

PII S0736-4679(02)00573-5



# RESPIRATORY COMPROMISE IN PATIENTS WITH RATTLESNAKE ENVENOMATION

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□ Abstract—Respiratory compromise after rattlesnake envenomation (RSE) is an uncommon yet potentially lethal complication. We were interested in determining the frequency of respiratory compromise in patients treated for RSE. The incidence and indications for intubation were also determined. A retrospective chart review was conducted of all patients treated by medical toxicologists at a tertiary referral hospital between July, 1994 and November, 2000. Out of 294 total patients, 289 charts were reviewed. Of all 289 patients, 214 (74%) received Crotalidae Polyvalent Antivenin (Wyeth-Ayerst) and 23 (8%) had clinical evidence of respiratory compromise. Thirteen of 289 patients (4.4%) were intubated following RSE. No one was intubated for antivenin-induced complications. There were no deaths among studied patients during acute hospitalization. Respiratory compromise following RSE is rare, occurring in only 8% of studied patients. Only 2 patients (0.7%) required intubation as a direct consequence of RSE. No one required intubation for antivenin-induced hypersensitivity reactions. © 2002 Elsevier Science Inc.

□ Keywords—respiratory compromise; rattlesnake envenomation; intubation; antivenin

# **INTRODUCTION**

In 1999, there were almost 1000 rattlesnake envenomations (RSE) reported to the American Association of Poison Control Centers (1). Respiratory compromise is an uncommon yet potentially lethal complication following RSE and is rarely reported in the literature (2-9). Each year our Medical Toxicology service admits approximately 50 patients with RSE to a tertiary care hospital. We were interested in determining the frequency of respiratory compromise and need for endotracheal intubation in patients admitted for RSE

## **METHODS**

This was a retrospective chart review of all rattlesnake bite patients admitted by medical toxicologists to a tertiary referral hospital between July, 1994 and November, 2000. Subjects included those who received Crotalidae Polyvalent Antivenin (Wyeth-Ayerst Laboratories, Philadelphia, PA) and those who received no antivenin therapy. Patients receiving CroFab Antivenom (Protherics Inc., Nashville, TN) were excluded because of enrollment in an experimental protocol (pre-clinical CroFab trial). Respiratory compromise was defined as airway obstruction, bronchospasm, soft tissue edema, or subjective symptoms including throat tightening or nasal congestion. Charts were also reviewed to determine frequency and indications for intubation.

# RESULTS

Of the 294 charts reviewed, 289 patients were included in the study. Five patients were excluded (three received

RECEIVED: 14 January 2002; FINAL SUBMISSION RECEIVED: 14 June 2002; ACCEPTED: 26 June 2002

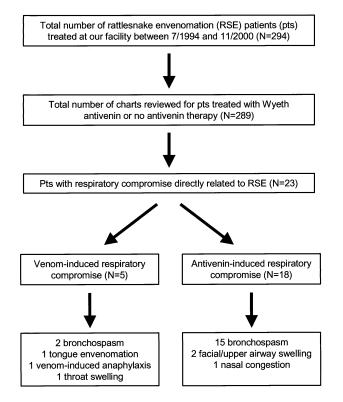


Figure 1. Flow chart of rattlesnake envenomation patients with identification and description of respiratory compromise.

CroFab and two charts could not be located). Of the 289 patients, 214 (74%) received Crotalidae Polyvalent Antivenin. The remainder received no antivenin.

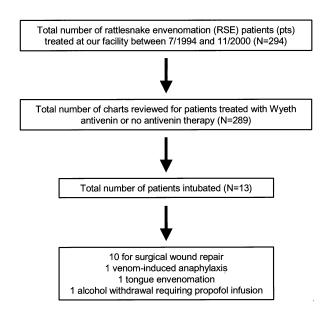


Figure 2. Flow chart of indications for intubation of patients treated for rattlesnake envenomation.



