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REVIEW ARTICLE

Scorpion sting, literature review and update

Picadura de escorpión, revisión de la literatura y actualización

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ABSTRACT

Introduction: scorpion stings are common in different parts of the world and are a real public health problem.
Objective: to describe scorpion species, venom characteristics, pathophysiology, clinical manifestations, severity classification, diagnosis and management in the intensive care unit.
Methods: a search for information was carried out in the period February-March 2023 in the SciELO, Scopus, PubMed/MedLine databases, the Google Scholar search engine, as well as in the ClinicalKeys services. The resulting documents were selected from those written in the last 10 years, in Spanish or English.
Development: There are approximately 2584 species of scorpions. The species Tityus (Tityus) sorataensis was described for Bolivia. Scorpion venoms have been studied for more than a century. The main clinical manifestations: urticarial plaques, swelling, erythema, ecchymosis and cellulitis with edema. Systemic manifestations range from one to two days after envenomation and may develop systemic signs: fever, pallor, fatigue, generalized edema. Diagnosis is based on a history of a scorpion sting and characteristic signs of envenomation. Treatment can be empirical, applying general measures, pain management and if some complications such as pulmonary edema, cardiogenic shock are present, management in an intensive care unit is necessary.

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Conclusions: intoxication by scorpion sting is a therapeutic challenge. It is advisable to administer antivenom together with supportive treatment. A better knowledge of scorpions may encourage interest in further research.

Keywords: Scorpion Stings; Scorpion Venoms; Scorpions; Poisoning.

RESUMEN

Introducción: las picaduras de escorpión son comunes en diversas partes del mundo y son un verdadero problema de salud pública.
Objetivo: describir las especies de alacranes, características del veneno, fisiopatología, manifestaciones clínicas, clasificación de la gravedad, diagnóstico y su manejo en la unidad de cuidados intensivos.
Métodos: se realizó una búsqueda de información en el periodo febrero-marzo de 2023 en las bases de datos SciELO, Scopus, PubMed/MedLine, el buscador Google Académico, así como en los servicios ClinicalKeys. De los documentos resultantes se seleccionaron aquellos redactados en los últimos 10 años, en idioma español o inglés.
Desarrollo: aproximadamente existen 2584 especies de alacranes. La especie *Tityus (Tityus) sorataensis* fue descrita para Bolivia. Los venenos de escorpión se han estudiado durante más de un siglo. Las principales manifestaciones clínicas: placas de urticaria, hinchazón, eritema, equimosis y celulitis con edema. Las manifestaciones sistémicas van de uno a dos días después del envenenamiento y pueden desarrollar signos sistémicos: fiebre, palidez, fatiga, edema generalizado. El diagnóstico se basa en una historia de una picadura de escorpión y signos característicos de envenenamiento. El tratamiento puede ser empírico, aplicar medidas generales, manejo del dolor y si está presente algunas complicaciones como edema pulmonar, choque cardiogénico es necesario su manejo en una sala de cuidados intensivos.
Conclusiones: la intoxicación por picadura de alacrán, es un reto terapéutico. Es recomendable la administración del antídoto (antiveneno) junto al tratamiento de sostén. un mejor conocimiento de los escorpiones, puede alentar el interés en realizar nuevas investigaciones.

Palabras clave: Picaduras de Escorpión; Venenos de Escorpión; Escorpiones; Intoxicación.

INTRODUCTION

Scorpion stings are common in various parts of the world and are a real public health problem in many countries.[1] Scorpion sting poisoning is common in tropical and subtropical regions so much so that it is considered a public health problem in some places such as Northern Sahara, Middle East, South India, China, Mexico, Brazil and Bolivia. Due to the high incidence, it can lead the patient from mild injuries to much more serious and life-threatening conditions. Scorpions are usually distinguished by the composition of their venom, clinical presentation and severity, as well as the different therapeutic approach.[2]

The consequences can be severe and possibly result in multisystem organ failure and even death. Several species are the causes of envenomation, including the genus Centruroides in North America and genus Tityus in South America.[3,4,5] The latter was extensively studied in South America, especially in Brazil,[6,7] and was described for Bolivia (Sorata) by Kraepelin, the species Tityus (Tityus) sorataensis.[8]

