Validation of a Severity Score for the Assessment of Crotalid Snakebite

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Study objective: No research tool exists for the clinical evaluation of crotalid snakebite. We sought to determine the correlation of the snakebite severity score (SSS) with the clinical assessment of physicians experienced in the management of crotalid snakebite.

Methods: We retrospectively used the SSS to quantify the severity of envenomation in 108 patients with crotalid snakebite. Two physicians experienced in the management of venomous snakebite independently and blindly assessed the severity of envenomation as detailed in medical records with the use of accepted clinical criteria. The correlation of the SSS and the physicians' consensus was determined with pointbiserial correlation.

Results: The SSS correlated well with the physicians' consensus at presentation (r=+.63, z score=6.52, $P<.000001$) and at the point at which the patient's condition was worst (r=+.70, z score=7.24, $P<.000001$). The SSS also correlated highly with the physicians' assessment of change in the patient's condition (r=+.51, z score= 6.10, $P<.000001$). With the physicians' consensus as the gold standard, the sensitivity of a change in the SSS of 1 point in detecting clinically significant worsening of the envenomation syndrome was .97; specificity was .81.

Conclusion: The SSS correlated well with the clinical condition of patients bitten by crotalid snakes as represented by the medical record. It provides a more objective instrument for the evaluation of severity and progression of envenomation in patients with crotalid snakebite.

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INTRODUCTION

The manifestations of crotalid snakebite in human beings vary widely. A crotalid snakebite produces effects ranging from puncture wounds without apparent clinical effects (the "dry bite") to life-threatening effects including coagulopathy, increased vascular permeability, and neurologic manifestations such as fasciculation, paresthesia, mental status depression, and weakness.[1] Most patients exhibit only a subset of the possible consequences, however, because of variability in the victim's response to venom and in the venom itself, which varies from species to species and from season to season.[2,3] All, some, or none of the anticipated manifestations of crotalid venom poisoning may develop in a given patient.

Other vagaries of crotalid venom poisoning include the time and rapidity of onset. Venom effects may begin within minutes or be delayed for hours. Even severe effects may not become evident for many hours.[4] Some patients exhibit alarming manifestations initially, but their condition fails to worsen. Authorities recommend repeated examination of the patient and the administration of antivenom if the patient's condition worsens.[1,5,6]

The unpredictable nature of crotalid snakebite makes assessment and management difficult. The literature is difficult to interpret because investigators use different methods of evaluation. Some investigators use no objective measurement at all, whereas others use indicators, such as swelling, that represent only part of the envenomation syndrome. Two classification systems for evaluation of snakebite have been widely disseminated (Figures 1 and 2).[1,5] Although both techniques have served well for many years, they lack resolution; snakebites are categorized into only three or four classes. Both systems are subjective. Some patients cannot be classified according to these systems. For example, a patient with a finger bite and swelling to the elbow after 4 hours but no coagulopathy or systemic effects would fall between categories of moderate and severe in one system and between grades II and III in the other. Thus, an investigator could categorize the patient in two different ways, making these tools imprecise. In addition, neither system has been validated as a clinical or research tool. Thus no proven instrument exists for the research evaluation of crotalid snakebite.

We developed a score to more objectively assess the severity of crotalid snake venom poisoning. The physical and laboratory findings used by physicians experienced in the treatment of crotalid snakebite were determined by means of review of the literature, textbooks in emergency medicine and medical toxicology, and discussion with authorities in the field. Our purpose was to determine the correlation of the snakebite severity score (SSS) with the clinical opinion of physicians experienced in the treatment of crotalid snakebite in the retrospective assessment of patients with crotalid snakebite.

Figure 1.
Minimal-moderate-severe scoring method.

Minimal envenomation: Local swelling and other local changes; no systemic manifestations; normal laboratory findings
Moderate envenomation: Swelling progressing beyond the site of bite and one or more systemic manifestations (eg, abnormal laboratory findings such as decreased hematocrit or platelets).
Severe envenomation: Marked local response, severe systemic manifestations, and significant alteration in laboratory findings.

MATERIALS AND METHODS

The Western Envenomation Database (WED) was created by the Section of Emergency Medicine of the University of Arizona and the Arizona Poison and Drug Information Center. The WED comprises the medical records of snakebite victims who contacted the poison center. All calls for information on the management of ongoing cases of snakebite were included. Each case was monitored closely until the patient was discharged from the health care facility, in keeping with standard poison center procedure. After the patient's discharge, the case was logged into the WED. Each patient was mailed a questionnaire 1 month after the bite; we asked the patient's permission to review the medical record. At 6 months a similar questionnaire was mailed to the patient. The WED contains 296 cases of crotalid envenomation in which the

Figure 2.
Grade I-IV scoring method.

