REVIEW ARTICLE

Diagnosis and treatment of patients injured by venomous snakes in the Bolivarian Republic of Venezuela

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Received: 12/11/2022 - Approved: 03/01/2023

ABSTRACT

Introduction: ophidian poisoning is considered a public health problem in most tropical countries. The Bolivarian Republic of Venezuela is considered one of the affected countries because highly venomous species are found there. A high quality antiophidic serum, produced by the University of Venezuela, Biotechnology Center, Pharmacy Faculty, has been able to reduce the mortality caused by these particular ophidians. Due to the specific circumstances of the Cuban Medical Mission, the need for learning about the management of patients injured by venomous snakes has been identified.
Objective: to deepen in the diagnosis and treatment of patients injured by venomous snakes during the performance in Emergency Services in the context of the Cuban Medical Mission in the Bolivarian Republic of Venezuela.
Method: detailed review of accidents caused by snakes of the Viperiade family in its different genera (Bothrops, Bothriechis, Bothriopsis, Porthidium, Crotalus and Lachesis) and of the Elapidae family or coral snake, genus Micrurus.
Conclusions: the diagnosis of the ophidian accident is based on the detailed knowledge of the characteristics of the clinical picture and the physiopathological activity of the envenomation. In the Bolivarian Republic of Venezuela most ophidian accidents are caused by snakes of the genus Bothrops. The treatment of the bothropic accident consists, in addition to the general measures, in the use of antivenom in adequate doses and intravenously.
Key words: ophidian accidents; venomous snakes; diagnosis; therapeutics

RESUMEN

Introducción: el envenenamiento ofídico es considerado un problema de Salud Pública en la mayoría de los países tropicales. La República Bolivariana de Venezuela es considerada uno de los países afectados porque allí se encuentran especies altamente venenosas. Un suero antiofídico de alta calidad, producido por el Centro de Biotecnología de la Facultad de

Farmacia de la Universidad Central de Venezuela, ha logrado disminuir la mortalidad causada por estos ofidios en particular. Debido a las circunstancias concretas de la Misión Médica Cubana se ha identificado la necesidad de aprendizaje sobre el manejo de los enfermos lesionados por serpientes venenosas.
Objetivo: profundizar en el diagnóstico y el tratamiento de los pacientes lesionados por serpientes venenosas durante el desempeño en los Servicios de Urgencia en el contexto de la Misión Médica Cubana en la República Bolivariana de Venezuela.
Método: revisión detallada de los accidentes provocados por serpientes de la familia *Viperiade* en sus diferentes géneros (*Bothrops*, *Bothriechis*, *Bothriopsis*, *Porthidium*, *Crotalus* y *Lachesis*) y de la familia *Elapidae* o serpiente de coral, género *Micrurus*.
Conclusiones: el diagnóstico del accidente ofídico tiene sus fundamentos en el conocimiento detallado de las características del cuadro clínico y la actividad fisiopatológica del envenenamiento. En la República Bolivariana de Venezuela la mayoría de los accidentes ofídicos son causados por serpientes del género *Bothrops*. El tratamiento del accidente *bothrópico* consiste, además de las medidas generales, en la utilización del antiveneno en dosis adecuadas y por vía intravenosa.
Palabras clave: accidentes ofídicos; serpientes venenosas; diagnóstico; terapéutica

INTRODUCTION

Ophidian poisoning is considered a public health problem in most tropical countries because there is a high number of fatal cases in these areas due to the high toxic level of the venoms of this category of snakes. The Bolivarian Republic of Venezuela is considered one of the affected countries because there are highly venomous species such as the butterfly tigra (*Bothrops Venezuelensis*), the mapanare (*Bothrops Colombiensis*) and the rattlesnake (*Crotalus Durissus Cumanensis*). A high quality antiophidic serum, produced by the Biotechnology Center of the School of Pharmacy of the Central University of Venezuela, has been able to reduce the mortality caused by these particular snakes.[1] Due to the specific circumstances of the Cuban Medical Mission, the need for learning about the management of patients injured by venomous snakes has been identified, so it is required that professionals deepen in a set of contents that are essential to achieve adequate care.
The objective of this review is to deepen in the diagnosis and treatment of patients injured by venomous snakes during the performance in Emergency Services in the context of the Cuban Medical Mission in the Bolivarian Republic of Venezuela.