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About 1,2 million scorpion stings are reported worldwide per year (average poisoning rate is 20/100 000 inhabitants) resulting in 3250 deaths. The exact incidence in developing countries is not known due to difficult access to health facilities in endemic areas, as well as parsimonious reporting of non-serious cases.[2] Scorpion stings are poorly studied, but the venom has partially benefited from advances in basic techniques and experimental toxicology. Worldwide, 90 % of scorpions produce stings that lead only to local manifestations, and 10 % of cases remain a serious medical emergency that can be life-threatening.[9]

The most frequent involvement involves the cardiovascular, neurological and gastrointestinal systems. Patients requiring admission to an Intensive Care Unit reach 12,500 per year worldwide and not all receive this level of complexity of care in resource-poor countries, which explains the paucity of evidence-based clinical recommendations.[1,2] Therefore, the present investigation was developed with the aim of describing the species of scorpions, venom characteristics, pathophysiology, clinical manifestations, severity classification, diagnosis and their management in the intensive care unit.

METHODS

A search for information was conducted in the period February-March 2023 in the databases SciELO, Scopus, PubMed/MedLine, Google Scholar search engine, as well as ClinicalKeys services.

Advanced search strategies were used to retrieve information by structuring search formulas using the terms "scorpion sting", "scorpion", "scorpion", "scorpion", "sting antidote", as well as their translations into English. Boolean operators were used to combine the terms, with search formulas according to the syntax requested by each database.

From the resulting documents, we selected those written in the last 10 years, in Spanish or English, that provided updated information on scorpion stings. In addition, with the aim of achieving a review based on the best possible evidence, only those studies of the case series, original articles or systematic review type were selected.

DEVELOPMENT

During the search and review of this entity, it could be seen that, in Latin America, research efforts on scorpion stings have increased. However, in Bolivia, data are scarce and limitations in research processes are evident. On February 27, 2023, through an official note, the Bolivian Ministry of Health and Sports regretted the death of a child due to a scorpion bite.[10] This is why there is an interest in acquiring basic knowledge to be exposed to the medical and scientific community, to guide in the early recognition of this disease.

Scorpion species

There are approximately 2584 described species belonging to 23 families of scorpions. The damage they cause is not uniform but almost all harmful species belong to the family Buthidae, including the most feared: the North African species Androctonus and Buthus, Parabuthus in South Africa, Leiurus in the Middle East, Mesobuthus in India, Centruroides in North and Central America and Tityus in South America. Different species may coexist in the same geographic area.[11] Temperature and humidity are important factors contributing to the variation in scorpion bite presentation.[12] The family Buthidae contains 972 described species in 80 genera.

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972 described species in 80 genera,[13] being the only family with species considered potentially dangerous to man, due to the active components of their venoms. The species Tityus (Tityus) sorataensis was described for Bolivia (Sorata) by Kraepelin.[8] It is a scorpion genus of medical importance in the region and present in Bolivia. In spite of this, the country does not present updated information on the subject, the most representative authors being Kraepelin, Lourenço and Acosta & Ochoa.[14]

Venom Characteristics

Scorpion venoms have been studied for over a century and have since revealed some interesting results. They are complex mixtures containing mucopolysaccharides, hyaluronidase, phospholipase, acetylcholinesterase, serotonin, histamine, protease inhibitors, histamine releasers and neurotoxins. Most of these toxins are small peptide toxins that target ion channels found in both mammals and insects. The greatest medical consequences result from the scorpion alpha toxins, which consist of 61 to 76 polypeptides that bind to a specific site in the mammalian voltage-dependent sodium channel.[15]

Alpha toxins produce a significant portion of human toxicity by binding to sodium channels in cell membranes and inhibiting inactivation of the action potential.[15,16] This action, together with the synergistic effects of other venom components, results in prolonged depolarization and excessive release of acetylcholine from parasympathetic ganglia and epinephrine and norepinephrine from sympathetic ganglia and adrenal glands. This excessive neurotransmitter release results in an autonomic storm.

