Paper

Use of antivenom serum in snake bite: a prospective study of hospital practice in the Gampaha district

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(Key words: Antiserum use, antiserum adverse reactions)

Abstract

Objective To record current practices in hospital management of snake bite, especially with regard to use of antivenom serum (AVS).

Methods Management of all snake bite victims admitted to the four main hospitals of the Gampaha district was prospectively studied during a 5-month period. A pretested data collection sheet was used. Relevant information was obtained from patients, accompanying persons, medical staff and hospital records.

Results 466 patients (M:F = 7:3; 402 adults and 64 children) were admitted following snake bite during the study. The offending snake was identified in 357 (76.6%) cases [172 (36.9%) by examining the dead snake, 185 by identification of the snake in a photograph]. 273 (76.5%) of the 357 admissions were due to hump nosed viper bite. AVS was given to 184 (39.5%) patients, including 99 (36.3%) with hump nosed viper bite. A sensitivity test of AVS was used in all 184 patients. Premedication with hydrocortisone and/or antihistamines before AVS infusion was given to 89 patients. Acute adverse reactions to AVS occurred in 102 (55.4%) patients given AVS. There was no significant difference in the rate of reactions whether premedication was given or not.

Conclusion Precise identification of the offending snake was not possible in many instances. Practices that are of no benefit in the treatment of snake bite are still widely used. Acute adverse reactions to AVS are common, and neither hydrocortisone nor antihistamines seem to be of benefit as prophylaxis. Evidence based management guidelines, especially with regard to AVS therapy, are urgently required.

Introduction

Sri Lanka has one of the highest snake bite fatality rates in the world (1). Much of the morbidity and about 95% of the mortality associated with snake bite here are associated with the bites of the highly venomous snakes, the cobra, Russell's viper, Sri Lankan krait and common krait (2). Information regarding management of snake bite from our hospitals is derived mainly from retrospective analyses of hospital records, in which the documentation is, in most instances, inadequate.

AVS is the only effective therapy available for treatment of snake bite envenomation. The AVSs available in Sri Lanka are polyvalent equine sera produced in India, namely, the Haffkine AVS and the Serum Institute of India AVS. These are effective against the venom of the cobra, Russell's viper, saw scaled viper and the kraits. Although these two polyvalent AVSs are made against venoms of Indian species and subspecies of these four snakes, clinical impressions are that they seem to be effective against envenoming by their Sri Lankan counterparts (3). Adverse reactions to AVS are common (4,5,6,7,8) despite improvements in manufacturing processes (9). They occur in about one-third to half the patients given AVS available in Sri Lanka (10,11). Anaphylaxis can be fatal unless emergency treatment is given. Several methods have been used in attempts to reduce acute adverse reactions to AVS. The use of a small test dose of AVS, administered intravenously, intradermally or to the conjuctiva, to detect patients who may develop reactions to antivenom, is no longer recommended as it is insensitive (5) and can give rise to anaphylaxis by itself (12). The prophylactic use of antihistamines before AVS infusion is widely practised, especially in many South American countries (13), but a recent placebo controlled study has shown promethazine to be ineffective in preventing acute adverse reactions to AVS in patients with *Bothrops* snake bite (14). Hydrocortisone takes time to act, and will not be effective prophylaxis against acute reactions that develop immediately after AVS. It has recently been shown that the prophylactic use of 1:1000 adrenaline, in a dose of 0.25 ml subcutaneously, immediately before infusion of AVS, significantly reduces the risk of acute adverse reactions to AVS (19).

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The aim of this study was to record current practices in the management of snake bite in the four main hospitals in the Gampaha district, especially with regard to use of AVS.

Methods

The Gampaha district has a population of about 1.6 million, and is served by one Teaching Hospital and three Base Hospitals. Admissions following snake bite to these hospitals are frequent. The management of all patients admitted with a history of snake bite to the four main hospitals in the Gampaha district – Colombo North Teaching Hospital at Ragama, Base Hospitals at Gampaha, Negombo and Wathupitiwela – during a 5-month period from 1 December 1997 to 30 April 1998 was studied prospectively. A data collection sheet was designed to obtain relevant information. It was pretested on a sample of 25 patients admitted to the Colombo North Teaching Hospital, Ragama, following snake bite before the main study.

Six medical students trained to gather relevant data visited the medical and paediatric ward of the four hospitals at least every other day. They were supervised by a registrar grade medical officer. Information was obtained from the patient, accompanying persons, ward staff and hospital records. The data were entered at the time of their visit to each hospital. Identification of snakes was considered accurate only if the dead snake was brought to the hospital or if the patient identified the snake when shown a photograph.

Results

There were 466 patients admitted with snake bite to the four hospitals during the study period. Of these 402 were adults [median age 38 years (range 14 to 68)] and 64 were children [median age 8.4 years (range 1 to 12)]. The male to female ratio was 7:3. The snakes responsible and the number of patients given AVS therapy are shown in the Table. The snake was identified in 357 (76.6%) of cases. 172 (36.9%) patients brought the dead snake to the hospital, and the offending snake was identified by the patient when shown a photograph in 185 cases. In total, AVS was given to 184 (39.5%) of the 466 patients. Indications for AVS therapy were systemic envenomation in 70 patients and significant local envenomation (swelling of more than half the bitten limb, necrosis at the site of the bite or regional lymphadenopathy) in 114. There were two deaths (0.43%), one from renal failure following a Russel's viper bite and the other from respiratory failure following a cobra bite.

