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Treatment of pediatric black widow spider envenomation: A national poison center's experience

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ABSTRACT

Background: Black widow species (*Latrodectus* species) envenomation can produce a syndrome characterized by painful muscle rigidity and autonomic disturbances. Symptoms tend to be more severe in young children and adults. We describe black widow spider exposures and treatment in the pediatric age group, and investigate reasons for not using antivenom in severe cases.

Methods: All black widow exposures reported to the Rocky Mountain Poison Center between January 1, 2012, and December 31, 2015, were reviewed. Demographic data were recorded. Patients were divided into 2 groups. Group 1: contact through families from their place of residence, public schools and/or cases where patients were not referred to healthcare facilities. Group 2: patient contact through healthcare facilities.

Results: 93 patients were included. Forty (43%) calls were in Group 1 and 53 (57%) in Group 2. Symptoms were evident in all victims; 43 (46.2%) were grade 1, 16 (17.2%) grade 2 and 34 (36.5%) grade 3, but only 14 patients (41.1%) of this group received antivenom. Antivenom use was associated with improvement of symptoms within minutes, and all treated patients were discharged within hours, without an analgesic requirement or any complications. Reasons for not receiving antivenom included: skin test positive (2/20), strong history of asthma or allergies (2/20), physician preference (2/20), non-availability of the antivenom at the health care facility (14/20).

Conclusion: In our study, most symptomatic black widow envenomations were minor. Relatively few patients received antivenom, but antivenom use was associated with shorter symptom duration among moderate and major outcome groups.

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1. Background

In the United States, there are five species of widow spiders: *Latrodectus mactans* (black widow), *Latrodectus hesperus* (Western black widow), *Latrodectus variolus*, *Latrodectus bishopi* (red widow) and *Latrodectus geometricus* (brown widow). They are present in every state except Alaska [1]. Black widow spiders are considered the most medically relevant spider in the United States, due to their proximity to residential areas [2], although other species, especially *geometricus*, have increasingly accounted for emergency department visits [3].

Black widow spider venom contains five latrotoxins, which are specific neurotoxins: alpha, beta, gamma, delta and epsilon [4,5]. The toxins have great affinity for nerve terminals and interact with synaptic vesicle proteins forming a complex that leads to a massive release of neurotransmitters. Clinical manifestations resulting from the release of these neurotransmitters are part of the envenomation syndrome known as latrodectism [6]. Severity depends on the amount of venom delivered, and is influenced by factors such as the number of bites and patient age.

Envenomations generally produce systemic neurologic syndromes without significant local injury [7]. Latrodectism is characterized by painful muscle rigidity and autonomic disturbances such as tachycardia, hypertension and diaphoresis, typically lasting for 1–3 days. Some bites do not progress to systemic illness, while other patients may show severe neuromuscular symptoms within 30–60 min – always spreading contiguously from the bite site [8]. Despite the risk of severe symptoms

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in pediatric patients, treatment recommendations after black widow spider envenomations are inconsistent.

The objective of this study was to describe black widow spider bite exposures in a large cohort of pediatric patients, to assess treatments and outcomes, and to investigate the reasons for not using antivenom in severe cases.

2. Methods

This was a retrospective study of all calls to the Rocky Mountain Poison Center in Denver, Colorado, USA, involving envenomations by a black widow spider between January 1, 2012, and December 31, 2015. The Rocky Mountain Poison Center covers a wide geographic area, including Utah, Montana, Colorado and Wyoming. Diagnosis of black widow envenomation was established by identification of the spider by affected individuals, and by typical clinical findings such as progressive, contiguous radiating pain. In some cases, envenomation was inferred if the patient recovered after the administration of Black Widow Spider Antivenom® (Merck).

For each envenomation, the date of occurrence, age of patient, gender, area where the bite occurred, time elapsed since the bite, affected limb, systemic and local manifestations, as well as treatment and clinical outcomes were recorded. Patients 18 years and older were excluded from this study.

