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Review Article

THE PREVALENCE OF INDIAN COMMON KRAIT ENVENOMATION AND ITS CLINICAL COMPLICATIONS AMONG THE RURAL POPULATIONS OF INDIA

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ABSTRACT

Snake envenomations have been a serious yet often overlooked public health threat especially in tropical and subtropical countries, including Southeast Asia. The medically important venomous land snakes in Southeast Asia include snakes from the Elapidae and Crotalidae families. Among the elapids, there are only 12 species that are considered of medical importance, represented by the kraits (*Bungarus caeruleus*, *B. candidus*, *B. fasciatus*, *B. flaviceps* and *B. multicinctus*). The incidence of snakebite is high in India. Apart from mortality, the morbidity is due to various complications. The common krait (*Bungarus caeruleus*) is the most toxic snake found commonly in the plains of throughout the India and the number of snakebites in the rural areas of India was recorded by this snake. The present article highlights the prevalence and the clinical complications of Indian common krait envenomation among the rural populations of India.

Keywords: snake bite, common krait, clinical complications and rural area

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INTRODUCTION

Alexander the Great who invaded India in 326 BC, was greatly impressed by the skills of Indian physicians, especially in the treatment of snakebites (Jaggi, 2000). Since then, India has remained notorious for its venomous snakes and the effects of their bites. With its surrounding seas, India is inhabited by more than 60 species of venomous snakes, some of which are abundant and can cause severe envenoming (Whitaker, 2004).

Snake envenomations have been a serious yet often overlooked public health threat especially in tropical and subtropical countries, including Southeast Asia

(Kasturiratne *et al.*, 2008; Chippaux, 2006). The medically important venomous land snakes in Southeast Asia include snakes from the Elapidae and Crotalidae families. Among the elapids, there are only 12 species that are considered of medical importance, represented by the kraits (*Bungarus caeruleus*, *B. candidus*, *B. fasciatus*, *B. flaviceps* and *B. multicinctus*), the Asiatic cobras (including *Naja kaouthia*, *N. sumatrana*, *N. siamensis*, *N. sputatrix*, *N. philippinensis* and *N. atra*), and the king cobra (*Ophiophagus hannah*) (Warrell, 1999).

The incidence of snakebite is high in India. Apart from mortality, the morbidity is due to various complications

(Narvencar, 2006). Approximately 10000 to 50000 snakebite related deaths occur in India each year (McNamee, 2001). A majority of the deaths are caused by neurotoxic envenoming by kraits and cobras in India's rural population (McNamee, 2001; Warrell, 1999). Snakebite is common in subtropical countries with heavy rainfall and humid climates (Banerjee, 1978).

Snake bite affects South Asia than anywhere else in the world with very high morbidity and mortality. Identification of the offending snake often facilitates clinical management of the patient (Alirol, *et al.*, 2010). Awareness of the fact had led the public to carry offending snakes killed or alive, to hospital together with snake bite victims when possible. However, even if the offending snake is authenticated, incorrect authentications also had led to inappropriate management (Nishioka and Silveira, 1994; Ariaratnam *et al.*, 2009).

Some snake species are often misidentified due to morphological resemblance to other snakes. For example, highly venomous Kraits are often misidentified as non-venomous Wolf snakes or vice-versa due to notoriously similar colour patterns (Fernando, 1997).

Immunodiagnostic techniques like Enzyme linked Immunosorbent Assay is increasingly being used to accurately authenticate the offending snake in snake bite cases in some countries (Ho *et al.*, 1986). However, since these techniques are not yet available in routine practice in India, conventional snake identification methods like morphological studies are still useful.

Indian common krait (*Bungarus caeruleus*)

The *B. caeruleus* snake has strong neurotoxic venom, envenomation by *B. caeruleus* causes hemorrhage, tissue necrosis and hemostatic disorders in the experimental animal. Furthermore, it shows high proteolytic activity towards casein and human fibrinogen (Rajana *et al.*, 2013).

The common krait (*Bungarus caeruleus*) is regarded as the most dangerous species of venomous snake in the Indian subcontinent (Theakston *et al.*, 1990). The most villagers in India usually sleep on the floor of their area, which are often surrounded by dense vegetation (Bawaskar, 2002). Although not vicious by nature, the krait may strike a person sleeping on the ground if the person accidentally touches or rolls over onto the snake (Kulartane, 1997). Also, the snake could mistakenly identify an exposed body part as prey. Most bites occur during the cooler months of June to December when snakes may, during the course of their hunting activity, linger in a person's bedding to take advantage of the warmth therein (Bawaskar, 2002; Kulartane, 1997). The common krait (*Bungarus caeruleus*) is the most toxic snake found commonly in the plains of Northwest India and bites typically occur during July–September (Sharma *et al.*, 2005; Chauhan *et al.*, 2005; Aggarwal *et al.*, 2005). Kraits are elapid snakes and within the single genus *Bungarus*, 12 species are found (Keogh, 1998). They are generally nocturnal, shy and non-aggressive. Their diet consists of other snakes and it will therefore pursue them into human habitation, where the prey

species are hunting for rodents. Bites generally occur when kraits are disturbed by sleeping humans moving, either naturally, or during rapid eye movement (REM) sleep (Kularatne, 2002).

