. Studies of prophylaxis, non-trauma patients, isolated head trauma or in non-emergency department settings were excluded.

Participants in the included study had a mean age of 34 years. They had experienced blunt or penetrating trauma within 12 hours of trauma centre admission and required at least six units of packed red cells within four hours of admission. The intervention consisted of three intravenous injections of rFVIIa (initially 200µg/kg then 100µg/kg). Controls received three intravenous injections of placebo. Reported outcomes relevant to the review were 48-hour and 30-day mortality and thromboembolism. None of the secondary review outcomes were reported in the primary studies.

The authors did not state how the papers were selected for the review.

Assessment of study quality
Assessment was based on published criteria (Guyatt 1993, 1994). Components of study quality assessed were: randomisation method; allocation concealment; comparability of baseline characteristics; blinding; follow-up; cointervention; and use of intention-to-treat analysis (ITT).

The authors did not state how the assessment was performed.

Data extraction
Risk ratios (RRs) and 95% confidence intervals (CIs) were extracted or calculated from the number of events in the two study groups. Outcomes were stratified by type of injury (blunt or penetrating).

The authors did not state how many reviewers performed data extraction.

Methods of synthesis
Not applicable.

Results of the review
One double-blinded RCT was eligible for inclusion (n=277). The study groups were well balanced. Losses to follow-up were minimal. Participants and care providers were blinded. Analysis was by intention-to-treat. However, methods of randomisation, enrolment and allocation concealment were inadequately described and/or maintained and there was some potential for confounding.

There was no statistically significant difference between the two groups in risk of mortality or thromboembolism. Relative risks for mortality were close to unity, with wide confidence intervals. Stratification by type of injury did not materially affect the results.

The review also reported additional outcomes measured by the primary study.

**Authors’ conclusions**

There was no evidence that use of rFVIIa had a significant effect on mortality rates among patients with severe trauma.

**CRD commentary**

Objectives and inclusion criteria of the review were clear. Relevant sources were searched for published and unpublished studies without language restriction. It was unclear whether steps were taken to minimise risks of reviewer bias and error in study processes, such as having more than one reviewer independently undertake study selection, validity assessment and data extraction. Relevant details about characteristics and findings of the included study were reported. An additional potentially relevant study (n=576) mentioned in the text appeared to support the review findings. This study was terminated by the manufacturers of rFVIIa when futility analysis predicted a low likelihood of reaching a successful outcome on the primary efficacy endpoint and it was excluded from the review. Although the review was limited by failure to provide relevant details of review processes, the authors’ cautious conclusions and call for more research appear well founded.

**Implications of the review for practice and research**

**Practice:** The authors stated that there was insufficient evidence to support the use of rFVIIa for severe trauma.

**Research:** The authors stated that further studies were required to evaluate efficacy and safety of rFVIIa for patients with severe trauma.

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