Role of prazosin on cardiovascular manifestations and pulmonary edema following severe scorpion stings in Saudi Arabia

Abdulrahman K. Al-Asmari, MSC, PhD, Abdulaziz A. Al-Seif, MD, PhD, Mohsen A. Hassen, MD, DPaeds, Nabil A. Abdulmaksood, MD.

ABSTRACT

هدف هذا التقرير الإشارة لفعالية دواء البرازوسين لمعالجة الأعراض القلبية والإحتشاء الرئوي الناجمة عن لدغات العقارب للمرضى بالسعودية. حيث استقبل قسم الطوارئ، بمستشفى البرك العام، منطقة عسير، ثلاث حالات (طفلين وفتاة) حضروا للمستشفى في أوقات متفاوتة. ولوحظ على كل مريض ألم شديد وعلامات تعرق، تسارع في ضربات القلب والتنفس، قلق، إفراز شديد للعاب، نعوظ مستمر للولد، إحتشاء رئوي وصدمة قلبية. أعطي كل منهما مصل العقرب المتوفر وبعض الأدوية المساندة ولكن حالتهم زادت سوءا فتم تحويلهم للعناية المركزة. أعطي كل مريض جرعة من دواء البرازوسين وقد لوحظ فعالية هذا الدواء حيث عكس تأثير السم وقلل من الأعراض القلبية والرئوية الناجمة عن لدغة العقرب تدريجيا وشفي المرضى تماما. لوحظ عدم فعالية المصل المتوفر في معالجة الأعراض القلبية والرئوية لهولاء المرضى وكذلك الأدوية المساندة الأخرى. أثبتت تلك النتائج ولأول مرة في السعودية قدرة دواء البرازوسين في علاج المشاكل القلبية والرئوية الناجمة عن لدغة العقرب بينما لوحظ عدم فعالية المصل في معالجة تلك الأعراض.

We report the ameliorating effects of prazosin on the cardiovascular (CV) manifestations and pulmonary edema (PE) after treatment with antivenom (AV) failed to improve the conditions of scorpion stung patients. Three cases of scorpion envenoming, 2 children and one adult, were received at the Accident and Emergency Department of Al-Birk Hospital, Asir Region, Saudi Arabia. They presented to the hospital late with features of severe perspiration, tachypnea, restlessness, drooling of saliva, priapism, sinus tachycardia, PE, and shock like syndrome. When polyvalent scorpion (PVS) AV and intensive supportive treatment failed to show any improvement, prazosin was administered to the patients, which resulted in dramatic improvement in the conditions of the patients. We conclude that PVS AV may not be beneficial in all cases of scorpion envenomation, and prazosin may be an effective alternative for treating scorpion sting cases with CV manifestations and PE.

Saudi Med J 2008; Vol. 29 (2): 299-302

From the Department of Research Center and Medicine (Al-Asmari, Al-Seif), Riyadh Military Hospital, Riyadh, and the Department of Pediatrics and Medicine (Hassen, Abdulmaksood), Al-Birk General Hospital, Asir, Kingdom of Saudi Arabia.

Received 4th August 2007. Accepted 4th November 2007.

Address correspondence and reprint request to: Dr. Abdulrahman K. Al-Asmari, PO Box 7897 (775S), Riyadh 11159, Kingdom of Saudi Arabia. Tel. +966 (1) 4777714 Ext. 25100. Fax. +966 (1) 4777714 Ext. 6896. E-mail: abdulrahman.alasmari@gmail.com

Scorpion stings (SS) are a common occurrence throughout the tropical and subtropical world, and the majority of cases present with local pain at the site of sting, and follow a benign clinical course.[1] Severe intoxication may include cardiac and respiratory dysfunction leading to multi-system organ failure and death.[2] Death associated with scorpion envenoming (SE) appears to be rare, as compared to the significant annual incidence of stings. In Saudi Arabia, the protocol implemented for the management of SS includes administration of antivenom (AV) raised against only 2 species of scorpions, *Leiurus quinquestriatus*, and *Androc tonus crassicauda*, while more than 23 species have been recorded from different regions of Saudi Arabia,[3] around 10 species were collected from Al-Birk Town, in the Asir region (**Figure 1**), imposing difficulties in identification by clinicians or victims due to the similarities of different species in their color (yellow or black). Until now, no medication has achieved acceptance as the gold standard for treating SS and AV is currently the focus of a wide debate regarding its actual efficacy[4,5] hence, alternative approaches, especially symptomatic treatment, are warranted. Based on recent insights into the pathophysiology of the cardiopulmonary consequences of severe scorpion envenoming, (SE) it was suggested that prazosin, commonly used to treat

Figure 1 - Common scorpion species collected from Al-Birk Town, Asir Region, Saudi Arabia, 1) *Androctonus ausralis*, 2) *Scorpio maurus fiscus*, 3) *Parabuthus liosoma* 4) *Leiurus quinquestriatus ssp*, 5) *Compsobuthus werneri* ssp, 6) *Orthochirus innesi*, 7) *Androctonus crassicuda*, 8) *Vachonioulus minipectinibus*, and 9) *Leiurus quinquestriatus* ssp.