METHODS

A detailed review of accidents caused by snakes of the Viperidae family, in its different genera (*Bothrops, Bothriechis, Bothriopsis, Porthidium, Crotalus* and *Lachesis*), and of the *Elapidae* family, coral snake, was carried out in different databases; articles written in Spanish and English were reviewed.

DEVELOPMENT

Brief epidemiological review

Ophidism, ophidiotoxicosis or ophidian accident is the name given to the morbid state caused by the bite of an ophidian.[2] Venomous snakes or ophidians are found

almost everywhere in the world (including many oceans), with the exception of a few islands, frozen environments and high altitudes. Envenomations and deaths from snakebites are a major public health problem in tropical countries;[3] up to five million people suffer snakebites each year. An estimated 2.4 million snakebite poisonings and 94,000-125,000 deaths occur each year, in addition to some 400,000 amputations and other serious health consequences such as infections, tetanus, scar deformities, contractures, and psychological sequelae. Poor access to health care and a shortage of anti-toxins increase the severity of injuries and their outcomes; the people most affected are those living in resource-poor rural areas, who base their livelihoods on low-cost, non-mechanized agriculture and other rural activities. Farmers, women and children are the groups that most frequently suffer snakebites.[4]

In Venezuela, being a tropical country, there are considerable rates of snakebite accidents. The country has a wide variety of venomous snakes distributed throughout the national territory, which cause around 4,000 cases of poisoning per year. Between 1980 and 1999, 1,494 people died in Venezuela as a result of contact with different zoological groups of vertebrates and invertebrates that produce venom. Ophidian poisoning was the leading cause of mortality due to poisoning, with 921 deaths (61.7%).[5] However, the number of accidents is underreported, the amount of which is unknown because not all ophidian accidents are reported.[6,7]

Poisonous snakes in Venezuela

There are 2,700 species of snakes in the world, of which 200 are considered venomous. In the Venezuelan territory there are 8 families with more than 150 species, of which about 25 are venomous.[7] These venomous snakes are grouped in two families.[1,5,6,7,8,9,10]

Viperidae:

- Genera *Bothrops, Bothriopsis, Bothriechis and Porthidium* (mapanare, mapaná, tigra mariposa, terciopelo, barba amarilla, yarará, jergón, cuatro narices, equis)
- Genus *Chrotalus* (rattlesnake, chonono)
- Genus *Lachesis* (cuaima, concha de piña, verrugosa, cascabel muda, cascabel púa, pucarara, surucucucú, matabuey, tamagá)

Elapidae:

- Genera *Leptomicrurus* and *Micrurus* (coral or coralline)

It should be taken into account that the common names of snakes vary, even within the same region. In the Venezuelan territory there are different indigenous ethnic groups, so the species of venomous snakes have a characteristic or common name that varies according to each ethnic group.[11]

According to the potency of the venom, the poisonous corals (Figure 1) would be the most dangerous, but it happens that most of them are not very aggressive, with very small mouths, and they are elusive, that is why accidents caused by this family are very rare. The few cases were bitten when handling the snake and playing with it because they considered it harmless.[1,9]

Figure 1. Coral snake[11]

The rattlesnake (Figure 2) has yellow eyes, can grow up to 1.5 m long and live more than 25 years. They have a rattle-like structure at the end of their tail that they shake when they are about to attack. Due to the activity of their venom they should be in second place. In Brazil and Venezuela, mortality from the bite of these snakes is very high, about 72% without treatment and about 10% even with dosage of polyvalent antiophidic serum. Fortunately, accidents are not so frequent because they are less aggressive than *Bothrops*, and because of the noise they make with the *Crepitaculum corneum* (rattle), which alerts of their presence.[1,5,9]

