Cross reactivity and lethality neutralization of venoms of Indonesian Trimeresurus complex species by Thai Green Pit Viper Antivenom

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ABSTRACT

Arboreal pit vipers of the Trimeresurus complex group are medically important species in Indonesia (west of Wallace's line) but there is no specific antivenom produced in the country for treating related envenomation. Instead, the existing trivalent Indonesian antivenom, Bioavé® Serum Anti Bisa Ular (SABI), indicated for envenoming by Malayan pit viper, Javan spitting cobra and Banded krait is often misused to treat Trimeresurus envenoming resulting in poor therapeutic outcome. Here, we investigated the cross-reactivity and neutralization capability of Thai Green Pit Viper Antivenom (GPVAV) against the venoms of four Indonesian Trimeresurus species. Consistently, the venoms of Trimeresurus (Trimeresurus) insularis, Trimeresurus (Trimeresurus) porphyraceus, Trimeresurus (Paraha) nagini and Trimeresurus (Crassocophus) puniceps of Indonesia showed stronger immunoreactivity on ELISA to GPVAV than to Bioavé®. The findings correlated with in vivo neutralization results, whereby GPVAV was far more effective than Bioavé® in cross-neutralizing the lethality of the venoms by a potency of at least 13 to 80 times higher. The efficacy of GPVAV is partly attributable to its cross-neutralization of the procoagulant effect of the venoms, thereby mitigating the progression of venom-induced consumptive coagulopathy. The paraspecific effectiveness of GPVAV against Trimeresurus species envenoming in Indonesia awaits further clinical investigation.

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1. Introduction

Snake envenomation is a major public health problem that primarily affects the poor rural populations in the tropics. The global mortality of venomous snake is estimated to be between 20,000 and 125,000 deaths annually, with more suffering from debilitating complications (Chippaux, 1993; Kasturiratne et al., 2006; WHO, 2016). Despite presenting as a global challenge, snake envenomation needs to be addressed by region-specific strategy, in particular the development and the assessment of antivenom (Tan et al., 2015c; Warrell et al., 2013; WHO, 2016). The use of antivenom is restricted by its species-specificity and geographical relevance. Being an orphan drug targeted mainly for the poor, antivenom production generates low commercial value and attracts little pharmaceutical interest, in spite of its listing under the WHO class of essential medicines (http://www.who.int/medicines/publications/essentialmedicines/en/).

In many regions, the scientific literature of local snake venoms and their neutralization remains limited, further contribuating to the neglect of appropriate management for snake envenoming. Myths and inappropriate practices based on pseudoscience has dominated the subject of snake treatment, not only by traditional healers but also by ill-informed clinicians resulting in the unjustified or inappropriate use of antivenom. This is a phenomenon noticed in countries like Indonesia, where limited antivenom supply is compounded by diverse species of venomous snakes in a massive geographical area (Tan et al., 2016a). Snakebite is likely to affect the Indonesian population at a large scale (WHO, 2016); however, the relevant epidemiological reports from this country are extremely scarce and are mainly fragmentary data obtained...