The major neurotoxic component of krait venom is β -bungarotoxin, which has high affinity for presynaptic neuromuscular receptors. It irreversibly blocks these receptors and is completely resistant to anticholinesterase treatment (Watt *et al.*, 1986).

Components of krait venom

Krait venom possess a wide variety of toxins and enzymes including neurotoxins, membrane toxins, cardiotoxins, 3 finger toxins (3FTXs), PLA2s, metalloproteinases, cholinesterases, L-amino acid oxidases, serine proteases etc. (Rusmili *et al.*, 2014). α -bungarotoxin, the first postsynaptic neurotoxin isolated from *Bungarus multicinctus*, inhibited the response of acetylcholine receptor on motor endplate and irreversibly blocked the transmission (Chang and Lee, 1963; Lee and Chang, 1966; Jiang *et al.*, 1986). The other postsynaptic neurotoxins isolated from *Bugnagus sp.* include TI, TH, κ -bungarotoxin, κ 2-bungarotoxin and κ 3-bungarotoxin, ceruleotoxin, alphaN3 and Bucain (Hsu *et al.*, 1985; Grant and Chiappinelli, 1985; Chiappinelli *et al.*, 1990; Bon *et al.*, 1975; Karsani and Othman, 2009; Murakami *et al.*, 2009). β -bungarotoxin, γ -bungarotoxin and Toxin F are presynaptic neurotoxins isolated from *Bugnagus sp.* Venom (Chang and Lee, 1963; Rehm and Betz, 1984; Tsai *et al.*, 2007; Chang *et al.*, 2002; Loring *et al.*, 1984). Phospholipase A2 (PLA2) is also an important constituent of *Bungarus sp.* venom (Liu *et al.*, 1988; Liu *et al.*, 1989; Khow *et al.*, 2002; Tsai *et al.*, 2007). The enzyme L-amino acid oxidase (LAAO) found in *Bungarus sp.* venom plays a major role in inducing toxicity (More *et al.*, 2010; Wei *et al.*, 2009). A number of protease inhibitors have been identified from krait venom (Zhang *et al.*, 1995; Lu *et al.*, 2008; Chen *et al.*, 2015; Siang *et al.*, 2010; Khow *et al.*, 2003). Cholinesterase was also purified from *B. fasciatus* venom through fractional precipitation with ammonium sulfate (Ghosh and Chaudhuri, 1968).

Clinical complications of Krait venom:

Envenoming due to krait (Genus: *Bungarus*) bites is a common, serious health issue in South and South-East Asia. Common krait (*Bungarus caeruleus*) is distributed throughout South Asia, and is responsible for large numbers of cases of severe neurotoxic envenoming each year (Valenta, 2010). It results in a descending flaccid paralysis progressing to life threatening respiratory paralysis unless mechanical ventilation is available (Alirol *et al.*, 2010; Pe *et al.*, 1997; Kularatne, 2002). Krait bites typically occur at night and are not painful; so many patients do not notice the bite and continue sleeping (Bawaskar and Bawaskar, 2004; Warrell *et al.*, 1983; Ariaratnam *et al.*, 2008), which delays medical care. Neuromuscular paralysis in krait envenoming is characterized by progressive descending paralysis. Krait venom contains β -bungarotoxins, which are presynaptic neurotoxins with phospholipase A activity and considered to be the major cause of paralysis. The presynaptic action is irreversible and is the reason that once

paralysis develops it is not reversed with antivenom (Dixon, 1999).

The pathophysiology of neuromuscular paralysis in snake envenoming remains poorly understood. This is due to the lack of detailed clinical studies of authenticated bites that report the time course of paralysis, including the recovery of paralysis, and very few studies of neurophysiological function in snake envenoming. There is also little evidence for the effectiveness of antivenom in reversing neuromuscular paralysis (Johnston, *et al.*, 2012). Neurophysiological testing could provide objective evidence of the progression and recovery of neurotoxicity, and the response to antivenom. Previous neurophysiological testing in krait bites with nerve conduction studies and repetitive nerve stimulation tests provide some information on krait neurotoxicity. Single fibre electromyography (sfEMG) is a more sensitive test of neuromuscular function (Richardson, *et al.*, 2007). It has only been reported in one study of neuromuscular paralysis from Papuan taipan envenoming (Sanders, 2002). Better methods to measure neuromuscular dysfunction in neurotoxic envenoming will improve our understanding of neuromuscular paralysis and the clinical benefit of antivenom.

