Presented at North American Congress of Clinical Toxicology (NACCT) 2025 – Chicago, IL

Published in Clin Toxicol (Phila) 2025;63:56-57.

103. Late hemotoxicity after Fab and Fab2 administration for acute rattlesnake envenomation reported to the North American Snakebite Registry

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Background: Rattlesnake envenomation treated with Crotalidae polyvalent immune Fab (ovine) (Fab), is associated with an approximate 35% incidence of late hemotoxicity. The introduction of crotalidae immune F(ab')2 (equine) (Fab2) reduced this complication of late hemotoxicity to approximately 5%. Data on the protective effect of Fab2 when both antivenoms are initially administered, however, is limited.

Methods: This is an analysis of cases reported to the North American Snakebite Registry (NASBR) from 2019 to 2023. Inclusion criteria were rattlesnake envenomation, administration of both Fab2 and Fab, and at least one follow-up laboratory value. Cases were excluded if the alternate antivenom was only administered on follow-up. Hemotoxicity was defined as platelets <150 k/mm3 or fibrinogen <150 mg/dL. Collected data included case demographics, laboratory values, and antivenom administration, readmission, retreatment, and bleeding details.Summary statistics included medians and interquartile ranges (IQR) and relative frequencies (percentages). Statistical tests were computed to determine differences in factors associated with late hemotoxicity including Wilcoxon Rank Sum Tests for continuous variables and Fisher's Exact Tests with p-value simulations for categorical variables. All analyses were conducted in R 4.3.3.

Results: Sixty-five cases met inclusion criteria. Median age was 44 years (IQR 26–64), 72.3% (n= 47) were male. When reported (n=23), the most common reason for dual antivenom use was transfer from an outside hospital with alternate antivenom (n=22, 95.6%). Median time to antivenom was 2.5 hours (IQR 2.0–3.5). Median total vials of Fab and Fab2 were 6 (IQR 6–6) and 10 (IQR 8–20), respectively. Median total doses of Fab and Fab2 were 1 (IQR 1–1) and 2 (IQR 1–3), respectively. Most cases (93.8%, n=61) received Fab as the first antivenom administered. Initial hemotoxicity occurred in 55.4% (n=36) of cases: 77.8% (n=28) thrombocytopenia, 50% (n=18) hypofibrinogenemia, and 27.8% (n =10) thrombocytopenia and hypofibrinogenemia. Late hemotoxicity occurred in 20.0% (n=13) of cases, 84.7% (n=12) of which received Fab first. All 13 cases (100%) of late hemotoxicity were isolated thrombocytopenia (median nadir 116 k/mm3, IQR 97–133). 84.6% (n = 11) were recurrent and 15.4% (n =2) were delayed hemotoxicity. None was retreated with antivenom or readmitted for hemotoxicity. One had a late bleeding event characterized as scant epistaxis with nose blowing on day 5 post antivenom. There was no difference in type of antivenom administered first, time from bite to any antivenom, time from bite to Fab2, or total vials of Fab2 or Fab between cases with and without late hemotoxicity.

Conclusion: In the NASBR population, administration of both Fab and Fab2 for acute rattlesnake envenomation resulted in a 20% incidence of late hemotoxicity, all of which were thrombocytopenia, and most were recurrent (85%). The mechanism for the apparent loss of Fab2's protective effect on late hemotoxicity when administered with Fab, such as order, timing, and total dose of antivenom, was not detected in this analysis. Implications for repeated laboratory follow-up in patients receiving both Fab and Fab2 after rattlesnake envenomation should be considered, similar to cases in which only Fab is administered.