

IS LOW DOSE ANTI-SNAKE VENOM AS EFFECTIVE AS HIGH DOSE ANTI-SNAKE VENOM FOR SNAKE ENVENOMATION IN INDIAN SUB-CONTINENT? A SYSTEMATIC REVIEW

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Objectives: To provide evidence from existing randomised controlled trials (RCT) to answer whether low dose anti-snake venom (ASV) is as effective as high dose ASV for snake envenomation in the Indian sub-continent.

Methodology: In March 2012, we searched PubMed, CENTRAL (Cochrane Central Register of Controlled Trials, in The *Cochrane Library*, Issue 1) and the South Asian Database of Controlled Clinical Trials for RCTs done on people who were victims of snake bites, given low dose ASV (defined by the individual study) compared to ASV at high dose (defined by the individual study). Outcomes sought were mortality, time to normalisation (neurological and haematological parameters), ventilator support, renal failure, and duration of hospital stay. We extracted data, assessed risk of bias, synthesised data and assessed overall quality of evidence using the GRADE approach.

Results: We identified eight studies of which four were excluded as they were not RCTs. The four included RCTs recruited 266 patients with haemotoxic snake envenomation. Mortality did not differ between high or low doses of ASV (RR 0.78, 95% CI 0.38, 1.63; four trials; *low quality* evidence), nor did the incidence of acute renal failure (RR 1.04, 95% CI 0.65, 1.66, two trials). We were unable to pool data for other outcomes. There was considerable variability in the study designs and dosage schedules in the included studies. The incidence of allergic reactions and anaphylaxis with ASV was not adequately reported.

Conclusion: Current evidence does not suggest that high or low dose ASV differed significantly in reducing mortality or acute renal failure after haemotoxic snake envenomation. The included trials had serious study limitations, and variability in definitions used for high and low doses of ASV. The low overall quality of the evidence leaves considerable uncertainty about the effect estimates. Adequately powered, well conducted RCTs that use flexible doses depending on clinical and laboratory parameters, specific envenomation syndromes, and snake species from the region; and that minimise inter-batch variations in ASV potency, are urgently needed.