Figure 2. Rattlesnake[12]

In Venezuela, approximately 80% of ophidian accidents are caused by snakes of the *Bothrops* genus (Figure 3). These are very aggressive snakes and their

geographic distribution is wide within the country. They predominate in tropical and subtropical areas, mainly in humid forests, foothills, riverbanks and streams. These snakes have a less potent venom than *Micrurus* and *Crotalus*. Mortality for untreated cases is not so high, reaching 8%.[1,8,9,13]

Figure 3. Mapanare snake[11]

Differences between venomous and non-venomous snakes

It is important to know the differences between poisonous and non-poisonous snakes (Table 1 and 2). The author of this review, on three occasions in which he carried out medical collaboration in the Bolivarian Republic of Venezuela, observed that many injured persons come to the hospital services with dead snakes. Being able to identify them is useful for the conduct to follow.[1,5,9,10,11,13,14,15,16]

Table 1. Viperidae-crotalidae

External character	Poisonous	Non-poisonous
Head	Heart-shaped or arrowhead. Covered with small scales	Round, covered with large, smooth scales
Dentition	Solenoglyph: two large anterior fangs of the upper jaw, mobile	Aglifa: no fangs Opistoglifa: two posterior maxillary fangs
Neck	Narrow differentiated	Undifferentiated width
Body	Covered with carinate scales rough to the touch and opaque	Covered with non-fleshy scales, smooth to the touch and shiny
Pupil	Vertical, elliptical	Rounded in most cases
Loreal pit (thermoreceptors organs located between the nostril and the eye)	Present	Absent
Tail	Short and thick	Long and thin
Attitude	They are slow and take an attacking attitude	They are agile, do not attack and escape quickly

Table 2. Elapidae

External character	Poisonous	Non-poisonous
Head	Tall and short	Flat and sharp
Eyes	Small	Large
Scales	2	3
Dentition	Proteroglyphic: two anterior fangs of the upper jaw, fixed	Aglifa: no fangs; Opistoglifa: two posterior maxillary fangs
Neck	Not differentiated	Not differentiated
Tail	Short	Long
Rings	Complete blacks in odd number (1 or 3)	Incomplete black in even number

Sometimes, the shape of the bite helps to know if it is a venomous snake:[14]

- Non-poisonous snake bites usually leave small scratches in a row (superficial).
- Poisonous snake bites usually leave one or two large punctures (holes).

Poisonous snake accidents

A) Bothropic Accident

This type of poisoning is most frequently caused by Mapanares, Tigra mariposa and all species of the genus *Bothrops*. The venom of these snakes has proteolytic, coagulant and hemorrhagic action. Although there is no unanimous agreement, the predominance of one effect over the others would seem to be linked to the amount of venom inoculated, the age of the aggressor animal, its species and geographical location. The anatomical site of the bite, the weight and size, as well as the general physiological state of the bitten person are also very important elements to be taken into account.[13,16,17]

The inoculation orifices left by the aggressor snakes are micropunctures of approximately 1 cm apart, which depends on the size of the snake. The first clinical manifestation is intense pain, followed by profuse and continuous bleeding from the holes left by the snake's fangs. Other manifestations may include edema, necrosis, phlyctenas and ecchymosis (Figures 4, 5 and 6). Immediate death after the bite is rare and appears only when the inoculation of the venom is significant in quantity and takes place inside a blood vessel. Hours after the bite (four to six hours) there is lightheadedness, nausea, restlessness, bilious or bloody vomiting and, occasionally, hematuria, melena, epistaxis and gingivorrhage.[16,17,18]

The prognosis is unfavorable in untreated cases because mortality and necrosis phenomena with rebellious ulcerations and loss of limbs increase considerably.

In cases treated appropriately and within an adequate time, the evolution is favorable in more than 90% and there are no sequelae.