- Cholinergic excess manifests as marked bronchorrhea, salivation, bronchospasm, diaphoresis, priapism, lacrimation vomiting, diarrhea, and bradycardia. These effects usually last for only a few hours after a scorpion sting.[17]
- Sympathetic stimulation typically persists and produces hypertension, tachycardia, and agitation. Severe envenomation may progress to direct myocardial injury with arrhythmias, myocarditis, pulmonary edema, cardiogenic shock, and multisystem organ failure.[15]

The mechanism of cardiotoxicity with acute pulmonary edema after scorpion sting is debated, but probably reflects a complex interaction of multiple venom effects, including catecholamine-mediated coronary, cardiac microcirculatory, and systemic vasoconstriction; catecholamine-induced tachycardia and arrhythmias; and depression of myocardial contractility caused by direct venom effects and the proinflammatory response to envenomation.[12,18]

Pathophysiology

When the bite results in the introduction of venom into the body of the prey, clinically relevant envenomation only occurs if critical plasma levels of scorpion toxin are reached. In an experiment in dogs it was shown that after progressive administration of scorpion venom subcutaneously, typical manifestations of envenomation occur when a critical threshold has been reached, for Androctonus australis the critical plasma concentration is 1,14ng/ml and is reached within 30 minutes by injecting 0,2mg/kg of the purified toxin fraction but not with a lower dose 0,125 mg/kg, triggering neurohormonal and hemodynamic manifestations with massive release of neurohormonal mediators with vasoconstrictor effect (epinephrine, norepinephrine, endothelin and neuropeptide and causing a significant increase in systemic blood pressure and left ventricular filling pressures with decreased cardiac output (phase 1 or vascular).[19,20]

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This effect is neutralized by levosimendan and is not restored by the addition of glibenclamide (potassium-dependent ATPase channel inhibitor) suggesting that catecholamine release involves calcium homeostasis and is independent of potassium-dependent ATPase channels. These findings reveal why the vulnerability of children to scorpion sting given the low volume of venom distribution compared to adults when the same amount of venom is introduced into the body.

The vascular phase is followed by a sustained state of hypotension, termed the myocardial phase, in approximately two hours with altered left ventricular filling resulting in pulmonary edema and increased right ventricular afterload. There is convincing evidence that these cardiocirculatory alterations are mediated by catecholamines (level of catecholamine release) rather than by a direct effect of scorpion venom. Phase two or myocardial phase is characterized by altered contractility (myocardial stunning), low cardiac output and hypotensive state. This may be persistent for days to weeks, similar to Takotsubo cardiomyopathy with multiepicardial vascular vasospasm, however, the latter usually presents circumferential and apical ventricular hypokinesia as well as basal hypercontractility.[2]

Clinical Manifestations

Scorpion stings most frequently affect the lower extremities. Patients seek medical attention for cutaneous manifestations.[18] In clinical practice, typically 95% of scorpion stings result in only local manifestations.[21] They often occur at night while the patient is sleeping and are often not noticed until morning. Initial symptoms usually consist of mild stinging and pain at the site of the sting.[22,23]

During the next 24 hours after the sting, other cutaneous findings may develop:[17]

- Concentric, pruritic urticarial plaques centered around the sting site; local necrosis, swelling, erythema, and ecchymosis are seen especially in children
- Cellulitis with edema (more frequent in adults and in stings on the extremities)
- Local or generalized erythematous rash that may have regions of clustered red papules
- Local punctate purpuric plaques without signs of inflammation, induration or ulceration
- Purpuric bullae up to 5 cm in diameter at or near the bite site

Systemic manifestations

One to two days after envenomation, patients may develop systemic signs: fever, pallor, fatigue, generalized edema.[23,24] These findings are most likely to develop mostly in the infant population (under five years of age) and indicate the presence of acute hemolysis. Petechiae, easy bruising and bleeding point to DIC. The most severe cases may be related to cardiorespiratory symptoms logically associated with subsequent alteration in the state of consciousness (75 %). Vomiting may also occur in 72 % of patients.[2] Multiple attempts have been made to create scales that predict the need for hospitalization; however, their external validity is still under study. In addition, the addition of complementary studies indicating myocardial damage (electrocardiogram, troponin and natriuretic peptide) may improve the performance of these scales. Some systemic forms of presentation have also been reported with disseminated intravascular coagulation, anaphylaxis, acute pancreatitis, acute liver failure, acute renal failure, metabolic acidosis, late demyelinating polyneuropathy, stroke, cerebral edema and even brain death.