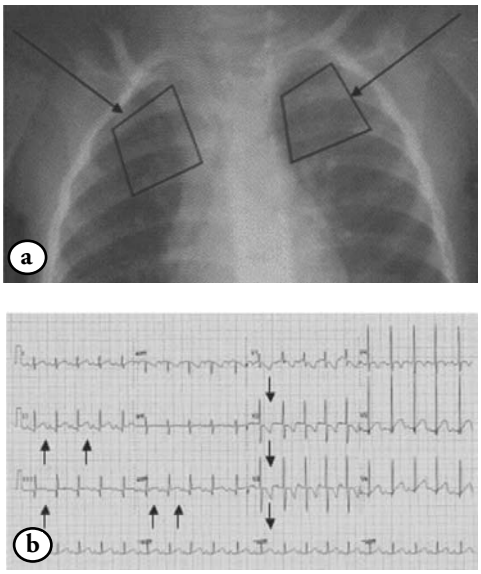

Figure 2 - Investigations of a one-year-old baby girl stung by a venomous scorpion showing **a)** chest x-ray taken when the case became stable, with ill defined alveolar infiltrates and patch ground glass opacity at both upper lobes, more in the left side, and **b)** Electrocardiogram taken after the first dose of prazosin, it showed sinus rhythm, regular, heart rate 125/m with normal PR and QT interval, normal axis. There is no signs of chamber enlargement, inverted T waves in RP precordial leads, which is normal for age. There are signs of elevated J point inferior leads, which may represent early repolarization.

hypertension might be useful in the setting of severe SE.[5] We report herein, the effects of prazosin in 3 scorpion stung patients with evidence of cardiac complications and pulmonary edema (PE) from Al-Birk town, in the Asir Region.

Case Report. ***Patient One.*** A 5-year-old Saudi boy was stung on the sole of the left foot by a scorpion in the Al-Birk area of Asir region. He presented to the emergency department one hour later with no mark of SS, no swelling, no tenderness, but severe excruciating, burning pain at sting site that was relieved by infiltration of local anesthetic (2% xylocaine). The clinical features were severe perspiration, tachycardia, tachypnea, restlessness, priapism, cold, clammy, hyperglycemia, and drooling of saliva (spitting saliva). The laboratory investigations showed oxygen saturation (SPO_2): 65%, heart rate (HR)152 beat/minute [min] (60-100), respiratory rate (RR): 34 breath/min (15-20), random blood sugar (RBS): 187 mg/dl (70-125), bleeding time (BT): 2 min, prothrombin time (PT) 16 sec (10-15), activated partial prothrombin time (APTT): 30 sec, creatinine 0.4mg, urea: 40mg/dl (7-18), and potassium 3.4 mmol/L (3.3-5.). Five ampules (5 ml IV infusion) of AV with normal saline were administered, however, his condition continued to deteriorate and he developed PE. He was started with oxygen (O_2) nebulization. The chest x-ray was normal but showed pulmonary haziness. He received furosemide 20 mg IV, and hydrocortisone 200 mg, IV fluids on flow and promethazine 25 mg injection. He developed convulsions the next day and was given diazepam IV (tachycardia, SPO_2 100 and continuous drainage was established). He was conscious and stable for a short period of time, and then became restless and irritable, developed dyspnea, convulsions, PE, and haziness were seen in chest x-ray and his general condition deteriorated despite all supportive measures. Digoxin 250 µg injections were given, without improvement and then aminophylline IV, was slowly administered and kept oxygen (O_2) on flow. At this stage the pediatrician was advised to start prazosin 250 µg oral and keep aminophylline (if necessary). The child totally improved from the symptoms within 3 hours.

