Utilisation of Crotalidae polyvalent immune fab (ovine) for Viperidae envenomations in children

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CRD summary
The review concluded that Crotalidae polyvalent immune fab (Ovine) was a safe and effective treatment for Viperidae envenomations in children, but the dose required was unclear. The limited evidence of uncertain quality from low numbers of patients and limitations in the review process implied that the authors’ conclusions should be treated with caution.

Authors’ objectives
To evaluate the safety and effectiveness of Crotalidae polyvalent immune fab (ovine) for Viperidae envenomations in children.

Searching
MEDLINE (from 1950 to February 2008), EMBASE (from 1988 to February 2008), International Pharmaceutical Abstracts (from 1970 to February 2008) and The Cochrane Library (from 1996 to June 2008) were searched for publications in English. Search terms were reported. The search was repeated later in Google Scholar. Abstracts of National American Congress of Clinical Toxicology were reviewed from 2002 to 2007.

Study selection
All types of study design that evaluated the safety and effectiveness of Crotalidae polyvalent immune fab (ovine; FabAV; a polyvalent antivenom derived from sheep for Crotalid envenomations) for Viperidae envenomations (snakebites) in children and adolescents aged 18 years or younger were eligible for inclusion. Eligible studies had to evaluate initial and maintenance dosing regimes and adverse events (acute and late reactions). Most of the patients had rattlesnake bites (one patient injected himself with intravenous rattlesnake venom in a suicide attempt); two patients had copperhead bites. Ages ranged from 1.2 to 17 years. Most patients (70.2%) had evidence of coagulopathy at initial treatment, but it appeared that only the most severely affected patients received blood products. The dosage range of FabAV for initial control was 2g to 18g and the maintenance doses used were mostly those recommended by the manufacturer: three doses of 2g every six hours. Patients were not routinely given prophylactic doses of antihistamines before FabAV treatment. The only included randomised controlled trial (RCT) compared the recommended FabAV dose with as-needed FabAV dosing.

One reviewer performed the initial screen for relevant papers and three authors performed the final study selection.

Assessment of study quality
The authors reported that they assessed quality, but no details were provided and the number of reviewers who performed the quality assessment was not reported.

Data extraction
The number of events for each outcome was extracted and overall percentages calculated. The authors did not report how many reviewers performed the extraction. Authors were contacted for missing information related to study questions.

Methods of synthesis
A narrative synthesis was performed since the authors expected variation in dosing, demographic factors and study design.

Results of the review
Ten relevant studies were identified (n=47, range one to 24): one RCT (n=4), six case reports and three descriptive reports. The RCT included older patients.
Efficacy and dosing (10 studies): Most patients achieved initial control (63.8% after only one dose). Most (63.8%) patients received additional maintenance doses as recommended by the manufacturer of FabAV; 19.1% patients received at least one additional maintenance dose and 17.0% patients did not receive any maintenance doses and were presumed to have more minor snakebites.

Recurrence of adverse events (nine studies): There were two incidences of recurrence of adverse effects (in 23 patients) following initial control; both patients were given FabAV maintenance doses. Late coagulopathy was reported in four of 23 patients following initial normal values. One retrospective study reported that five of 12 patients had episodes of thrombocytopenia (platelet count <150,000/mm³) during their hospital stay that did not respond to FabAV treatment.

Safety (10 studies): Three patients (6.4%) developed an acute infusion reaction. Symptoms noted included urticaria, cough, facial/periorbital oedema, voice change and tachycardia. The overall incidence of both acute and late adverse reactions was 8.5%.

Authors' conclusions
FabAV appeared to be a safe and effective agent for children as young as two years old with Crotalid envenomations.

CRD commentary
The review addressed a well-defined question in terms of participants, interventions, study design and relevant outcomes. Relevant databases were searched and unpublished studies were considered, but only studies published in English were included and so some relevant studies may have been missed. Publication bias was not assessed. It was unclear whether an assessment of study quality was made; no relevant details were provided. Little effort to avoid error and bias in the review process was reported. Some relevant study details were reported, but there was little detail of study design. Most studies were of less reliable study designs (case studies and retrospective data) and there was only one small RCT. A narrative synthesis was provided by the authors due to the variation in dosage regime used. The true percentages for incidence of recurrence of adverse events was unclear; the text implied that results were not available for all studies yet the final percentages were calculated for all patients. The authors noted that different types of snakebite may require different FabAV dosages.

In view of potential limitations in the review process, uncertainties about the quality of included studies and the low number of participants in the included studies, the authors’ conclusions should be treated with caution.

Implications of the review for practice and research
Practice: The authors suggested that clinicians use the dosage recommended by the manufacturers and adapt dosing recommendations used for adults until relevant evidence was available. They warned about underdosing. Clinicians should not exceed the recommended infusion rate for FabAV and should reduce the rate if adverse events were noted. There were additional concerns about the volumes required in infusing very young children. The authors noted that different types of snakebite may require different FabAV dosages.

Research: The authors identified a need for well-designed trials to confirm the efficacy and safety of FabAV as a treatment for children with snakebite and identify dosing recommendations for children.

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