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ORIGINAL RESEARCH

Effectiveness of A Clinical Protocol Implemented To Standardize Snakebite Management In Iran: Initial Evaluation

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Objective.—This study was designed to evaluate the effectiveness of a new protocol implemented to standardize snakebite management in Iran.

Methods.—In this study, 27 patients treated according to the new protocol in 2012 (P+) were compared with 22 patients treated according to the previous modality in the year before implementation of the protocol (P–) in Mashhad Medical Toxicology Centre (MTC). Demographic characteristics and treatment details of all patients were recorded prospectively. Envenomation severity of each victim was assessed according to snakebite severity score (SSS).

Results.—After implementation of the protocol, a smaller percentage of patients received antivenom (AV) therapy (78% vs 95%; $P = .079$). In spite of no significant difference in baseline severity of envenomation between the 2 groups (SSS [mean ± SD], 34.8 ± 18.1 vs 35.5 ± 17.4; $P = .801$), the P+ group received significantly fewer AV vials (8.4 ± 6.8 vs 12.1 ± 5.6 vials; $P = .042$) and had a significantly shorter length of hospital stay (2.2 ± 1.5 vs 3.2 ± 1.8 days; $P = .027$). Moreover, smaller proportion of P+ patients experienced recurrence of venom-induced effects; however, the difference was not significant (18.5% vs 36%; $P = .159$). The reduction in use of antiallergy treatments to prevent or treat acute hypersensitivity reactions approached statistical significance (41% vs 68%; $P = .051$). These findings denote a reduction in AV use of approximately 4 vials and a reduction in hospital stay of 1 day for each patient, which translates to approximately $196/patient in healthcare cost savings.

Conclusions.—Implementation of a snakebite management protocol at MTC reduced overall antivenom usage, use of antiallergy interventions, and length of hospital stay.

Key words: antivenoms, clinical protocols, comparative effectiveness research, Iran, snakebite

Introduction

Snakebite is a toxicologic emergency that was primarily treated according to anecdotal evidences, local experiences, and empirical basis until recent decades.[1–3] Thus, considerable attention has been devoted to development of unified integrated protocols for standardizing management of snakebite in different parts of the world.[3–6] In Iran, a comprehensive protocol has been recently introduced that conjoined antivenom (AV) dosage plan and recommendations for supportive treatments.[7] This is the first Iranian protocol that has been designed to standardize the AV dosage and indications to overcome shortcomings of previous guidelines and to clarify indications of supportive treatments.

Annually, snakebite involves 4500 to 6500 victims in Iran, causing 3 to 9 deaths.[2,8] The most prevalent medically important snakes in this country are *Echis sochureki, Macrovipera lebetina obtuse*, *Pseudocerastes persicus persicus,* and *Naja oxiana*: the first 3 belong to the Viperidae family, and the fourth is an Elpidae snake.[9,10] The current commercially available AV in Iran (Polyvalent Snake Antivenin, Razi Serum and Vaccine Research Institute, Iran) that has been manufactured during the past 5 decades is capable of counteracting the venoms of these snakes.[11]

Conflict of interest: The authors declare that they have no conflict of interest.

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Mashhad Medical Toxicology Centre (MTC) in Imam Reza Hospital is a referral medical toxicology department in northeast Iran that admits 25 to 60 snakebite victims each year with less than 1% mortality rate.[2] Snakebite events in this part of the country mostly occur during April to late October.[12] During the past 3 decades, a local treatment modality for snakebites mainly designed according to western references has been practiced in MTC.[2,8] Although the treatment modality has been effective in terms of saving many lives, its cost-benefit has remained obscure. Moreover, its effectiveness has been affected by differing interpretations of the grading of envenomation severity, undefined therapeutic response (or initial control), and unspecified indications for supportive treatments.[7] Hence, through elaborating the modality, rectifying its defects, and enhancing neglected aspects, an integrated protocol has been developed in MTC by a focus group of medical toxicologists and expert physicians in other areas of medicine.[7] The new protocol includes: 1) a grading scale that enabled a more objective assessment of victims (snakebite envenomation severity scale, SESS); 2) an algorithm consisting of planned course of action and AV dosing (Figure); and 3) a table of instructions for supportive treatments.

The aim of this study was to evaluate the effectiveness of the new protocol according to the overall AV volume administered to patients, morbidities, and duration of admission after its institution in 2012.

Methods

DESIGN AND SETTING

This was a prospective comparative study of snakebite victims admitted to MTC during 2011 and 2012. The study was started prospectively in 2011 with precise data collection of patients who were treated according to previous modality and continued with careful observation of the patients treated according to the new protocol in 2012.

PATIENTS

The patients treated according to the new protocol between April 1, 2012, and October 30, 2012 (P+), were compared with patients who received treatment according to the previous modality in the same period of the year before implementation of the protocol (P–). Demographic characteristics and clinical manifestations of all patients as well as treatment details were recorded in a predesigned checklist by 2 of us (S.M.M. and B.D.). At presentation, the envenomation severity of each victim was also assessed by these researchers according to the snakebite severity score (SSS).[13]

TREATMENTS

To start attacking the venom and promptly reversing the venom effects, a specified amount of the AV called the attack dose (or initial dose in other internationally recognized protocols) should be given to the patient at a relatively rapid rate. The attack dose may be repeated according to the patient's condition (subsequent attack dose). For maintaining a steady AV level in the blood to prevent venom–AV mismatch and recurrence of venom effects, the maintenance dose of AV should be infused at a slow rate. Differences between the 2 treatment plans rely on the definition of these doses, the rate of AV administration, the time to repeat antivenom, indication of supportive treatments, etc. The characteristics of the new protocol and the previous modality are summarized in Table 1. As shown, in the new protocol compared with the previous treatment modality:[7,8]

1. The grading system (SESS) has been defined with more details and has been simplified into 3 grades.
2. The extent of <2.5 cm has been defined as the threshold of edema that does not need to be treated. However, for bites on digits, any level of edema has been determined as an indication for AV administration.
3. The systemic venom effects have been clarified with more detailed definitions in the grading scale.
4. The highest AV volume at each attack dose has been limited to 10 vials, half of the amount recommended in the previous treatment modality.
5. The infusion rate of the attack dose has been increased.
6. Therapeutic response has been defined and its assessment has become mandatory.
7. Administration of subsequent attack doses depended on the failure to achieve the therapeutic response.
8. The maintenance dose and the dose for recurrence of venom-induced effects have been fixed at 5 vials.
9. The maximum of total attack doses (upper limit of AV attack dosage) has been set at 20 vials except for uncontrollable bleeding and critically ill patients.
10. The skin test has been discontinued.
11. Pretreatment for immediate allergic reactions (IARs) has been limited to severe atopic syndrome and previous sensitization to biological products.
12. The time to discharge has been defined as 18 hours after admission after 4 normal 20-minute whole-blood clotting tests (20-minute WBCT) for minimal cases and 24 hours after stabilization of severe and very severe cases.