Patient 2. A 24-year-old Saudi female was stung on the right foot by an unknown scorpion. She arrived to the Accident and Emergency (A&E) Department 3 hours after the sting. She was in shock and with severe pain and swelling on the right foot. Her blood pressure (BP) was 80/50 mm Hg and she was sweating profusely. Her extremities were cold and she was short of breath, with dyspnea and sinus tachycardia (ST). Her HR was 140 beats/min. She was given intravenous IV drip of normal saline rapidly with hydrocortisone (200 mg), and 5 ampules (5 ml) of scorpion AV. The chest x-ray showed

cardiomegaly, and confirmed extensive PE. The initial ECG showed ST. She was admitted to the intensive care unit (ICU) and given oral prazosin 500 µg every 3 hours, she responded to prazosin and her vital signs (VT) became stable. She was kept under observation for another 24 hours and discharged the next day.

Patient 3. A one-year-old baby girl, was stung on her buttock and left foot by a scorpion, and the child's mother informed that the scorpion was big and yellow in color. She presented to the A&E Department, 2 hours after the SS, she was very excitable, crying all the time, and in shock with marked sweating, dehydrated, hypothermic (temp. 35.2°c), markedly drowsy (semi conscious), and with bradycardia. Her pulse rate (PR) was 65/min, and bilateral pulmonary crepitation was also observed (**Figures 2 a & b**). An IV fluid and 5 ampoules (5 ml) of AV were administered by IV infusion to the child on arrival at the A&E Department, but her condition deteriorated and she was admitted to the ICU. Humid O_2 inhalation, 250 µg prazosin (crushed orally) and aminophylline 37.5 mg IV were given. Dramatic improvement was seen in the condition of the child within one hour after prazosin administration. Three hours later prazosin was repeated, her BP was monitored regularly. After 24 hours the child became almost normal and was discharged.

Discussion. The 3 patients presented to the hospital 1-3 hours after SS. The symptoms presented included cardiogenic shock (tachycardia, hypotension and acidosis), respiratory distress (tachypnea), hypoxemia, PE, and ST. The CV consequences of severe SE presented in our cases were similar to as described before.[6,7] The patients received AV (usual treatment protocol) after the SS, without improvement in their conditions. However, treatment with prazosin resulted in dramatic improvement in their condition. The use of AV has been subjected to a great deal of controversy.[8] First, queries on the effectiveness of AV in the treatment of scorpion envenomation and its clinical benefit have been raised over the last 2 decades for several reasons.[8,9] Second, no single control study has been published to document the effectiveness of AV in a prospective trial.[6] Furthermore, it has been suggested that AV fails to change the clinical course in PE, shock, hypertension, and central nervous system (CNS) disturbances of patients even several hours after the SS.[10] Gueron et al[11] also suggested that AV has no effect whatsoever and the experimental protocol implemented in Saudi Arabia should be avoided. Other reports also support this observation. A study from Al-Baha Region reported 2 deaths out of 86 admitted cases of SS over a 4 year period, and they concluded that the beneficial effects of AV in protecting against fatal complications are not proven.[12] Another study reported 2 deaths out of 96 children seen after SE over a one year period at the hospital in Al-Medina-al-Munawara.[9] Two cases of death out of 20 children were reported during 6 months from Al-Quawayah general hospital.[13] Cardiac arrest was observed following SE of a 51-year-old Saudi male, who presented to the National Guard Hospital 20 minutes after a SS. The patient died despite the administration of 5 doses of AV (25 ml IV infusions), and aggressive supportive therapy.[1] Furthermore, 2 deaths were reported in Al-Drab area of Jazan region. These patients also presented with CV complications due to SE and in spite of the AV administration and intensive therapy they did not survive.[14] Another study of 820 cases in the Hail region reported that management of 5 ml of AV was not superior to using one ml.[15]

The results of our study showed that AV was ineffective in controlling the severe complications of scorpion envenomation. Prazosin was effective in all the 3 cases of SS induced CV complications and PE. Prazosin is a selective alpha-adrenergic receptor blocker. It dilates veins and arterioles thereby reducing preload, and left ventricular impedance without rise in HR and rennin secretion, it also inhibits the sympathetic outflow in CNS.[5] Abroug et al[16] reported that prazosin reverses both inotropic (hypertension) and hypokinetic (PE, hypotension and tachycardia) phases evoked by SE. Thus, its pharmacological properties can antagonize the hemodynamic, hormonal, and metabolic toxic effects of scorpion venom.[5,16] Moreover, prazosin is easily available and free from aphylaxis. Bawaskar and Bawaskar[4] also reported the development of PE 4-8 hours after SS, and recommended early prazosin to prevent such complications. In Saudi Arabia, the majority of SS fortunately follows a benign course and can be safely treated with supportive measures alone without the use of AV.[1] While on most of the death cases, the AV was given at variable times, ranging from 20 mins to more than 10 hours after SS, making it unlikely to be of therapeutic benefit in severe SS.[4]

We conclude that management of severe human envenoming should be directed to neutralizing the over stimulated autonomic nervous system. An acceptable protocol regarding the use of prazosin should be developed aiming at its beneficial effect against severe SE.

