Mem. Inst. Butantan, 52 (supl.), 1990

SYSTEMIC ACTIVITIES OF BOTHROPIC VENOMS

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Bothropic venoms can affect animals both indirectly, through the liberation of pharmacologically active substances and directly through their action on cellular membranes.[11]

Among the many enzymatic activities presented by bothropic venoms only a few are important in the genesis of pharmacological effects namely proteolytic, coagulant, phospholipasic and hyaluronidasic activities.

The majority of bothropic venoms exhibit *in vitro* coagulant activities[1,2,8,4]; *in vivo* they can produce hypercoagulability followed by incoagulability through fibrigonen consumption.

We investigated[5,6] the effects of *B. jararaca* and. *B. erythromelas* venoms on arterial blood pressure of anaesthetized dogs following intravenous injection. The doses used were 100 μg/kg for *B. jararaca* and 25 μg/kg for *B. erythromelas.* With this dose *B. erythromelas* venom caused death in 60% of the injected animals, while no deaths were observed with *B. jararaca* venom. A fall of mean arterial pressure to shock levels (30 — 40 mm Hg) was observed in all survivors. Besides this effect we also observed thrombocytopenia and slight hemoconcentration. In the case of *B. erythromelas* venom (but not of *B. jararaca* venom) a brief tachypnea was followed by bradypnea and in some animals, by an apnea which was not counteracted by section of both *vagi.* Artificial respiration failed to maintain blood pressure.

Pretreatment with Metronidazole (125 mg/kg) was able to prevent the onset of shock and the thrombocytopenia induced by i.v. injection of *B. jararaca* venom[5]. This latter effect could be attributed to its anti-aggregating properties[6]. Heparin (200 IU/kg) and cellulose sulfate (40 mg/kg) protected the dogs against the lethal effects of *B. erythromelas* venom, but did not affect significantly either the fall of arterial blood pressure or thrombocytopenia. Pretreatment with mepyramine also failed to prevent the onset of shock suggesting that histamine release is not a major factor.

Bradykinin formation[7] may be involved as disappearance of circulating kininogen has been reported following the injection of *B. jararaca* venom in rats[9]. The liberation of EDRF is supported by the finding that pretreatment with an EDRF antagonist, nitro methylate arginine,[10] reduced the fall of blood pressure and pro-

moted recovery following i.v. injection of *B. erythromelas* venom. However, the coagulant activity remained unchanged.

Multiple hemorrhagic foci were present in all animals studied. Hemorrhagins have been detected in most bothropic venoms and could worsen the shock, not only by their direct action on collagen IV[3] but also by inhibiting the platelet aggregation induced by ADP. The inhibition of thrombin-induced platelet aggregation was one more detectable effect of *B. erythromelas* venom.

Many factors contribute to the genesis of shock following bothropic envenomation.

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