Clinical Practice Statement

How Should Native Crotalid Envenomation Be Managed in the Emergency Department?

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- Dr. Greene has disclosed a conflict of interest-served as a speaker for BTG/Boston Scientific.
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Recommendations:

1.Address airway, breathing, circulation, then assess for local, hematologic, and/or systemic toxicity indicative of envenomation.

2. Assess and determine the antivenom dosage needed.

3. Prophylactic antibiotics and surgical intervention are unnecessary and should be avoided.

Executive Summary

1. How should patients with potential snake envenomation be assessed?

After life-threatening airway, breathing, or circulatory conditions are identified and corrected, snakebite victims should be assessed for local, hematologic, and systemic toxicity. Clinicians should examine the affected extremity for swelling, tenderness, and hemorrhagic blebs every 15 – 30 minutes for a minimum of eight hours and until progression has halted [1].

All patients with possible snakebite envenomation should have the following laboratory tests performed:

- Complete blood count (CBC), Basic metabolic profile (BMP)
- Prothrombin time (PT), Fibrinogen, Creatine kinase (CK)

Serial dynamometry and negative inspiratory force (NIF) assessments may be used to identify muscular weakness following envenomations from snakes with neurotoxic venom components. Capnography can also be used to diagnose respiratory insufficiency.

2. What are the initial steps in snakebite management?

Life-threatening conditions must be immediately stabilized. Ensure airway patency and adequate oxygenation and ventilation. Intravenous crystalloids are recommended to maintain euvolemia.

Analgesia is an essential component to snakebite management. Intravenous opioids are preferred initially. NSAIDs are discouraged because of the potential inhibition of platelet function. The use of topical ice packs is discouraged because prolonged cryotherapy is harmful to tissue [2].

The crotalid-envenomated limb should be elevated once the patient has arrived at the hospital. This prevents the venom from accumulating in the extremity and reduces the hydrostatic pressures that can exacerbate tissue swelling.

3. What are the indications for antivenom?

Administer antivenom for any of the following:

- significant or progressive local tissue damage e.g., tenderness, swelling, hemorrhagic bleb.
- systemic toxicity, e.g., hypotension, airway swelling, neurological toxicity.
- Significant or progressive hematologic toxicity. Abnormalities that are particularly worrisome include fibrinogen < 50 mg/dL or platelets < 50K/μL.

If the swelling and tenderness are more than minimal and have extended beyond a major joint (e.g., wrist, ankle), antivenom is warranted [1]. If there is significant local tissue injury, e.g., necrosis, antivenom is also indicated, even if the swelling has not progressed across a joint. Minimal hematologic laboratory abnormalities, e.g., isolated fibrinogen levels between 100 – 150 mg/dL in an otherwise well-appearing patient, warrant serial testing but not treatment with antivenom. Antivenom is most effective when given early [3].

4. How should antivenom be dosed?

There are currently two antivenoms with FDA approval to treat native crotalid envenomations in adult and pediatric patients. Crotalidae Polyvalent Immune Fab Ovine (CroFab®, FabAV) is ovine (sheep)-derived and prepared using the venoms from four snakes found in the U.S.:

- Western diamondback rattlesnake (*Crotalus atrox*)
- Eastern diamondback rattlesnake (*C. adamanteus*)
- Mojave rattlesnake (*C. scutulatus*)
- Cottonmouth (*Agkistrodon piscivorus*)

Initial dosing of CroFab®) is 4 – 12 vials [4]. If control is achieved within one – two hours, maintenance dosing consisting of two vials of every six hours for three doses is recommended starting six hours after the initial dose. There is evidence that maintenance dosing may not always be necessary when a snakebite expert can serially assess the patient at the bedside [5]. If no such expert is available, maintenance doses should be administered. If control is not initially achieved, another 4 – 6 vials should be administered. CroFab® should be used with caution in patients with allergy to latex, papaya, pineapple, papain, bromelain, and sheep.