Acknowledgments. *This work is a part of National Project supported by King Abdulaziz City for Science and Technology, Riyadh, Saudi Arabia. The authors would like to thank the Director of MSD, Major General Dr. Ketab Al-Otaibi for his encouragement and continued support.*

References

1. Dittrich K, Ahmed R, Ahmed Q. Cardiac arrest following scorpion envenomation. ***Ann Saudi Med*** 2002; 22: 87-90.
2. Tarasiuk A, Khvatskin S, Sofer S. Effects of antivenom serotherapy on hemodynamic pathophysiology in dogs injected with L. quinquestriatus scorpion venom. ***Toxicon*** 1998; 36: 963-971.
3. Al-Sadoon M, Al Faraj S. Scorpions of Saudi Arabia. Riyadh: Al-Mehmas Press 2001. p. 46-71.
4. Bawaskar H, Bawaskar P. Prazosin therapy and scorpion envenomation. ***J Assoc Physicians India*** 2000; 48: 1175-1180.
5. Bawaskar H, Bawaskar P. Utility of scorpion antivenin vs prazosin in the management of severe Mesobuthus Tamulus (Indian red scorpion) envenoming at rural setting. ***J Assoc Physicians India*** 2007; 55: 14-21.
6. Gueron M, Illa R, Sofer S. The cardiovascular system after scorpion envenomation. A review. ***J Toxicol Clin Toxicol*** 1992; 30: 245-258.
7. Bawaskar H, Bawaskar P. Prazosin for vasodilator treatment of acute pulmonary oedema due to scorpion sting. ***Ann Trop Med Parasitol*** 1987; 81: 719-723.
8. Gueron M, Yaron R. Cardiovascular manifestation of severe scorpion stings. Clinicopathologic correlations. ***Chest*** 1970; 57:156-162.
9. El-Amin E. Issues in management of scorpion sting in children. ***Toxicon*** 1992; 30: 111-115.
10. Gueron M, Margulis G, Sofer S. Echocardiographic and radionuclide angiographic observations following scorpion envenomation by Leiurus quinquestriatus. ***Toxicon*** 1990; 28: 1005-1009.
11. Gueron M, Margulis G, Ilia R, Sofer S. The management of scorpion envenomation 1993. ***Toxicon*** 1993; 31: 1071-1083.
12. Brennan R, Kumar E, Jaggarao N. Scorpion sting in Al-Baha Region. ***Saudi Med J*** 1989; 10: 25-27.
13. Ismail S.A. Clinical Pattern of scorpion stings at El-Quawayah general hospital, Riyadh region, Saudi Arabia. ***Saudi Med J*** 1995; 16: 312-314.
14. Hakim J, Ukabam S. Fatal myocarditis and pulmonary edema following scorpion sting: Report of two cases. ***Saudi Med J*** 1995; 16: 108-112.
15. Hisham, M, Sharif E. Scorpion stings, is it health problem in Saudi Arabia? Evaluation of management of 820 cases. ***Saudi Med J*** 1996; 17: 315-312.
16. Abroug F, Ayari M, Nouira S, Gamra H, Boujdaria R, Elatrous S. Assessment of left ventricular function in severe scorpion envenomation: combined hemodynamic and echo-Doppler study. ***Intensive Care Med*** 1995; 21: 629-635.

Illustrations, Figures, Photographs

Four copies of all figures or photographs should be included with the submitted manuscript. Figures submitted electronically should be in JPEG or TIFF format with a 300 dpi minimum resolution and in grayscale or CMYK (not RGB). Printed submissions should be on high-contrast glossy paper, and must be unmounted and untrimmed, with a preferred size between 4 x 5 inches and 5 x 7 inches (10 x 13 cm and 13 x 18 cm). The figure number, name of first author and an arrow indicating "top" should be typed on a gummed label and affixed to the back of each illustration. If arrows are used these should appear in a different color to the background color. Titles and detailed explanations belong in the legends, which should be submitted on a separate sheet, and not on the illustrations themselves. Written informed consent for publication must accompany any photograph in which the subject can be identified. Written copyright permission, from the publishers, must accompany any illustration that has been previously published. Photographs will be accepted at the discretion of the Editorial Board.