Patients were described in two groups:

Group 1: contact was through families from their place of residence, public schools and/or cases where patients were not referred to healthcare facilities.

Group 2: patient contact was through healthcare facilities or was continued through healthcare facilities after being started elsewhere.

Demographic information, clinical data, complications, and outcome data were extracted from the Rocky Mountain Poison Center electronic database which includes records of all patient consults made at the center. Data were abstracted by a single investigator from the Rocky Mountain Poison Center and transferred to an electronic spreadsheet (Excel 2007). Demographic and clinical features are shown as numbers or percentages for categorical variables; the continuous variables are shown as the median and 25th and 75th percentiles (interquartile interval, IQI). Statistical comparisons of variables were performed using non-parametric association tests (Chi-square or Fisher's exact test), with $p < 0.05$ indicating significance.

2.1. Definitions

The severity of the envenomation was separated into three categories [9]:

Grade 1: Ranging from no symptoms to local pain at the envenomation site with normal vital signs.

Grade 2: Muscular pain at the site with migration of pain to the trunk, diaphoresis at the bite site, and normal vital signs.

Grade 3: Grade 2 symptoms with abnormal vital signs; diaphoresis distant from the bite site, generalized myalgias of back, chest, and abdomen, nausea, vomiting and headache. Pediatric Advanced Life Support (PALS, American Heart Association) parameters were used to define tachycardia and hypotension (defined as systolic blood pressure < 5 th percentile) in accordance with age [10].

Control of envenomation was defined as cessation pain progression, systemic signs and Symptoms.

If the physician decided to perform a skin test for horse serum sensitivity, a 1:10 dilution of antivenom intradermally was utilized [11]. Since a type I immune reaction (acute hypersensitivity) and type III immune reaction (serum sickness) are potential adverse events associated with the intravenous administration of this antivenom, signs of these events were specifically sought and recorded by the poison center.

This study was approved by research ethics committee of the Rocky Mountain Poison Center.

3. Results

During the three-year study period 93 patients with black widow spider envenomations were treated. Ages ranged from 0 to 18 years with a median of 11 years; 54 (58%) were male (Table 1). The interval between bite and call to the poison center ranged from 0.2–55 h (median 3 h). Forty (43%) calls were in Group 1 (calls from homes, schools or institutions with management on site) and 53 (57%) in Group 2 (calls from healthcare facilities or calls which ended in a healthcare facility).

All envenomations occurred in and around the home including the garage; 61 (65.5%) were diagnosed by identification of the spider using photographs or direct examination of the spider in the hospital. The upper limb was affected in 53.8% and lower limb in 26.9% of cases with no difference in envenomation severity by site (Table 1). The number of bites ranged from 1 to 4.

Clinical manifestations were evident in all patients; 43 (46.2%) were grade 1, 16 (17.2%) grade 2 and 34 (36.5%) grade 3. There

Table 1

Demographic characteristics, presentation and outcomes of children bitten by black widow spiders.

	Patients (n = 93)
Demographic data	
Mean age (SD), years	10 (6)
Median age, years	11
Age range, years	0.1–18
IQI, years	4–16
Male gender, n (%)	54 (58)
Calls to the Poison Center (electronic database)	
From the residence/schools, n (%)	40 (43)
From healthcare facilities, n (%)	53 (57)
Median time from bite to the call (range), hours	3 (0.2–55)
Q1, Q3, hours	1, 6
Anatomic area involved, n (%)	
Upper limb	50 (53.8)
Lower Limb	25 (26.9)
Back	10 (10.8)
Face	7 (7.5)
Abdomen	2 (2.2)
Neck	1 (1.1)
Chest	0 (0)
Number of bites seen	
Median (range)	1 (1–4)
Single bite, n (%)	67 (72)
Clinical manifestations, n (%)	
Grade of envenomation	
Grade 1	43 (46.2)
Grade 2	16 (17.2)
Grade 3	34 (36.5)
Local signs/symptoms	
Local pain	66 (71)
Erythema at site	14 (15)
Puncture marks	12 (13)
Systemic signs/symptoms	
Muscle rigidity/cramping	24 (25.8)
Abdominal pain	20 (21.5)
Migration of the pain (chest/back)	17 (18.3)
Restlessness	8 (8.6)
Vomiting	7 (7.5)
Diaphoresis	6 (6.5)
Neurologic features	4 (4.3)
Priapism	1 (2.1)