Clinical complications:

Indian Krait is distributed in India, Bangladesh, Pakistan, Nepal and Sri Lanka. Bites by these snakes lead to high morbidity and mortality in the region, often leading to death of the victim, if not intervened (Warrell, 1995). Indian Krait is known to cause most of the bites during night, when the victim is sleeping (Kularatne, 2002). Indian Kraits cause a clinical syndrome characterized by negligible local envenoming, vomiting, abdominal pain and descending paralysis that at times start as soon as 30 min after the bite which could be delayed for up to 4 h (Ariaratnam *et al.*, 2008). Although ptosis, external ophthalmoplegia, dysphagia, drowsiness, altered consciousness and deep coma also had been commonly reported following envenoming by this snake, reports on prolonged WBCT in Indian Krait bite victims has been very rare (Kularatne, 2002). On the contrary, Sri Lankan Russell's viper (*Daboia russellii*) frequently causes both neurotoxicity and coagulopathy in the victims (Kularatne, 2003). However, Kularatne reported mottling haemorrhages in viscera and adrenal bleeding in one victim of Indian Krait who died due to shock, however with no clinical details (Kularatne, 2002). In addition, the same study revealed occurrence of mucosal haemorrhages in stomach of 3 of the 16 deceased victims of Indian Krait bite. Therefore, altered coagulation and haemorrhages as evident from the laboratory and post-mortem findings of the victim suggest rare clinical presentations of anti-coagulant effects of Indian Krait venom.

Treatment of Snakebite:

The treatment of snakebite is as variable as the bite itself. The only available treatment is the usage of antivenom against snakebite. The first antivenom (called an anti-ophidic serum) was developed by Albert Calmette, a French scientist of the Pasteur Institute in

1895, against the Indian cobra (*Naja naja*). Antivenom binds to and neutralizes the venom, stopping further damage, but do not reverses the damage already done. Some individuals may react to the antivenom with immediate hypersensitivity reactions. Other alternative treatment involves the usage of folk and traditional medicines in snake bites. Medicinal herbs are the local heritage in the global importance. Various plants have been used against snake bite, in folk and traditional medicine. In Ayurvedic system of medicine different plants and their compounds are reported to possess antisnake venom activity. But they also possess these individual toxicities and most of the folk medicinal plants have no scientific validation (Gomes *et al.*, 2010; Cannon *et al.*, 2008).

Currently, a large number of plants and plant materials are being screened for pharmacological activities especially those used in traditional or folk medicine against different diseases. Over the years, many attempts have been made for the development of snake venom antagonists especially from plant sources in spite of the existence of antiserum. Many Indian medicinal plants or plant materials are recommended for the treatment of snakebite and some are tested, but so far no systematic analysis has been done (Alam and Gomes, 2003; Chopra, *et al.*, 1956; Nazimudeen *et al.*, 1978).

The common krait (*Bungarus caeruleus*) is the most toxic snake found commonly in the plains of Northwest India and bites typically occur during July—September (Sharma *et al.*, 2005; Chauhan *et al.*, 2005; Aggarwal *et al.*, 2005). Kraits are elapid snakes and within the single genus *Bungarus*, 12 species are found (Keogh, 1998). They are generally nocturnal, shy and non-aggressive. Their diet consists of other snakes and it will therefore pursue them into human habitation, where the prey species are hunting for rodents. Bites generally occur when kraits are disturbed by sleeping humans moving, either naturally, or during rapid eye movement (REM) sleep (Kularatne, 2002). A significant number of patients die before they reach the hospital, largely due to the fact that the bite does not inflict sufficient pain or as a result of the bite itself or venom action and the victims are therefore unaware that they have been bitten.

Common venomous snakes found in the Indian subcontinent are kraits, cobras, and carpet vipers (*Echis carinatus*). Kraits are nocturnal, terrestrial snakes that enter human dwellings in search of prey such as rats, mice, and lizards (Bawaskar, 2002).

Spectacled cobra (*Naja naja*), common krait (*Bungarus caeruleus*), saw-scaled viper (*Echis carinatus*) and Russell's viper (*Daboia russellii*) have long been recognised as the most important, but other species may cause fatal snakebites in particular areas, such as the central Asian cobra (*Naja oxiana*) in the far north-west, monocellate cobra (*N. kaouthia*) in the north-east, greater black krait (*B.niger*) in the far north-east, Wall's and Sind kraits (*B. walli* and *B. sindanus*) in the east and west and hump-nosed pit-viper (*Hypnale hypnale*) in the south-west coast and Western Ghats (Whitaker, 2004).

Herbal remedies for Snakebite

Extracts from plants have been used among traditional healers, especially in tropical areas where there are plentiful sources, as therapy for snakebite for a long time. Several medicinal plants, which appear in old drug recipes or which have been passed on by oral tradition, are believed to be snakebite antidotes. Many Indian medicinal plants are recommended for the treatment of snakebite (Meenatchisundaram *et al.*, 2008). Accurate records to determine the exact epidemiology or even mortality of snake bite cases are generally unavailable. Hospital records fall far short of the actual number, owing to dependence on traditional healers and

practitioners of witchcraft, especially in developing countries. It has been reported that in most developing countries, up to 80% of individuals bitten by snakes first consult traditional practitioners before visiting a medical centre. Owing to the delay, several victims die during journey to the hospital (Hasson *et al.*, 2009)

CONCLUSION

Snakebite is being one of the dangerous health hazards in tropical countries especially in India. The data present in this paper will help the reader to understand the snake venom, Indian common krait, composition of krait venom and the clinical complications of the krait bite treatment.

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