0 No envenomation: fang marks and minimal pain.
I Minimal envenomation: fang marks, pain, 1 to 5 inches of edema, and erythema during the first 12 hours; no systemic symptoms
II Moderate envenomation: fang marks, pain, 6 to 12 inches of edema, and erythema in the first 12 hours; systemic symptoms may be present, along with rapid progression of signs from grade I; may be bloody ooze at bite site
III Severe envenomation: Fang marks, pain, edema greater than 12 inches in first 12 hours; systemic symptoms, including coagulation defects after pit viper bites; signs of grades I and II appear in rapid progression, with immediate systemic signs and symptoms
IV Very severe envenomation: local reaction develops rapidly; edema may involve ipsilateral trunk; ecchymoses, necrosis, and blebs and blisters develop; at tightly restrictive fascial planes, tension may become great enough to obstruct venous or even arterial flow.

poison center was consulted between the inception of the WED (January 1, 1986) and December 30, 1990. A complete description of the WED has been published.[3]

To be included in this study, the medical record had to contain the poison center chart and the hospital medical record. The hospital record had to contain the admitting physician's clinical comments, as well as the patient's laboratory values at presentation and at the point of his or her worst condition. Of the 296 cases in the WED, 108 met these criteria.

Calculation of the SSS involves the evaluation of six areas that experienced clinicians use in the evaluation of crotalid snakebite (Figure 3). The SSS range of severity is 0 to 3 or 0 to 4 for each area of evaluation; a higher score indicates more severe effects. The score total ranges from 0 to 20 points. Early versions of the score had fewer areas of clinical evaluation and narrower scoring ranges but, when assessed with a small number of charts, were judged insufficiently sensitive in the detection of clinically significant changes in the envenomation syndrome.

Each medical record was evaluated independently and the SSS calculated with the use of a standardized abstract form by a single research assistant blinded to the physicians' assessment. The SSS at presentation was calculated with the medical record and laboratory values from the initial assessment of the patient at a health care facility

Figure 3.
The SSS.

Criterion	Points
Pulmonary system	
No symptoms/signs	0
Dyspnea, minimal chest tightness, mild or vague discomfort, or respirations of 20 to 25	1
Moderate respiratory distress (tachypnea, 26 to 40 breaths/minute, accessory muscle use)	2
Cyanosis, air hunger, extreme tachypnea, or respiratory insufficiency/failure	3
Cardiovascular system	
No symptoms/signs	0
Tachycardia (100 to 125 beats/minute), palpitations, generalized weakness, benign dysrhythmia, or hypertension	1
Tachycardia (126 to 175 beats/minute) or hypotension, with systolic blood pressure greater than 100 mm Hg	2
Extreme tachycardia (>175 beats/minute), hypotension with systolic blood pressure <100 mm Hg, malignant dysrhythmia, or cardiac arrest	3
Local wound	
No symptoms/signs	0
Pain, swelling, or ecchymosis within 5 to 7.5 cm of bite site	1
Pain, swelling, or ecchymosis involving less than half the extremity (7.5 to 50 cm from bite site)	2
Pain, swelling, or ecchymosis involving half to all of extremity (50 to 100 cm from bite site)	3
Pain, swelling, or ecchymosis extending beyond affected extremity (more than 100 cm from bite site)	4
Gastrointestinal system	
No symptoms/signs	0
Pain, tenesmus, or nausea	1
Vomiting or diarrhea	2
Repeated vomiting, diarrhea, hematemesis, or hematochezia	3
Hematologic symptoms	
No symptoms/signs	0
Coagulation parameters slightly abnormal: PT, <20 seconds; PTT, <50 seconds; platelets, 100,000 to 150,000/mL; or fibrinogen, 100 to 150 μg/mL	1
Coagulation parameters abnormal: PT, <20 to 50 seconds; PTT, <50 to 75 seconds; platelets, 50,000 to 100,000/mL; or fibrinogen, 50 to 100 μg/mL	2
Coagulation parameters abnormal: PT, <50 to 100 seconds; PTT, <75 to 100 seconds; platelets, 20,000 to 50,000/mL; or fibrinogen, <50 μg/mL	3
Coagulation parameters markedly abnormal, with serious bleeding or the threat of spontaneous bleeding: unmeasurable PT or PTT; platelets, <20,000/mL; or undetectable fibrinogen; severe abnormalities of other laboratory values also fall into this category	4
Central nervous system	
No symptoms/signs	0
Minimal apprehension, headache, weakness, dizziness, chills, or paresthesia	1
Moderate apprehension, headache, weakness, dizziness, chills, paresthesia, confusion, or fasciculation in area of bite site	2
Severe confusion, lethargy, seizures, coma, psychosis, or generalized fasciculation	3

PT, prothrombin time. **PTT,** partial thromboplastin time.
Points are assessed on the basis of manifestations caused by the venom itself (antivenom reactions not included). Ranges given are for adults; appropriate compensation should be made for age

(eg, emergency department record). The worst-condition SSS was calculated with the medical record description and laboratory values for the patient's worst condition at any time during hospitalization. We calculated the change in SSS by subtracting the SSS at presentation from the SSS at the point of the patient's worst condition.