was no statistical association between the age of the patient and grade of envenomation (p -value = 0.67). The most common symptoms were local pain including subsequent back, chest and abdominal pain with muscle cramping. One patient developed priapism. Another patient developed fever two days after envenomation, possibly reflecting a systemic inflammatory response. There were no deaths.

L. mactans antivenom (Merck & Co, Inc., West Point, PA, USA) was administered to 14 (43%) patients (Table 2), all of whom were grade 3 severity. The median time from envenomation to antivenom administration was 12 h (IQR: 15–20 h; limits: 0.5–48 h). One patient was treated with antivenom 48 h post bite; he was 1.7 years old and presented to the emergency department with severe abdominal pain, rigid abdomen and irritability. He was worked up for intussusception, with ultrasound and computerized tomography of the abdomen to rule out appendicitis, which were both normal. After consulting with toxicology, antivenom administration was recommended and symptoms improved within 20 min, suggesting that envenomation occurred. No patient required an additional dose of antivenom, and most began to improve within 20–40 min of starting the antivenom infusion. Resolution of the clinical syndrome within 1 h was seen in all patients treated with antivenom. All patients treated with antivenom had received intravenous benzodiazepines and morphine and intravenous fluids before receiving antivenom. One patient developed an urticarial rash during the infusion without airway compromise and was treated with intravenous antihistamines and steroids with improvement. One six-year-old male developed mild swelling of the hand contralateral to the infusion site; he had no fever, pain, or other symptoms, no proteinuria and a normal serum creatinine.

Twenty patients with grade 3 envenomation did not receive antivenom for the following reasons: skin test positive (2/20), strong history of asthma or allergies (2/20), physician preference (2/20), and no available antivenom at the health care facility (14/20).

4. Discussion

Our study showed that black widow spider envenomation is not rare and can affect children of all ages. Most bites occurred residually and many were clinically significant. Antivenom therapy was uniformly helpful to patients for whom it was administered, although many patients with grade 3 severity did not receive this therapy. Black widow spider envenomation frequently occurs during the summer [12], both inside and near the home; in our series, all reported envenomations occurred in and around the home and garage. Local pain usually occurs within 30–120 min. By 3–4 h, painful cramping and muscle fasciculations developed involving the extremities with centripetal progression towards the chest, back, or abdomen. There are no specific laboratory tests for diagnosing black widow spider envenomation [13].

In humans, from 2000 through 2008, a total of 23,409 black widow spiders exposures were reported in 47 states; 65% reported minor clinical effects, 33.5% moderate and 1.4% major effects, and there were no deaths [14]. Close to half the patients in this study - 43% of the calls coming from Group 1 - avoided unnecessary hospitalization, instead calling in directly to the poison center. The majority of patients require analgesia with the possible addition of a benzodiazepine, or no treatment at all. These patients can generally be managed at home through telephone consultation with the poison center, especially if the spider has been positively identified. Transport to a medical facility familiar with treating this condition is important for severe cases; we recommend transfer only in cases of worsening pain and/or for antivenom administration. In this case it is essential that health care practitioners recognize the signs and symptoms of envenomation as quickly as possible to initiate optimal care for patients.

To diagnose *Latrodectus* envenomation, it is invaluable for healthcare providers to actually see the suspected spider. If this is not possible, envenomations are diagnosed through a detailed analysis of history and clinical findings. Evidence of the classic “target” lesion can aid

Table 2
Characteristics of children requiring antivenom therapy.

