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Continued overleaf

Anti-venom for snakebite in Sri Lanka

We need an effective, low reactogenic, affordable and polyvalent AVS

Sri Lanka has one of the highest snakebite rates in the world. Although there are 92 species of snakes in this country, much of the morbidity and about 95% of the mortality associated with snakebites are due to the highly venomous cobra, Russell's viper and kraits (1). The hump-nosed viper, a moderately venomous snake, accounts for about 27% of all snakebites in Sri Lanka, with marked geographical variation (1,2). Its bites cause predominantly local effects such as pain and swelling at the site of the bite, but coagulopathy from excessive fibrinolysis has been reported to occur in about 20% of cases (3). Renal impairment has also been reported, but death due to hump-nosed viper bite is rare (1,2,3,4).

In the year 2000, over 37 000 patients were treated for snakebite in Sri Lankan government hospitals (5). The national figure for snakebite is likely to be much higher, as many of the victims do not have the opportunity for or do not seek hospital treatment. Hospital mortality has fallen greatly over the last 15 years from a hospital case fatality rate of 3.5% in 1985 to 0.5% in 2000 (5). The current low hospital case fatality rates have been confirmed by several independent studies (6,7,8). The most important reason for this fall in mortality is the wide availability and prompt administration of anti-venom serum (AVS), the only effective treatment for snakebite envenoming. Other probable contributing factors are an increased public awareness of the availability of effective treatment for snakebite that encourages early presentation to hospital, and improvements in intensive care in many hospitals situated in areas where snakebite is common (8).

One of the obstacles faced by doctors treating snakebite in this country is that precise identification of the offending snake is often not possible, as the snake is brought to hospital with the victim in less than half the cases (6,7). This may be because the majority of bites occur in men working in paddy fields or forests where it may be difficult to see or kill the snake. Other reasons may include the night biting habits of kraits, and cultural and religious reasons for not killing cobras. Immunodiagnosis of the offending species is not available in Sri Lanka. This procedure, though useful as a research tool, is time consuming, and would add to the already high cost of snakebite management. It is unlikely to be practicable in the rural hospitals where many patients with snakebite seek treatment. Under these circumtances it is much more appropriate to use polyvalent rather than species specific monovalent AVS; it may be positively dangerous to use monovalent AVS when the identity of the offending snake is in doubt.

AVS currently available in Sri Lanka is polyvalent equine serum manufactured in India. Both the widely used Haffkine (Haffkine Laboratories, Mumbai) and Serum Institute of India (Pune) products are effective against venoms of the cobra, Russell's viper, common krait and saw-scaled viper. They are not effective against the venom of the hump-nosed viper (9). These anti-sera have been used in Sri

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Lanka for decades, and although they are produced against venoms of the Indian subspecies of these snakes, the clinical evidence, published and otherwise, is that they are effective against the venoms of their Sri Lankan counterparts as well. In fact, a recent trial found that the currently available polyvalent Haffkine AVS was more effective than a monovalent AVS – Polonga-Tab – that is prepared specifically against Sri Lankan Russell's viper venom (10).

Adverse effects of AVS are common, and include anaphylaxis. Several methods have been used in attempts to reduce them. A small test dose of AVS to detect patients who may develop reactions to antivenom is insensitive, can itself give rise to anaphylaxis, and is no longer recommended (11). The prophylactic use of antihistamines is ineffective (12). As hydrocortisone takes time to act, this too is unlikely to be effective. Low dose adrenaline given subcutaneously immediately before administration of AVS to snakebite victims significantly reduces incidence of acute adverse reactions to the serum (7). Its use in this manner has now been recommended in the Cochrane database (13). However, a major concern regarding use of adrenaline is the risk of intra-cerebral haemorrhage (14). A paper published in this issue of *CMJ* investigating the safety of subcutaneous adrenaline reports a death due to probable cerebral haemorrhage (15). Although the death in this instance was unlikely to be directly related to the use of adrenaline, the authors recommend further studies on the safety of this treatment before it is used routinely. For the present the most acceptable alternative to prevention is the early detection of adverse reactions to AVS, especially anaphylaxis, and the ready availability of drugs such as adrenaline for their prompt treatment.

The reported rates of adverse reactions to the polyvalent AVS used in Sri Lanka vary from about 30% to 68% (6,7,8,16,17,18), but only a small proportion (5% to 10%) of these reactions appear to be severe (6,7,8). The overall rate of adverse reactions reported with the monovalent antivenom Polonga-Tab is 34% (19), and this too at what the authors themselves admit to being sub-optimal doses of the antiserum (10). There is also concern about the possibility of more frequent adverse reactions with the use of a more effective higher initial dose of Polonga-Tab (10).

Another important consideration regarding treatment of snakebite envenoming with AVS is cost. Firstly, AVS should not be used inappropriately. Unfortunately, practices such as administering Haffkine AVS for hump-nosed viper bites still continue (6) and must be strongly discouraged. The average dose (10 g) of the presently available Haffkine polyvalent AVS costs about Rs. 8 000 per patient. The monovalent Polonga-Tab costs Rs. 43 000 per patient, and this too at a sub-optimal dose of 1g (10). Snakebite is a major health problem in many parts of India (20,21) causing an estimated 10 000 to 50 000 deaths annually (22). AVS exports from India to Sri Lanka are probably only a small fraction of the quantity that is manufactured in that country. Hence there are no grounds for undue concern regarding either the continued production of AVS in India, or of adequate supplies to Sri Lanka. Although development of less reactogenic local antivenoms should be encouraged it is important to bear in mind the cost factor, and the situation here, where identifying the offending snake is a problem most of the time as a consequence of which AVS must necessarily be polyvalent. What may be important is to develop an anti-venom against the venom of the hump-nosed viper, and include it in the polyvalent AVS 'cocktail', rather than attempting to develop expensive new substitutes to currently available, effective, and relatively much cheaper AVS.

What doctors treating snakebite envenoming in Sri Lanka require is an effective, low reactogenic, cheap, and most importantly, a polyvalent AVS. Until that becomes available the currently available antisera imported from India, seem good enough. To increase the safety of the Indian AVS inappropriate use should be avoided and adverse reactions that may occur should be detected and treated promptly.

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