Recombinant Factor VIIa Use in Amniotic Fluid Embolism: A Systematic Review

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Introduction: Patients with amniotic fluid embolism (AFE) (major cardiac and pulmonary symptoms plus consumptive coagulopathy (DIC)) have high circulating levels of tissue factor. Recombinant factor VIIa (rVIIa) has been used, and recommended, to treat DIC-induced hemorrhage in AFE. We hypothesized that rVIIa can combine with circulating tissue factor, leading to thrombotic complications and worse outcomes in patients receiving rVIIa. We systematically reviewed case reports from 2003 to 2009 of patients with massive hemorrhage due to AFE who were and were not treated with rVIIa.

Methods: We searched MEDLINE for case reports of rVIIa use in AFE patients (rVIIa cases). We then re-searched MEDLINE for AFE patients in which surgery was used to control bleeding and there was no use of rVIIa (controls). Additional rVIIa cases were obtained from the FDA and the Australian and New Zealand Haemostasis Register. SOAP abstracts provided more rVIIa cases and controls. Demographic and clinical details were scrutinized to avoid duplicate reporting.

We considered the AFE diagnosis confirmed if patients had at least one cardiac (hypotension or cardiac arrest) and one pulmonary (dyspnea, hypoxemia, or respiratory arrest) symptom in addition to DIC. Patients not meeting this definition were not included.

Chi square (3x2) tested the difference in the incidence of the 3 possible outcomes (full recovery, survival with permanent deficits, and death) between rVIIa cases and controls. We considered p<0.05 statistically significant.

Results: We identified 15 rVIIa cases and 27 controls. Surgery to control bleeding was performed in all 15 rVIIa cases: hysterectomy (n=7), hysterectomy plus additional surgery (n=3), exploratory laparotomy (n=4), and intrauterine balloon catheter insertion (n=1). The surgical operations in the 27 controls were hysterectomy (n=11), hysterectomy plus subsequent exploratory laparotomy (n=2), uterine artery embolization or ligation (n=5), exploratory laparotomy (n=5), B-Lynch suture (n=1) and dilation and curettage (n=3).

Full recovery occurred in 2 of 15 rVIIa cases and 17 of 27 controls (13% vs. 63%). Permanent disability was present in 5 rVIIa cases (coma, stroke x 2, pulmonary hypertension, new systemic hypertension) and 4 controls (left-sided motor weakness, short term memory loss x 2, panhypopituitarism). Death occurred in 8 of 15 rVIIa cases and 6 of 27 controls (53% vs. 22%). The outcome difference between rVIIa cases and controls was statistically significant.(p<0.01)

Discussion: AFE patients with DIC who received rVIIa had significantly worse outcomes than comparable patients who did not receive rVIIa. Death and complications that could have been caused by major organ thrombosis were common in patients receiving rVIIa.

References