Age in years/gender	Time from bite to antivenom (hours)	Clinical manifestation	Treatment before the antivenom	Outcome improvement (minutes)	Test antivenom	Adverse reaction
13/F	20	Severe back pain, muscle cramps	Morphine, benzodiazepines, fluids	45	No	No
6/M	8	Severe back pain, muscle cramps	Morphine, benzodiazepines, fluids	30	No	Yes ^a
13/M	24	Muscle cramps, chest pain, abdomen pain, hypertension, tachycardia	Morphine, benzodiazepines, fluids	30	No	No
12/F	22	Muscle cramps, chest pain	Morphine, benzodiazepines, fluids	40	No	No
3/F	12	Muscle cramps, irritability state	Morphine, benzodiazepines, fluids	30	Yes	No
17/M	20	Muscle cramps, back pain, diaphoresis	Morphine, benzodiazepines, fluids, ondansetron	20	No	No
1.5/M	36	Irritability state, grunting, tachycardia, diaphoresis	Morphine, benzodiazepines, fluids	20	No	No
1.7/M	48	Muscle cramps, rigid abdomen, grunting, priapism, fasciculation, tachycardia	Morphine, benzodiazepines, fluids	20	No	No
11/M	24	Muscle cramps, rigid abdomen, vomiting	Morphine, benzodiazepines, fluids	20	No	No
1/M	24	Muscle cramps, irritability state, rigid abdomen	Morphine, benzodiazepines, fluids	20	No	Yes ^b
4/M	24	Muscle cramps, irritability state	Morphine, benzodiazepines, fluids	40	No	No
18/M	18	Muscle cramps, diaphoresis, tachycardia, piloerection	Morphine, benzodiazepines, fluids	20	Yes	No
1.6/M	8	Muscle cramps, irritability state	Morphine, benzodiazepines, fluids	20	No	No
17/M	8	Muscle cramps, irritability state	Morphine, benzodiazepines, fluids	20	No	No

M = male; F = female.

^a Swelling on the opposite hand one week after the antivenom, follow up at the clinic, no fever, no renal dysfunction. Rule out serum sickness.

^b Hives on body, allergic reaction, no anaphylaxis. Treated with antihistamines and oral steroids.

diagnosis [2]. The site of the bite may develop a pale central area with surrounding erythema, fang marks may be visible, and there may be some swelling and redness of the involved area. Additionally, the presence of piloerection may be commonly seen. These signs may, however, be absent.

Wound evaluation and local care, including tetanus prophylaxis, are needed [15]. Pain management is essential, and immediate initiation of an oral non-steroidal anti-inflammatory agent is indicated. For more severe cases, intravenous opioids and benzodiazepines to control pain and muscle spasms may be necessary [16]. Calcium and dantrolene are not recommended.

Pediatric patients at times may require high doses of opioids or benzodiazepines and are at risk of developing adverse effects such as central nervous system and respiratory depression [17]. Hospitalization and possibly antivenom, however, should be reserved for patients exhibiting serious systemic symptoms or inadequate pain control.

Aside from immediate resuscitative measures and supportive therapy, management of black widow spider envenomation is based on the parenteral administration of animal derived antivenom. *L. mactans* antivenom (Merck & Co, Inc., West Point, PA USA), which is rapidly effective and curative [18]. The recommended treatment at a healthcare facility, for a suspected black widow spider envenomation, begins with intravenous diazepam (0.2–0.3 mg/kg) and morphine (0.05–0.1 mg/kg bolus slowly intravenously), with subsequent observation for several hours for grade 2 and 3 patients. Doses of both drugs can be repeated as necessary. If pain can be controlled for several hours without antivenom, patients can typically be discharged home with oral pain medications and strict return precautions.

