Cross Neutralization of Afro-Asian Cobra and Asian Krait Venoms by a Thai Polyvalent Snake Antivenom (Neuro Polyvalent Snake Antivenom)

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Abstract

Background: Snake envenomation is a serious public health threat in the rural areas of Asian and African countries. To date, the only proven treatment for snake envenomation is antivenom therapy. Cross-neutralization of heterologous venoms by antivenom raised against venoms of closely related species has been reported. The present study examined the cross-neutralizing potential of a newly developed polyvalent antivenom, termed Neuro Polyvalent Snake Antivenom (NPNAV). NPAV was produced by immunization against 4 Thai elapid venoms.

Principal Findings: In vitro neutralization study using mice showed that NPAV was able to neutralize effectively the lethality of venoms of most common Asiatic cobras (Naja spp.), Ophiophagus hannah and kraits (Bungarus spp.) from Southeast Asia, but only moderately to weakly effective against venoms of Naja from India subcontinent and Africa. Studies with several venoms showed that the in vivo neutralization potency of the NPAV was comparable to the in vitro neutralization potency. NPAV could also fully protect against N. sputatrix venom-induced cardio-respiratory depressant and neuromuscular blocking effects in anesthetized rats, demonstrating that the NPAV could neutralize most of the major lethal toxins in the Naja venom.

Conclusions/Significance: The newly developed polyvalent antivenom NPAV may find potential application in the treatment of elapid bites in Southeast Asia, especially Malaysia, a neighboring nation of Thailand. Nevertheless, the applicability of NPAV in the treatment of cobra and krait envenomations in Southeast Asian victims needs to be confirmed by clinical trials. The cross-neutralization results may contribute to the design of broad-spectrum polyvalent antivenom.

Introduction

The global figure of snake envenoming cases has been estimated to be greater than 1.8 million annually, with an annual death toll of more than 90,000. Most of the snake envenoming cases occurs in South Asia and Southeast Asia (estimated 720,000 cases, 53,000 fatality), followed by Africa (estimated 420,000 cases, 32,000 fatality) [1], and the main biting species are snakes from the Elapidae and Viperidae families. Among members of the Elapidae family, the cobras and kraits are the main causes of snake envenoming [2,3]. There are about 34 species of cobras belonging to 7 genera (Aiphielaps, Boaenglerina, Hemachatus, Naja, Ophiophagus, Pseudhaje and Wallironnestia). The genus Naja distributed extensively across large regions of the Africa (13 species) and Asia (12 species) [4]. Ophiophagus hannah or commonly known as the king cobra, is the only member of the Ophiophagus genus and is found only in Asia. Bungarus (the kraits), are represented by 12 species and their distribution is confined to the Indian subcontinent, Southeast Asia, as well as Southern China and Taiwan [4]. Cobra and krait envenomations are generally characterized by neurotoxic envenoming [5].

Antivenom therapy is the only effective treatment for snake envenomation. Monovalent antivenoms are raised with venom from one particular species and hence generally only effective in the treatment of envenomation caused by the particular species. Because of the difficulties in accurate diagnosis of the biting species, polyvalent antivenoms that offer parascriptic protection against several venomous snake bites have also been developed and become commercially available. It has been argued that monovalent antivenoms are generally more effective than polyvalent antivenoms, though this has not been firmly established. At present, several types of polyvalent antivenoms against Afro-Asian venomous snakes are available in the market, produced mainly by Asian or African commercial pharmaceutical firms or government institutions [5,6]. There is, however, a lack of rigorous evaluation of the parascriptic protective actions of these commercially available polyvalent antivenoms. Recently, Thai Red Cross Society produced a new polyvalent antivenom that offers...