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Severity classification

Several classification systems for scorpion envenomation with autonomic storm have been described based on species-specific regional findings or expert opinion.[7,9,25] We favor the system proposed by Isbister and Bawaskar because it directs treatment in addition to identifying severity and is applicable to all species (Table 1)

Table 1. Severity classification

Classification	Clinical Findings	
	Scorpion poisoning with neuromuscular toxicity	**Scorpion stings capable of causing autonomic storm**
I	Localized pain or paresthesias at site	Local pain, erythema and/or paresthesias at the site of the sting
II	Local and distant pain or paresthesias	Autonomic stimulation: -Parasympathetic: diaphoresis, hypersalivation, priapism, vomiting, bronchorrhea, bronchospasm, lacrimation. -Sympathetic: hypertension, tachycardia, cold extremities. Pancreatitis with severe abdominal pain (associated with bites of Leiurus [Middle East and Asia] and Tityus [South America and Trinidad and Tobago]).
III	-Parabuthus: salivation, vomiting and urinary retention more frequent.	-Pulmonary edema -Cardiac dysfunction (cardiogenic shock and cardiac arrhythmias) from induced autonomic myocarditis and myocardial ischemia -Coagulopathy with hemiparesis and stroke (associated with Hottentotta [formerly Mesobuthus] bites in India)
IV	All of the above features present	Coma, convulsions and multiorgan failure caused by prolonged cardiogenic shock with decreased systemic vascular resistance and myocardial depression

Source: Classification scale based on the system proposed by Isbister[15] and Bawaskar[25].

Diagnosis

The diagnosis of scorpion envenomation is based on the following findings:

- Recent visit to or residence in a scorpion endemic region.
- History of a scorpion sting (often not present).
- Characteristic signs of envenomation.

Supportive laboratory findings in patients with severe envenomation (grade III or IV include evidence of rhabdomyolysis and rarely, pancreatitis. Physicians should have a high suspicion of scorpion envenomation when caring for young children from endemic areas who present with unusual neurologic symptoms (such as agitation, choreiform movement, or abnormal eye movements) even when there is no history of a scorpion sting or presence of a scorpion.

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However, the physician should always consider other possible diagnoses when evaluating a patient with suspected scorpion envenomation.[25]

Treatment

The understanding of the pathophysiology of scorpion envenomation allowed a standardization in the symptomatic treatment and a better management of the same, in order to achieve a decrease in the number of deaths due to this entity.

Empirical

There is the experience of several countries which apply the use of empirical or folkloric popular treatments such as Mexico: the ingestion of garlic with tobacco, water until full, cacahuananche with salt, raw egg, lemon juice, milk, tea.[26] Spain folk remedies include: the bezoar, the application of the same scorpion in the area of the lesion once fried, the use of smoke from the combustion of vegetables such as rosemary, pine and elder, the local application of pressed garlic, pork fat among others.[27] However, these treatments do not have enough evidence and besides not solving the problem, they delay the beginning of an effective treatment.

It is important to remember that some actions such as cutting the skin around the bite or sucking out the venom have not been shown to be effective.[28] Tourniquets, local incision or application of potassium permanganate or herbal remedies are associated with local tissue infection and gangrene should be avoided.[25]

General measures

They consist of:

- Apply cold compresses or ice to the area of the sting. This will help reduce pain and produce vasoconstriction, slowing the release of venom.
  Use analgesics if necessary. If the pain is severe, subcutaneous lidocaine may be applied to the site of the sting.
- Place a venous access and ensure general supportive measures when necessary according to the severity of the envenomation.
- Monitor vital signs, continuous cardiorespiratory monitoring with pulse oximetry, hemodynamic status, water-electrolyte balance and renal function.
- Patients with local effects after a scorpion sting should be observed for up to 24 hours for signs of cholinergic excess and adrenergic stimulation in a setting capable of providing intensive care.

Pain management

Evidence for pain management after scorpion stings is limited. Oral nonsteroidal anti-inflammatory agents (e.g., ibuprofen) or acetaminophen are indicated for pain control. If pain is more severe they may benefit from topical anesthetics (e.g., topical lidocaine or tetracaine) or regional anesthesia (e.g., digital block) using a long-acting agent (e.g., bupivacaine).[29]

Management in the intensive care unit

Maintaining oxygen saturation equal to or greater than 90-92 % by mask oxygenation or mechanical ventilation is a primary goal. Routine care in the Intensive Care Unit can control pulmonary edema and cardiogenic shock.[30]