If pain progresses, antivenom is considered. Its use is reserved for patients whose systemic effects are designated grade 3. All treatments and reasons for treatment decisions were recorded in these patients. The starting dose of Black Widow Spider Antivenom® (Merck) is one vial (2.5 mL), diluted in 50 mL of normal saline for intravenous administration, infused over 1 h. Adverse events were recorded and categorized according to severity and apparent cause.

After intravenous administration, it distributes widely throughout the body and binds to venom. It is derived from foreign proteins and is capable of producing acute and delayed hypersensitivity reactions in humans. Antivenom administration in children follows the same guidelines as adults, with administration based on clinical presentation, especially severity of pain. It is efficacious for both systemic manifestations and marked, progressive pain if given within hours, but should also be considered for delayed systemic signs even >24 h after envenomation [18]. Only 14 of our patients received antivenom even though administration is associated with shorter symptom duration among moderate and major outcome groups. Antivenom use was associated with improvement of symptoms within minutes and all patients were discharged after some hours of observation without complication or need for further analgesia. Our results strongly suggest that Black Widow Spider Antivenom® (Merck) administration is relatively safe, with mild to moderate adverse effects seen in only a small percentage of patients. To produce this monovalent, whole immunoglobulin, equine species are hyper-immunized against *L. mactans* venom. Despite concern that the antivenom is an equine-derived whole IgG that can precipitate early hypersensitivity reactions, there are only three reported cases of anaphylaxis to the antivenom in the medical literature. One reported a boy who developed anaphylaxis within 45 min of administration. He received standard therapy for anaphylaxis and all signs and symptoms (including the pain secondary to the black widow envenomation) abated within 6 h [19]. The second report describes a 37-year-old male with a history of atopic asthma who developed a severe anaphylactic reaction resulting in cardiac arrest [20]. The third reported case was related to rapid infusion of undiluted antivenom over a very short period of time and the patient died [21].

In our study, 2/14 patients receiving antivenom had skin testing prior to administration, although this does not predict the occurrence

of hypersensitivity reactions [19,22]. We do not recommend skin testing, although if it is performed and is positive, patients should be considered high risk, in similar fashion to patients with asthma or allergies receiving horse serum products. These patients may benefit from pre-treatment with antihistamines and corticosteroids, with slower infusion of antivenom.

Controversy over when to administer black widow spider antivenom is influenced by reports of adverse events. In pediatric patients, a risk-to-benefit balance exists between adverse effects due to the antivenom and the risk of adverse effects due to opioids and benzodiazepines in high doses. In one of patients with grade 3 symptoms, who was pregnant, the decision was made to avoid antivenom administration (patient refused) even though untreated latrodectism can precipitate abortion due to muscle cramping.

Latrodectism must be considered among the causes of an apparent acute abdomen [23]; two of our patients underwent computerized tomography of the abdomen or ultrasound to rule out appendicitis and intussusception respectively. Latrodectism was suspected and antivenom was given with complete symptom resolution of symptoms.

There are limitations to this study. The study represents data from a single center. Adverse reactions to the antivenom may have occurred without being documented. Case ascertainment was, at times, based on criteria other than actual identification of the actual offending spider. Many patients who would, theoretically, have benefited from antivenom did not get this therapy since it was not stocked in some hospitals. Finally, while mortality from black widow spider envenomation is low, patients who may have died from envenomation would not have been reported in this study.

5. Conclusion

Although black widow bites are associated with severe muscle pain, cramping and autonomic disturbances, mortality is extremely low. Symptomatic treatment with non-steroidal analgesics, and in severe cases with benzodiazepines and morphine, is generally effective, although the duration of symptoms may necessitate hospitalization for 1–2 days. If symptoms fail to resolve, an equine monovalent immunoglobulin G (IgG) antiserum is available, and should be considered, especially for severe reactions such as hypertensive crisis, intractable pain, priapism and in pregnant woman.

The use of Merck black widow antivenom dramatically shortens the duration of symptoms, allowing outpatient care in most cases. It rarely results in serum sickness or severe allergic reactions.

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