Crotalidae Immune F(ab')2 Equine (Anavip®) is equine (horse)-derived and prepared using the venoms from two non-native snakes:

- Central American rattlesnake (*Crotalus simus*)
- Terciopelo (*Bothrops asper*)

The recommended starting dose of Anavip® is 10 vials [6]. An additional 10 vials should be given if initial control is not attained within one – two hours. Maintenance dosing is not recommended for Anavip®, and it should be used with caution in patients with allergy to horses, pepsin, and cresol.

The choice of which product to use should be based on patient allergies, prior adverse reaction to either product, availability, and familiarity/comfort with each product.

5. Should copperhead envenomations be managed differently from other crotalid envenomation?

Although the average copperhead envenomation tends to be less severe than a typical rattlesnake envenomation, any native crotalid envenomation can result in significant local and systemic toxicity. Furthermore, many snakes go unidentified or misidentified by patients or healthcare professionals.

Moderate and severe envenomations should be treated regardless of what crotalid was responsible. In a mild envenomation from a confirmed copperhead, the physician and patient should engage in shared decision-making regarding treatment with antivenom. It is important to acknowledge the expense and the low (1.4 – 2.7% for FabAV) risk of acute adverse reactions associated with antivenom therapy as well as the potential financial and health consequences of going untreated [7,8]. A randomized clinical trial demonstrated that copperhead envenomations recover more quickly when treated with CroFab® compared to placebo [9]. CroFab® also reduced total opioid requirements [10].

6. To what unit should snakebite patients be admitted?

Not all crotalid bites require hospitalization. Patients with "dry" bites, in which there are no venom effects, should be monitored for a minimum of eight hours, because what appears insignificant at first may progress to something more severe. If no signs or symptoms develop, the patient can be discharged. Patients with evidence of envenomation should be monitored for a minimum of 12 – 24 hours. The level of care should be determined by patient severity, likelihood of progression to severe envenomation, use of antivenom, and capabilities of the individual facility. Many patients can be safely monitored in an ED observation unit or a general medical floor. Admission to the ICU is recommended for patients with significant systemic toxicity. Early medical toxicology consultation is encouraged. Hospital length of stay is decreased by an average 21 hours when a toxicologist is involved in patient care, with no difference in readmission rates [11]. Poison control should be contacted for complex cases when medical toxicology is unavailable.

7. What is the role of antibiotics following crotalid envenomation?

Infection is uncommon following crotalid envenomation [12]. Prophylactic antibiotics have not proven to be beneficial, and indiscriminate use of antibiotics can cause side effects and contribute to antimicrobial resistance [12,13]. Therefore, antibiotics should not be administered unless there is clinical evidence of infection.

8. What are the indications for surgical consultation for snakebite in the ED?

Acute surgical intervention is rarely necessary following crotalid envenomation. Excising tissue around the bite site confers no benefit and will exacerbate local tissue damage [14]. Compartment syndrome is an exceptionally uncommon complication from crotalid envenomation, and prophylactic fasciotomies are not recommended. Even in a confirmed compartment syndrome, the initial treatment should be additional doses of antivenom, not fasciotomy. Fasciotomy should only be considered in those patients with persistently elevated compartment pressures despite adequate antivenom therapy [14,15].

9. Should pediatric patients be treated differently from adult patients?

Indications for treatment with antivenom are the same in the pediatric population and the adult population. A study by Levine et al. found that pediatric patients were less likely to exhibit edema than adult patients [16]. Adults developed tissue necrosis more often than children, but this difference resolved when rates were adjusted for the bite location. There was a trend for more systemic toxicity in adults, but it did not reach statistical significance. Pediatric patients were more likely to develop elevated PT and hypofibrinogenemia, but the rates of bleeding were similar.

In the randomized clinical trial of FabAV for copperhead bites by Gerardo et al., there was a trend for pediatric patients to recover faster from copperhead bites, irrespective of antivenom therapy, but this did not reach statistical significance [9].

Antivenom dosing should not be adjusted for age or weight, because the amount of venom injected is not dependent upon the size of the victim. Initial doses are the same as listed above. However, the antivenom should be reconstituted for smaller patients to avoid volume overload.