Recombinant factor VIIa for the prevention and treatment of bleeding in patients without haemophilia

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BACKGROUND: Recombinant factor VIIa (rFVIIa) is licensed for use in patients with haemophilia and inhibitory allo-antibodies. It is also increasingly being used for off-license indications to prevent bleeding in operations where blood loss is likely to be high, and/or to stop bleeding that is proving difficult to control by other means. OBJECTIVES: To assess the effectiveness of rFVIIa when used therapeutically to control active bleeding, or prophylactically to prevent (excessive) bleeding in patients without haemophilia. SEARCH STRATEGY: We searched the Cochrane Injuries Group's Specialised Register, CENTRAL, MEDLINE, EMBASE and other specialised databases up to March 2006. We also searched reference lists of articles and contacted experts in the field. SELECTION CRITERIA: Randomised controlled trials (RCTs) comparing rFVIIa with placebo, or one dose of rFVIIa with another, in any patient population with the exception of those with haemophilia. There was no restriction by outcomes examined, but this review focuses on mortality, blood loss or control of bleeding, red cell transfusion requirements, number of patients transfused and thromboembolic adverse events. DATA COLLECTION AND ANALYSIS: Two authors independently assessed potentially relevant studies for inclusion. Data were extracted and methodological quality was examined. Studies using rFVIIa prophylactically and those using rFVIIa therapeutically have been considered separately. Data were pooled using fixed and random effects models, but random effects models were preferred because of the variability in clinical features of the included studies. MAIN RESULTS: Thirteen trials met the inclusion criteria; all were placebo-controlled double-blind RCTs.Six trials involving 724 participants examined the prophylactic use of rFVIIa; 379 received rFVIIa. There were no outcomes by which any observed advantage, or disadvantage, of rFVIIa over placebo could not have been observed by chance alone. There were trends in favour of rFVIIa for a number of outcomes, particularly the number of participants transfused, pooled RR 0.85 (95% CI 0.72 to 1.01) but this was balanced by a trend against rFVIIa with respect to thromboembolic adverse events, pooled RR 1.25 (95% CI 0.76 to 2.07).Seven trials involving 1214 participants examined the therapeutic use of rFVIIa; 687 received rFVIIa. There were no outcomes where any observed advantage, or disadvantage, of rFVIIa over placebo could not have been observed by chance alone. There was a trend in favour of rFVIIa for reducing mortality, RR 0.82 (95% CI 0.64 to 1.04), although no other clear trends in favour of rFVIIa were noted for other desired outcomes. Interpretation of these results must take into account one study which could not be included in the quantitative summary but which showed results strongly in favour of rFVIIa for the treatment of intra-cerebral haemorrhage. There was a trend against rFVIIa with respect to thromboembolic adverse events; the RR 1.50 (95% CI 0.86 to 2.62). AUTHORS' CONCLUSIONS: Although rFVIIa has a role in the management of patients with haemophilia, its effectiveness as a more general haemostatic drug, either prophylactically or therapeutically, remains uncertain. Its effectiveness as a therapeutic agent, particularly for intra-cerebral haemorrhage, looks more encouraging than prophylactic use. The use of rFVIIa outside its current licensed indications should be very limited and its wider use await the results of ongoing and possibly newly commissioned RCTs. In the interim, rFVIIa use should be restricted to clinical trials.
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