B) Micruric accident

In almost 100% of the cases the bites occur on the hands. The accidents caused by coral snakes are characterized by the immediate appearance of poisoning symptoms, which is explained by the rapid absorption and low molecular weight of the neurotoxin. The action of the venom is essentially neurotoxic, but also

Figure 4. Extensive homorrhagic blisters and edema[19]

Figure 5. Necrosis, edema and infection secondary to venomous snakebite[20]

Figure 6. Proteolysis, necrosis and infection secondary to poisonous snake bite[10]

cardiotoxic and rhabdomyolytic. In the area of the bite there is usually only slight burning or pain, accompanied by a hypoesthetic sensation. Occasionally, there is scarce edema circumscribed to the bite area. A few minutes after the bite, dizziness, headache and nausea may appear, suggesting the sensory-motor involvement that covers the affected limb and then generalizes to the cranial nerves, configuring a typical neurotoxic fasciitis. Physical examination revealed swallowing disorders (velopalatine paralysis), dysarthria, suffocation crisis, respiratory muscle paralysis, hypotensive crisis and flaccid paralysis of the limbs. The presence of progressive mydriasis is a sign of poor prognosis.[9,13,16,17,18]

C) Crotalic accident

Next in frequency to *Bothrops* poisoning is crotalic (rattlebell) poisoning. The stings often appear as small punctures that become congested and reddened. The effect of the venom is essentially neurotoxic, although it may also be myotoxic, coagulant, nephrotoxic, and rhabdomyolytic. Local manifestations are not very obvious, with erythema and paresthesia. Systemic manifestations include myasthenic facies (Figure 7), diplopia, ophthalmoplegia, dysphagia, myalgia, respiratory muscle paralysis, myoglobinuria, disseminated intravascular coagulation, hemorrhage, respiratory failure, renal failure, etc. The prognosis is worsened by the appearance of uremia that shows no signs of decreasing at 24 and up to 36 hours.[9,13,16,17,18]

Figure 7. Myasthenic facies[21]

D) Lachesic accident

The effect of the poison is proteolytic, coagulant, hemorrhagic. The clinical manifestations are similar to those observed in bothropic poisoning, with the exception of a vagal excitation syndrome that occurs in the first hours. There is

severe pain at the bite site and invasive ecchymotic edema. Profuse bleeding may be observed from the penetration holes of the snake's fangs. At the systemic level, hematologic, gastrointestinal, cardiovascular, and neurologic changes dominate the clinical picture.[9,13,17,18]

Prevention of ophidian accidents[4,9,10,16,19,22,23]

1. Walking without footwear should be avoided. The use of high rubber or leather boots prevents between 50% and 75% of accidents because the feet and legs are the most affected anatomical regions.
2. Before starting agricultural work in areas with a high prevalence of ophidian accidents, the worker should be alerted about the risk so that he/she takes double care in his/her work.
3. As there are snakes that live in trees, great attention should be paid when harvesting fruits.
4. The use of gloves is necessary when harvesting sugar cane, coffee and rice, and in land clearing work because 20% of snake accidents involve the hands and forearms.
5. Do not introduce your hands into holes in trees or in the ground. Do not remove fallen logs or stacked firewood without taking precautions because these are places where snakes frequently rest.
6. Building sidewalks around houses, covering cracks in the floor and walls and placing small walls that interrupt the space between the door and the floor of the house can prevent accidents. It is important to keep the area around houses clear of vegetation.
7. Animals such as cats, poultry and rabbits help to keep the domestic and peridomestic area free of snakes.
8. On days out or vacations, camping should be avoided in places close to plantations and pastures. The banks of rivers and lakes are places usually populated by snakes, so you should be alert when visiting them.
9. Venomous snakes usually have evening or nocturnal habits; during this period of time, you should avoid wandering around without taking the necessary preventive measures.
10. Natural enemies of snakes (foxes, hawks, rabbits and nocturnal birds) should be preserved.
11. Avoid panic and any sudden movement. Move away from danger gradually.
12. Act in a manner that the animal at no time feels threatened or cornered (when confronted with any snake do not run, move away gently. If it is very close, throw something on it to distract it and then run away in the opposite direction).