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There are cases in which the success of noninvasive mechanical ventilation has been reported. Thus, intubation and mechanical ventilation with application of positive end-expiratory pressure and pulmonary protective mechanical ventilation are indicated when acute respiratory failure is associated with altered consciousness or cardiogenic shock. Intravenous nitrates and diuretics may be considered. Dobutamine is usually used in the most severe cases with cardiogenic shock, titrated according to the systemic blood pressure (so as not to produce or worsen hypotension).[31]

With the current paradigm shift from ischemic cardiomyopathy to Takotsubo syndrome, concerns have been raised about the use of dobutamine as a bridge therapy to recovery from scorpion toxin poisoning, since it has been argued from a biochemical standpoint that it would not seem appropriate to use catecholamines to treat a catecholamine-induced cardiomyopathy, yet cardiomyopathy secondary to pheochromocytoma that is also catecholamine-induced is usually treated with dobutamine or dopamine. [32]

The frequency of systemic hypertensive crisis depends on the scorpion species with the lowest rate with A Australis and the highest with the Indian red scorpion Mesobuthus. Remember that hypertension is usually transient followed by normal blood pressure or even vascular collapse, thus when elevated blood pressure is present it should not be systematically treated and antihypertensive medication should be administered only in patients with pre-existing chronic hypertension, hypertensive crisis or with acute pulmonary edema.

When it is decided to treat hypertension, hydralazine, clonidine, nifedipine and prazosin are recommended, among which prazosin,[33] stands out as an alpha 1 antagonist with phosphodiesterase inhibitory effect, and it is speculated that this vasodilator effect could reduce left ventricular preload and impedance without elevating heart rate. Studies such as those of Bawaskar et al. state that patients treated with prazosin plus antivenin recovered earlier than those treated with prazosin alone.[33,34] Parenteral corticosteroids (steroids) do not show clinical benefit and are therefore not recommended.[1]

Specific treatment

Immunotherapy has been of interest due to its efficacy against snake venom, however there are two important differences, the first in relation to toxicokinetics since there is an important imbalance between scorpion venom and antivenom kinetics since scorpion venom has a lower molecular weight compared to snake venom which is important for absorption from the subcutaneous tissue into the blood (bioavailability), distribution to tissues and elimination time.

Evidence supports the use of antivenom,[35] especially to treat systemic toxicity after envenomation by Hottentotta (formerly Mesobuthus), Leiurus and Tityus. Countries such as Mexico, Brazil and the USA have shown that when the correct antivenom is applied in a timely and appropriate manner, mortality from scorpion poisoning is exponentially reduced.[36,37,38]

In addition, in many occasions the available antivenoms are not always adequate and medical training and assistance in our country is usually insufficient. Therefore, the decision to administer antivenom to patients with scorpion envenomation and autonomic dysfunction requires careful consideration of the potential scorpion and the risks and benefits of the specific antivenom. Timely supportive care or toxicity is critical for good outcomes.

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Recommendations for the use of scorpion-specific antivenoms vary according to the specific scorpion species: For patients stung by Tityus or Leiurus species, which inhabit our country, show signs of systemic scorpion envenomation, we suggest treatment with a scorpion-specific IV antivenom. No trials have addressed the efficacy of these antivenoms. However, small observational studies suggest a potential benefit in patients with cardiotoxicity.[39]

The second difference represents the most serious obstacle to immunotherapy, based on mediation by neurohormones (catecholamines), making it futile to seek neutralization of the venom when the consequences have already been unleashed, at least 2 hours after the sting.[1] However, even a second administration of antivenom has been recommended, especially in children.[9] Also add that the antivenom may produce anaphylaxis.[40]

Critical obstetrics

More severe forms of poisoning have been described in pregnant women with a potential risk of fetal loss, premature delivery or placental abruption, although the effect on the product in the long term has not yet been fully evaluated. Thus, the obstetric population is also a population at risk for this poisoning.[2]

CONCLUSION

A general approach was made of all the information obtained and emphasis was placed on the clinical manifestations according to classification and their management. Intoxication by scorpion sting, although rare, is a therapeutic challenge; it seems to be advisable to administer antivenom together with supportive treatment. At present, only a very limited number of species are used in the study of venoms and toxins, mainly because they pose a threat to humans. However, a better knowledge of scorpions in general by non-experts may encourage interest in their study and further research, particularly those that can provide more information on intensive care management.

Conflict of Interest
The authors declare that there is no conflict of interest.

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All authors participated in conceptualization, research, writing - initial draft, writing - revision and editing.

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