All patients who required AVS were given Haffkine polyspecific antivenom serum (Haffkine Laboratories, Mumbai, India) by intravenous infusion. The intial dose was 10 to 20 vials of AVS in adults and 5 to 10 vials in children. AVS was repeated as required. An intravenous test dose of antivenom before administering the full infusion (sensitivity testing) was given to all patients who received AVS. Premedication before the AVS infusion was given in 89 patients. The premedication given included intravenous hydrocortisone alone (n=33), promethazine alone (n=4), chlorpheniramine alone (n=3) or various combinations of these drugs (n=49). Adrenaline was not used as a premedication in any patient. Acute adverse reactions to AVS occurred in 102 (55.4%) of the 184 patients given antivenom. The reactions were considered by the doctors treating the patients to be mild in 64 patients, moderate in 30 and severe in 8. They were treated with adrenaline, hydrocortisone and either promethazine or chlorpheniramine. There was no significant difference in the rate of reactions to AVS between the patients given some form of premedication 47 (52.8%) compared to patients who did not receive any premedication 55 (57.9%).

Table. Type of snake responsible for bite and the number of patients given AVS therapy

Type of snake	*Number bitten*	*Number (%) given AVS*
Unidentified	109	28 (25.7)
Non venomous	18	Nil
Hump-nosed viper	273	99 (36.3)
Russell's viper	52	45 (86.5)
Cobra	11	9 (81.8)
Kraits	3	3 (100)
Total	466	184 (39.5)

Discussion

Hospital mortality from snake bite was low, and this is probably due to early use of AVS. The high proportion of bites by the hump nosed viper, a moderately venomous snake, may be another reason for the low mortality. One of the first problems encountered in the management of snake bite is the identification of the offending snake. Species immunodiagnosis is not available in Sri Lanka. Many victims do not bring the dead snake to hospital (3,15,16). In the present study less than 40% did so. Examining the dead snake is the gold standard for species identification. Identification by showing a photograph or specimen of the snake to the victim is possible, but not as reliable as examining the dead snake. Other methods of identification are inaccurate. The problem regarding identification of the snake has an important implication for AVS therapy, in that, monovalent antivenoms may be inappropriate to treat many of our snake bite victims.

About 40% of the victims required AVS in the present study. This relatively low figure is probably because 58.6% of the bites were by the hump nosed viper. The appropriateness of AVS therapy, the dose selected, use of sensitivity testing for AVS, premedication for prevention of adverse reactions to AVS and the rate of AVS infusion in our hospitals, are usually arbitrarily decided, and depend on individual doctors. Some of the practices in snake bite management observed in our study reveal this unsatisfactory state of affairs. Despite clinical evidence that Haffkine AVS is not effective against hump nosed viper venom (11), 36.3% of patients with bites by this snake were given this AVS. There is no other effective antivenom available against venom of the hump nosed viper which accounts for a majority of snake bites in Sri Lanka (2). A specific antiserum against its venom is clearly required.

Acute adverse reactions to AVS are common. Even monovalent antivenoms have a high frequency of adverse effects (18). Adverse reactions occurred in about 55% of patients in the present study. Despite being an insensitive and potentially dangerous procedure, sensitivity testing was performed on all patients. The use of premedication to prevent acute adverse reactions to AVS was also not based on scientific evidence. Various combinations of hydrocortisone and antihistamines were used without any apparent benefit. In a double blind placebo-controlled trial conducted in Polonnaruwa we found that premedication with adrenaline significantly reduces the risk of acute adverse reactions to AVS (19). Before our trial, a few uncontrolled retrospective studies from Australia (20) also suggested that adrenaline was safe and seemed to be effective in reducing acute adverse reactions to AVS. A major concern regarding the use of adrenaline as premedication is the potential risk of intracerebral haemorrhage and hypertension. This has led to a reluctance to use adrenaline. Few studies have analysed the risk of cerebral haemorrhage following adrenaline. Of 7 cases of fatal intracerebral haemorrhage following snake bite documented in Australia, only 3 had received adrenaline as premedication (8). Fears of development of hypertension following low dose adernaline also seem unfounded (21). No adverse effects attributable to adrenaline were observed during the trial in Polonnaruwa (19).

The present study shows up some shortcomings in the management of snake bite in our hospitals. Two of the most important are need for development of a specific antivenom against the hump nosed viper, and the use of effective prophylaxis against acute adverse reactions to AVS. We recommend that clear management guidelines be made available soon, especially with regard to AVS therapy. These guidelines should preferably be based on evidence rather than on the experience of individuals.

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Early problems with the NHS (UK)

One general practitioner sent many of his patients straight to the medical or surgical outpatient department at the hospital where I worked. They would be carrying his business card with a note scribbled on the back that might say "check abdomen" if the patient had complained of a bellyache or "check chest" if the poor soul had a cough. One day, my mentor at the hospital responded to one of these occurrences by writing on the card, sealing it in an envelope, and asking the patient to return it to the general practitioner.

"What did you write?" I innocently asked, wondering at the smirk on my senior colleague's face.

"I wrote 'chest present' " he replied. "Now, for once, the lazy bugger will have to sort it all out by himself."

Anderson EG. Doing the right thing for US healthcare. *Postgraduate Medicine* 2000; **107**: 13-15 (Editorial).