BRIEF REPORT

A Retrospective Review of Early Gastrointestinal Symptoms in the Prediction of Crotaline Envenomation Severity

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Objectives.—Rattlesnake envenomations are cited to cause gastrointestinal (GI) symptoms, which may be indicators of systemic envenomation. We sought to identify whether the presence of early GI symptoms, defined as occurring within 4 hours of the bite, could be used to predict antivenom use or bite severity.

Methods.—We performed a retrospective review of a statewide poison system's database for all cases of rattlesnake envenomation from January 2000 to December 2009. Data collected included presence of GI symptoms and antivenom use. The GI symptoms were further classified as early (within 4 hours) or late. Bite severity was determined using the minimal to moderate to severe scoring system from collected data. Data were then analyzed with a χ^2 test and Fisher's exact test to evaluate for association between early GI symptoms and either antivenom use or bite severity.

Results.—There were 2570 reported rattlesnake exposures in the database. Sixty-one (2.4%) of these had GI symptoms reported. Of these, 36 (59%) had symptoms develop within 4 hours of envenomation. A total of 49 patients (80%) received antivenom. Early GI symptoms were seen in 31 (63%) of patients receiving antivenom versus 5 (42%) of patients not receiving antivenom ($P = .20$). Early GI symptoms were seen in 4 of 6 (66%) of the severe group, 19 of 29 (66%) of the moderate group, and 13 of 26 (50%) of the minimal group ($P = .47$).

Conclusions.—Gastrointestinal symptoms after rattlesnake envenomations were rarely reported in this poison center study, and the presence of early GI symptoms did not predict bite severity or the use of antivenom.

Key words: rattlesnake, envenomation, antivenom

Introduction

Every year more than 1000 envenomations from North American (NA) rattlesnakes resulting in significant morbidity and occasional mortality are reported to the American Association of Poison Control Centers' National Poison Data System.¹ The venom of NA rattlesnakes primarily causes local tissue destruction with pain and swelling, and hemotoxic effects such as coagulopathy.² In addition, rattlesnake envenomations are frequently cited to cause early gastrointestinal (GI) symptoms such as nausea, vomiting, or diarrhea.^{3–5} The exact mechanism by which this occurs is

unknown, but some suggest that these GI symptoms could be an early marker for systemic envenomation or bite severity. We retrospectively reviewed a regional poison control system's database in an attempt to identify whether the presence of early GI symptoms, defined as occurring within 4 hours of the bite, could be used to predict antivenom use or bite severity.

Methods

Our institution's Human Research Protection Program approved this retrospective observational case series. A retrospective case review of the California Poison Control System (CPCS) electronic database (Visual Dotlab, Madera, CA) for all cases of rattlesnake envenomations between January 1, 2000, and December 31, 2009, was

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Table. Minimal, moderate, severe scoring method

Bite severity	Signs and symptoms
Minimal	No systemic manifestations; normal laboratory findings
Moderate	Swelling progressing beyond the site of bite and 1 or more systemic manifestations (eg, abnormal laboratory findings such as decreased hematocrit or platelets)
Severe	Marked local response; severe systemic manifestations; significant alteration in laboratory findings

performed. Cases were included if the presence of GI symptoms defined as nausea, vomiting, diarrhea, altered gustation, or oral paresthesias were documented. Data collected include gender, age, location of bite, presence of nausea, vomiting, diarrhea, altered gustation or oral paresthesias, antivenom use, presence of urticaria or wheezing, antiemetic use, and opioid analgesic use. The GI symptoms were further classified as early (within 4 hours) or late (occurring 4 hours or more after the bite). Bite severity was determined using the minimal, moderate, severe scoring system.⁶ The criteria for this scoring system are shown in the Table. The determination of bite severity was made by the study authors upon reviewing the CPCS chart for each case. Data collected for bite severity determination included local and distal pain, local and distal swelling, ecchymosis, neurological complaints (ie, fasciculations), thrombocytopenia, and hypofibrinogenemia. Data were then analyzed with a χ^2 test and Fisher's exact test to evaluate for statistically significant association between early GI symptoms and either bite severity or antivenom use.