Figure 3. Rattlesnake envenomation of tongue resulting in airway compromise and nasotracheal intubation. © 2002 Department of Medical Toxicology, Good Samaritan Regional Medical Center.

Twenty-three of 289 patients (8%) exhibited clinical evidence of respiratory compromise. (Figure 1) Five of these 23 (1.7% of total) developed venom-induced respiratory compromise (3 developed throat tightening with or without urticaria and 2 developed bronchospasm). Eighteen of these 23 patients (6.2% of total patients, 8.4% of those receiving antivenin) developed antivenininduced respiratory compromise (15 experienced bronchospasm, 2 developed facial and upper airway swelling, and one developed nasal congestion).

Thirteen of 289 patients (4.4%) were intubated after RSE (Figure 2). Ten patients were intubated for surgical fasciotomy, dermotomy, or wound care, one for venominduced anaphylaxis, and one for severe alcohol withdrawal requiring airway protection. One patient was intubated for tongue envenomation with airway swelling (Figure 3) (7). No one was intubated for antivenininduced complications. There were no deaths among our patients during acute hospitalization following rattlesnake envenomation.

Interestingly, of all 289 patients, only 29 (10%) reported a previous history of rattlesnake bite (how many

#### Table 1. Indications, Contraindications and Dosing of Wyeth Crotalidae Polyvalent Antivenin, and Drugs to Treat Adverse Reactions

Indications for antivenin:

- Progressive swelling beyond a major joint (e.g., wrist for hand bites and ankle for foot bites)
- Severe or progressive coagulopathy, hypofibrinogenemia, or thrombocytopenia
- Neuromuscular toxicity

Shock

Contraindications to Wyeth Crotalidae Polyvalent Antivenin:\*

- Reactive airway disease or atopy
- Previous exposure or allergy to horse serum
- Use of beta-blocking agents
- History of coronary artery disease or other contraindication to epinephrine use
- Administration of Wyeth-Antivenin:
  - Patient placed on cardiopulmonary monitor, with precautionary epinephrine drip, H<sub>1</sub>- and H<sub>2</sub>-antihistamines and corticosteroids available at bedside
  - Initial dose: 20 vials of antivenin/500 cc NS (begin at  $\leq$  5 cc/h and titrate to 250–500 cc/h)†
  - Subsequent doses: Reassess laboratory studies and clinical examination to determine if further antivenin is needed (generally, 10–20 vials; average # of total vials given = 28.5 vials/rattlesnake bite patient)
  - Hold antivenin infusion if anaphylactoid or anaphylaxis reaction develops. Start Epinephrine drip at 2-4 mcg/min and administer H<sub>1</sub> and H<sub>2</sub>-antihistamines and corticosteroids. Consider consultation with a toxicologist before reinitiating antivenin infusion at a slow rate after signs and symptoms of allergic reaction have resolved. Continue epinephrine drip during entire antivenin infusion, after reinitiation, and do not infuse more than 8 vials/hr.

Dosing of Drugs to Treat Antivenin-induced Anaphyloid or Anaphylaxis Reactions (adult doses given):

- Epinephrine drip: 1 mg epinephrine/250 cc D<sub>5</sub>W, starting at 2 to 4 mcg/min
- Methylprednisolone (intravenous): 1-2 mg/kg
- Hydroxyzine (parenteral): 0.5–0.75 mg/kg
- Ranitidine (intravenous): 150-300 mg

Other Treatments:

- Intravenous fluid bolus
- Wound care and tetanus prophylaxis
- Limb elevation in full extension with noncompressing splint

\* If the patient has a life-threatening envenomation, antivenin treatment is considered

† A similar number of vials of antivenin is used in pediatric patients, but a smaller, age-appropriate volume of normal saline (NS) may be utilized.