Each chart was independently and blindly reviewed by two physicians experienced in the management of crotalid envenomation. Both physicians were familiar with the SSS. Physicians were blinded to each other's assessments, as well as to the SSS calculated by the research assistant. Each physician assessed the patient's condition on presentation to the health care facility and at the time of the worst clinical condition. The physicians' assessment of the envenomation was categorized as none, minimal, moderate or severe with the method described by Russell.[1] The progression of envenomation during hospitalization was assessed separately and categorized as none or slight, moderate, or marked worsening. In cases in which the two physicians disagreed in their assessment of envenomation, the case was reviewed jointly and a consensus assessment reached.

The correlation between the physicians' assessment of severity and the SSS was determined with Pearson's correlation coefficient.[7] The correlation between the clinical assessment of the change in envenomation severity and a change in the SSS was determined with a point biserial correlation.[7] The sensitivity and specificity of a change in the SSS in the detection of clinically significant worsening (as assessed on the basis of the physicians' consensus) were also calculated.[8] In addition, we performed multiple-regression analysis to evaluate the relative contribution of each component to the total SSS and to determine whether the various components correlated too highly with each other and were therefore redundant or, alternatively, contributed very little to the total SSS.[9]

RESULTS

It was the physicians' consensus that at presentation 11 patients had no evidence of venom effect and 48 showed minimal, 38 moderate, and 11 severe effects (Table 1). For all patients, the SSS at presentation was 3.0±.3 (mean±SEM, Table 1). The scores for patients with no effect and minimal, moderate, and severe effects were 1.3±.5, 2.1±.2, 3.2±.3, and 8.5±1.0, respectively. The correlation between the physicians' assessment of severity and the SSS at the time of presentation was highly statistically significant (r=+.63, z score= 6.52, $P<.000001$). The physicians disagreed on the severity of envenomation at presentation in 12 cases; in four cases the consensus favored physician 1.

It was the physicians' consensus that at the point of worst condition, 8 patients had no clinical evidence of venom effect, whereas 11 were judged to have minimal, 55 moderate, and 34 severe effects (Table 1). The SSS at the point of worst condition was 6.0±.4 (mean±SEM, Table 1). The scores for patients with no effect and minimal, moderate, and severe effects were .6±.2, 3.5±.6, 4.5±.3, and 9.6±.6, respectively. The correlation of the same parameters for worst condition was also highly statistically significant (r=+.70, z score=7.24, $P<.000001$). The physicians disagreed on the severity of envenomation at the point of worst condition in nine cases; in two cases the consensus favored physician 1.

The physicians' consensus was that 21 patients did not show worsening during hospitalization, whereas 87 did: 44, slight, 30 moderate, and 13 marked (Table 2). A point biserial correlation between physician assessment of worsening and change in SSS was highly significant (r_{pb}=+.51, t=6.10, $p<.000001$). Wilcoxon sign testing indicated no

Table 1.
SSS and physician assessment of crotalid snakebite.

	Presentation		Worst Condition	
Extent of Envenomation	**Score***	**No. of Patients**	**Score***	**No. of Patients**
None	1.3±.5	11	.6±.2	8
Minimal	2.1±.2	48	3.5±.6	11
Moderate	3.2±.3	38	4.5±.3	55
Severe	8.5±1.0	11	9.6±.6	34
Total		**108**		**108**

*Data expressed as mean±SEM.

Table 2.
SSS and change in severity.

	Change in SSS	
Assessment of Change	**No. of Patients**	**Mean±SEM**
No worsening	21	.2±.5
Slight worsening	44	1.9±.2
Moderate worsening	30	3.8±1.7
Marked worsening	13	6.6±2.0

significant change in SSS from the baseline values in subjects clinically judged to have no worsening ($z=1.83$, $P=.07$) but a highly significant change from baseline in subjects clinically judged to have worsening after presentation ($z=7.96$, $P<.000001$). The physicians disagreed on the extent of worsening in 13 cases; in 6 of these cases the consensus favored physician 1.

With the physicians' consensus as the gold standard, the sensitivity of a change in the SSS of 1 point in detecting clinically significant worsening of the envenomation syndrome was .97; the specificity, .81.