Immediate care[2,6,9,10,13,14,15,16,17,18,19]

1. After the accident, the patient should be kept at rest, avoiding walking or running as much as possible; otherwise, the absorption of the poison may be favored. The patient should be transferred to a medical center immediately.
2. Clean the affected anatomical area with soap and water.

3. Do not use tourniquet under any circumstances or make incisions in the affected anatomical area because these measures aggravate the local lesions and may complicate the clinical picture, with subsequent superimposed infections.
4. Avoid drinks such as alcohol because, far from helping, they complicate the patient's evolution.
5. Before starting serotherapy, blood samples should be taken for the pertinent laboratory tests:
   a. Coagulation tests:
      - Partial thromboplastin time (PTT)
      - Prothrombin time (PT)
      - Clotting time (CT)
      - Fibrinogen
   b. Hemogram and leukogram
   c. Urea and creatinine
   d. Hemogasometry
   e. Creatinfosfokinasa (CPK) and lactate dehydrogenase (LHD)
   f. Urine test
6. If there is clinical or laboratory evidence of poisoning, initiate serotherapy with specific serum (antibothropic, anticrotalic or antimicuric) or, failing that, polyvalent antiophidic serum (antibothropic-anticrotalic).
7. The edema of the affected limb may compromise its circulation. Early movement and elevation at an angle of 45° can be of great help. The application of warm compresses can improve circulation.
8. Administer analgesics and reassure the patient. Avoid the use of central nervous system depressant drugs.
9. Monitor the patient's vital signs and urine volume periodically.

Specific treatment[2,6,9,10,13,14,15,16,17,18,19]

1. In case of cardiorespiratory arrest, apply resuscitation according to CABDE
2. Assessment of vital signs
3. Cardiorespiratory monitoring
4. Supportive treatment
5. Tetanus prevention
6. Local antiseptics: hydrogen peroxide or alcohol
7. Antibiotic therapy: in the case of secondary infection, in addition to the adequate drainage of the collections (abscesses), it is necessary to consider the use of antibiotics that act on germs of the oral cavity of the animal: *Morganella Morganii*, *Escherichia Coli*, *Providencia spp.* and *Streptococcus* of group D, among the most frequent, as well as germs of the skin of the patient. In a broad manner, amoxicillin/clavulanic acid, ampicillin/sulbactan and clindamycin plus quinolone can be considered in the first term. The culture of the secretions of the lesions should be performed early and the antibiotic treatment should be adapted according to the microbiological result.
8. Analgesics and sedatives: no non-steroidal anti-inflammatory drugs due to the risk of bleeding.
9. Antiophidic serotherapy:

a) Polyvalent antiophidic serum (PAS), (10 ml vials), for the treatment of bites of venomous snakes of Central and South America, except corals and sea snakes. Each 10 ml neutralizes 25 mg of bothropic venom, 20 mg of lachesic and 20 mg of crotalic (Figure 8).
b) Monovalent anticoral antiophidic serum (Figure 9).

Figure 8. Anti-poison for specific hospital use to treat poisoning caused by bites of most of the snakes of medical importance in Central and South America[24]

Figure 9. Anti-poison for specific hospital use to treat envenomations caused by bites of most coral snakes in Central and North America[24]

Clinical criteria to determine the severity of the poisoning and the dose of antiophidic serum[2,6,9,10,14,15,16,17,18,19]

- Mild: local effects of edema and pain but without systemic alterations, administer five ampoules or vials
- Moderate: local effects (edema, pain and bleeding) accompanied by non-severe systemic alterations (coagulopathy and arterial hypotension), administer 10 ampoules or vials
- Severe: prominent local effects and important systemic alterations, such as coagulopathy, systemic bleeding, hypotension and renal alterations, administer 15 ampoules or vials.

The serum should be diluted in 500 or 1,000 ml of 0.9% saline in adults and 200 ml in children; infusion is started with a slow drip for 15 minutes and, if no reactions occur, the flow is increased so that all the serum is administered in one hour. Be prepared for anaphylactic reactions.