Results

The initial review identified 2570 reported NA rattlesnake envenomations in the database. Seventy-five (2.9%) of these had GI symptoms recorded in the database. Fourteen of these cases were miscoded and were not true rattlesnake envenomations. Of the remaining 61 cases, 50 patients (82%) were older than 18 years of age and 47 (77%) were male. A majority were bitten on the hand (56%, $n = 34$). The median time from alleged envenomation until CPCS contact was 1.5 hours. In 36 (59%) of the patients, GI symptoms developed within 4 hours of the reported rattlesnake bite. Of these, 24 (39%) had nausea alone, 16 (26%) had vomiting alone, 5 (8%) had both reported, 5 (8%) had altered gustation, 9 (15%) had oral paresthesias, and no patient had diarrhea reported. Eighteen patients (29%) received antiemetics, including 15

of the patients with early GI symptoms documented. Three patients with early GI symptoms were given opioid analgesics before symptoms being reported. Six (9%) of the bites met the definition of severe, 29 (47%) were moderate, and 26 (42%) were rated as minimal severity. Early GI symptoms were seen in 4 of 6 (66%) of the severe group, 19 of 29 (66%) of the moderate group, and 13 of 26 (50%) of the minimal group ($P = .47$). A total of 49 of 61 patients (80%) was given antivenom. No urticaria or wheezing was documented after antivenom administration. Early GI symptoms were seen in 31 (63%) of patients receiving antivenom versus 5 (42%) of patients not receiving antivenom ($P = .20$). Among different age groups, 7 of 11 pediatric patients had early GI symptoms, and all pediatric cases were given antivenom; 30 of 50 adult cases had early GI symptoms, and antivenom was given 38 times.

Discussion

The venom of NA rattlesnakes is a complex mixture of various proteins, lipids, ions, and carbohydrates leading to local tissue destruction, hemotoxic effects, and occasional neurotoxicity.⁷ Gastrointestinal symptoms such as nausea, vomiting, diarrhea, and altered gustation are frequently attributed to NA rattlesnake envenomations.⁸ They are included as part of the Snakebite Severity Score (SSS) and thus considered markers of systemic venom effect.⁹ The biological mechanism by which NA rattlesnake venom causes GI symptoms is not fully known. Animal studies have described GI symptoms as a prominent feature of envenomation in a canine model but not in a primate model.^{10,11} Recently, a component of *Crotalus viridis viridis* venom has been shown to cause contraction of smooth muscle in rat and guinea pig gastric fundus.¹²

The true incidence of GI symptoms caused by NA rattlesnake venom is not known. Several pediatric case series have found the incidence of GI symptoms, primarily vomiting, to range from 16.6% to 31%.^{4,13,14} Only a few adult case series address GI symptoms and have reported incidences as high as 40%.^{5,15} Case reports sporadically describe GI symptoms.¹⁶ Of note, GI symptoms were prominent in a case of intravenous administration of *Crotalus atrox* venom.¹⁷ Surprisingly, we found a very low incidence (2.5%) of GI symptoms associated with NA rattlesnake envenomations reported to our poison control system. Among persons who did have GI symptoms, we chose to look specifically at early GI symptoms with the theory that early manifestation would indicate more severe envenomation. However, we could find no significant association between early GI symptoms and bite severity or need for antivenom.

It should be noted this study has several potential limitations. First, it was a retrospective review of a poison

control system's database, which is subject to underreporting and incomplete data collection. In the CPCS database, the absence of GI symptoms is not explicitly documented in every case. It was not possible to determine the number of cases for which GI symptoms were asked about and found to be lacking. It is thus possible that CPCS staff did not consistently ask about GI symptoms, resulting in underreporting. Conversely, health care providers may have considered GI symptoms to be unrelated to the envenomation and failed to report them. In addition, GI symptoms may have occurred but resolved before the patient's presentation and thus may not have been reported. It is also possible, although unlikely, that severe envenomations, which may have had more GI symptoms, may not have been reported to the CPSC.

A second limitation is that the decision to classify oral paresthesias as a GI symptom may be criticized, as many would view it as a neurological process. We included it in our search criteria because we were concerned that it is perhaps difficult for patients to differentiate between altered gustation and oral paresthesias. Third, we utilized the mild, moderate, severe scoring system and not the more objective SSS owing to inherent limitations of a retrospective review. The minimal, moderate, severe scoring system is not validated, but before the development of the SSS, it was frequently used,^{6,18,19} and it has numerous limitations. It has a large subjective component and is an all-or-nothing scale that scores local and hematologic symptoms equally. The SSS is a validated scoring system that is a useful research tool; however, attempts to apply it to the CPCS records were unsuccessful as recorded data are simply not detailed enough.

As a fourth limitation, it is possible that ethanol or opioid analgesic use could be confounders. Although we could not account for ethanol use, we did find a low rate of analgesic administration, which is unlikely to have influenced the final results. Finally, it is theoretically possible that allergic reactions to the antivenom (Antivenin [Crotalidae] Polyvalent or Crotalidae Polyvalent immune Fab) may cause nausea and vomiting. There were no documented cases of urticaria or wheezing in our dataset, however, making this an unlikely confounder.

Conclusions

In this retrospective review of NA rattlesnake envenomations, we could find no association between the presence of early GI symptoms and bite severity or the requirement for antivenom administration. Furthermore, we found a low incidence of GI symptoms after NA rattlesnake envenomation reported to our poison control system.

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