Sources: Holstege CP, Miller MB, Wermuth M, et al. Crotalid snake envenomation. Crit Care Clin 1997;13:889–921, and Tanen DA, Ruha A-M, Graeme KA, et al. Epideminology and hospital course of rattlesnake envenomations cared for at a tertiary referral center in central Arizona. Acad Emerg Med 2001;8:177–182.

of these were dry bites is unknown). Of the 23 patients suffering from respiratory compromise, 3 (13%) reported a prior rattlesnake bite.

## DISCUSSION

This study directly evaluates respiratory compromise following rattlesnake envenomation, specifically identifying the incidence of respiratory compromise as well as the incidence and indications for intubation. Previous work reported immediate antivenin reactions in 36% of patients receiving Crotalidae Polyvalent Antivenin and operative procedures in 3.4% of patients following rattlesnake envenomation, however, that study did not specifically address respiratory compromise (2). There are several case reports of facial envenomations with subsequent airway compromise but they fail to discuss overall incidence (10-12).

Jurkovich et al. reviewed 8 years of records and identified 40 patients treated for Crotalidae envenomation, 23 of whom received Crotalidae Polyvalent Antivenin. They reported that 6 of these 23 (26.1%) patients developed acute anaphylaxis, 3 (13%) of whom displayed 'dyspnea.' No other information on respiratory compromise or intubation was reported (13).

A European article reported 7 of 42 (16.7%) patients experiencing 'potentially life-threatening anaphylactoid reactions' including dyspnea, angioedema, and hypotension following envenomation from foreign snakes in Switzerland (3).

In our study, 18 of 214 (8.4%) patients developed hypersensitivity reactions, manifested as respiratory compromise, while receiving Crotalidae Polyvalent Antivenin. None of these patients required intubation. We have a protocol for the administration of antivenin that requires a physician and pre-primed epinephrine drip at the bedside (see Table 1). The presence of a physician allows early identification of respiratory distress and immediate intervention. Even subjective complaints of upper airway congestion are taken seriously if they develop during antivenin infusion. If respiratory compromise develops, the antivenin infusion is held and the epinephrine infusion is started at 2-4  $\mu$ g per min. The patient receives IV histamine receptor antagonists, steroids, and an inhaled beta agonist. The antivenin infusion is slowly restarted after termination of allergic signs and symptoms.

Intubation after RSE was rare in this study. Two of 289 patients (0.7%) were intubated as a direct result of RSE, and another 11 patients were intubated for surgical procedures or co-existing medical issues. The majority of intubations were done electively for surgical procedures requiring general anesthesia.

There are several limitations to this study. First, we used a very broad definition of respiratory compromise, which may overestimate the number of patients with this finding. Although our definition includes subjective symptoms, we felt it was most important to recognize all potential early warnings of life-threatening respiratory compromise. Second, the data were collected retrospectively and, therefore, may underestimate the true incidence of airway compromise. Minor symptoms may not have been documented in all charts.

Third, our findings may not be generalizable to other geographical areas with different species, particularly those with neurotoxic venoms. Although our patients are rarely able to identify the responsible species, the most common snake encountered in our region is the Western Diamondback (*Crotalus atrox*). In central Arizona, even patients with a known Mojave Rattlesnake (*Crotalus scutulatus scutulatus*) envenomation rarely exhibit severe neurotoxicity, unlike some of the Mojave envenomations in other areas that result in respiratory failure (14). This is due to geographical differences in venom components (15).

## CONCLUSIONS

Respiratory compromise after rattlesnake envenomation was rare, occurring as a direct result of envenomation or required therapy in only 23 of 289 (8%) patients. Five of these 23 patients developed venom-induced respiratory compromise (two requiring intubation) and 18 developed antivenin-induced respiratory compromise. Three of these patients reported a prior rattlesnake bite, but it is unknown if these were true envenomations. No one required intubation for antivenin-induced hypersensitivity reactions. There were no deaths among our patients during acute hospital admission for rattlesnake envenomation during this 6-year study period. The use of Crotalidae Polyvalent Antivenin appears to be safe when administered in the intensive care unit under an experienced physician's supervision.

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