In children bites are usually more severe, so the dose of PAS should be equal to the adult dose.

Administer an additional dose of five to 10 vials of PAS if after 10 hours there are no favorable changes in coagulation tests or if the local picture and systemic bleeding persist. Consideration should be given to the possibility that signs and symptoms may reappear after 12 to 24 hours, probably due to the late release of accumulated venom in the tissues after the poisoning has been controlled. In these cases it is advisable to administer five more bottles of PAS.

Coagulation time (CT) interpretation[9,10,15,16,19]

1. Normal up to 10 minutes
2. Prolonged 10 to 20 minutes
3. Incoagulable> 30 minutes.

If after six hours the CT is incoagulable, additional serum therapy with four to five ampoules or vials is recommended.

In cases where severe poisoning is demonstrated or the nearest Health Center is more than four hours away, before applying the serum, a hypersensitivity test to the product should be performed if the patient's history identifies any allergic history. The skin test can be used, although it is not absolutely reliable.

Skin test in the field

Administer 0.1 ml of serum diluted 1/10 or 1/100 intradermally on the forearm. The test is positive if there is redness and itching at the site of inoculation within 20 minutes; if the test is positive, the serum should not be administered to the person bitten in the field, it should be administered in the hospital. If the test is negative, the serum should be administered intramuscularly, never intravenously; in the gluteal region the total dose should be administered only once.[6,17,18]

Patient desensitization

Apply hydrocortisone succinate in an amount of 200 mg intravenously, prior to the administration of the antiophidic serum. Administer the therapeutic dose of the serum: 50 ml, that is, five vials fractionally, always subcutaneously. Start with 0.1 ml, after 15 minutes inject 0.5 ml and then at 10-minute intervals, if no symptoms of adverse reaction are noted, administer 1 ml, 2 ml and 5 ml. Finally, five minutes

after the last injection, the rest of the dose will be administered. A 1:1000 adrenaline solution should be ready for intravenous or intramuscular injection if symptoms of severe anaphylactic shock occur.[6,17]

Serum sickness

The administration of PAS can trigger serum sickness, which manifests 5 to 20 days after serotherapy and is characterized by fever, urticaria, joint pain and lymphadenopathy. This reaction is treated with corticosteroids and antihistamines.[13,18,23] In more than 200 patients attended by the author of this review in Venezuela (years 2005-2008 and 2010-2012) and Nicaragua (years 2013-2015), as a collaborator of the Medical Brigade in those countries, serum sickness was a rare complication.

Forecast

The factors that condition a worse prognosis are the greater length of the attacking animal, the later administration of specific serotherapy, the patient being younger than nine years of age and the initiation of treatment after eight hours of the accident. Mortality has been associated with patients over fifty years of age and late diagnosis of complications. Amputation of the affected limb, one of the most feared sequelae, is related to coagulation alterations, the localization of lesions on the fingers, the development of blisters and abscesses, the installation of real insufficiency and the initiation of treatment after ten hours after the accident. The occurrence of abscesses seems to be related to a decrease in prothrombin and fibrinogen less than 100 mg/dl.[25]

CONCLUSIONS

The diagnosis of an ophidian accident is based on a detailed knowledge of the characteristics of the clinical picture and the pathophysiological activity of the envenomation, which, depending on the genus or family of the snake, can be summarized as follows:

- accidents in which local and systemic pathology dominates (edema, ecchymosis, phlyctenas and coagulation disorders), caused by *Bothrops* and *Lachesis* venom.
- accidents dominated by systemic pathology (neurotoxicity, rhabdomyolysis and acute renal failure), caused by *Crotalus* and *Micrurus* venom.

In the Bolivarian Republic of Venezuela most ophidian accidents are caused by snakes of the *Bothrops* genus. The treatment of bothropic accidents consists, in addition to the general measures, in the use of antivenom at adequate doses and intravenously.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.