No component correlated highly with another component, with correlations ranging from +.17 to +.39. However, all components correlated highly with the total SSS, with correlation ranging from +.51 to +.70. Thus none of the component scores was redundant, and all component scores correlated highly with the total SSS.

DISCUSSION

Research on the treatment of snakebite has been limited by the lack of an objective assessment of severity of envenomation. For example, the authors of one study concluded that antivenom was not needed for the treatment of crotalid snakebite in southeastern Texas.[10] This conclusion was based on the finding that patients with crotalid snakebite (copperhead, 31; water moccasin, 12; rattlesnake, 10; unknown, 14) had good outcomes even though they were not treated with antivenom. This provocative finding has been misinterpreted by some authors as justification of a "conservative" approach to the treatment of all crotalid snakebites (ie, treatment without antivenom). This reasoning is flawed, however, because most of the patients were bitten by the copperhead snake (*Agkistrodon contortrix*), a snake known to generally cause only minor injury. Authors commonly indicate a reduced need for antivenom in copperhead bites, and no deaths resulting from copperhead bites have been reported in the medical literature.[1,11] The extrapolation of this data to all crotalids, particularly the rattlesnakes (*Crotalus* sp), is therefore misleading and potentially dangerous.

The use of a scoring system could help physicians avoid this problem by allowing comparison of snakebite severity between studies. The typical copperhead bite at presentation would be scored as a 1 or 2 on the SSS (1 or 2 points for swelling, no points for other organ systems). The most severe score in the typical copperhead snakebite would probably be 2 or 3, for increased swelling and perhaps minor alterations in respiratory rate or heart rate. For example, analysis of the copperhead subgroup in the WED revealed that the mean SSS for such bites at presentation was only 2.0±1.1 points; no patient demonstrated worsening during hospitalization. In contrast, a typical bite by the western diamondback rattlesnake would be scored 4 or 5 initially and, if untreated, could easily be scored as 12 to 15 with the development of coagulopathy and alterations in respiratory rate or heart rate. Use of a scoring system would have allowed recognition of the Texas study as verification of the relatively benign nature of copperhead snakebite, not a rationale for avoiding the use of antivenom.

We found that the correlation between the SSS and the physicians' assessment at baseline and at the point of the patient's worst condition was highly statistically significant, indicating that the score increased in proportion to the patient's condition at baseline or worst condition. This makes the SSS a promising tool for describing the severity of crotalid snakebite under research conditions. The SSS also correlated highly with the physicians' assessment of worsening in the patient's condition. Change in the patient's condition, such as worsening, is also an important parameter because it indicates disease progression. A scoring system that reliably detects worsening would permit meaningful comparisons among different treatment methods.

Other criteria for the evaluation of a test are its sensitivity and specificity. It should be noted that we studied the ability of a change in the score, not of the absolute value of the score in detecting worsening. For research purposes we are interested mainly in sensitivity (assurance of detection of all patients whose condition worsens). The SSS worked well in this regard, detecting 97% of patients the physicians judged to have worsened.

Limitations of this study involve that fact that the scoring system was developed mainly as a research tool with which to quantify the manifestations of crotalid snakebite. To develop such a tool, one must know which patients are affected by the disease. In the case of crotalid snakebite no test uniformly indicates that envenomation has occurred. Traditionally, symptoms and signs have been used to determine whether antivenom should be administered. Therefore clinical assessment is the gold standard for the diagnosis of crotalid snakebite.

Bias was minimized because the physicians performed independent, blinded assessment. Another limitation is the accuracy of the medical record. An accurate record is an implicit assumption in studies based on the medical record. We addressed this weakness by using only cases with complete records and using the records as the basis for both the physicians' assessment and determination of the SSS. Another limitation of the SSS is the fact that the

score does not distinguish between effects of the envenomation syndrome and acute reactions to antivenom. Because severe envenomation and anaphylaxis can cause similar clinical effects (tachypnea, tachycardia, hypotension), the potential for misinterpretation of the cause of such clinical effects is unavoidable. We addressed this potential problem by considering the timing of signs and symptoms relative to the administration of antivenom and the clinical impression of the treating physician as recorded in the medical record. Sixteen of 108 patients were believed to have experienced an acute reaction to antivenom; in 7 of these patients the reaction consisted only of a rash or chills, which would not have affected the SSS.

We used the SSS to accurately assess the clinical condition of patients bitten by crotalid snakes as represented by the medical record. An increase in the SSS correlated well with worsening in the patient's condition. Although this study is a promising beginning, a prospective trial is needed to determine the ease of use of the SSS under clinical research conditions, its interrater reliability, and its effect on clinical decisionmaking.

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