Ciencia animal 20(2):111-114, 2010

EFEITOS DO VENENO DA SERPENTE *Crotalus durissus cascavella* NA PRESSÃO ARTERIAL EM RATOS

(Effects of *crotalus durissus cascavella* snake venom on arterial blood pressure in rats)

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RESUMO

O presente estudo objetivou investigar os efeitos do veneno da serpente *Crotalus durissus cascavella* na pressão arterial sanguínea em ratos. O veneno foi inoculado através de uma cânula introduzida na veia jugular, em doses crescentes (100 μg/Kg; 300 μg/Kg); salina foi injetada nos animais controles. A concentração de nitrito foi determinada pela reação de Griess, após os experimentos de pressão arterial. As pressões sistólicas e diastólicas, bem como a Pressão Arterial Média (PAM), diminuíram de forma dose-dependente após a inoculação do veneno. Foi observado um aumento sanguíneo na produção de nitrito e o envolvimento do Óxido Nítrico no efeito hipotensor do veneno. Para analisar a significância das diferenças entre os grupos foi utilizado a Análise de Variação entre grupos (ANOVA) seguida do teste de Student-Neuman-keul. Foi considerado significante um $p< 0,05$. Este projeto foi aprovado pelo Comitê de Ética para Uso de Animais da Universidade Estadual do Ceará, processo nº 08670084-7.

PALAVRAS-CHAVE: veneno *Crotalus durissus cascavella*; pressão arterial média; efeito hipotensor.

ABSTRACT

The present study aimed at investigating the effects of the *Crotalus durissus cascavella* venom on the arterial blood pressure in rats. The venom was injected through a cannula into the jugular vein, with increasing dose (100 μg/Kg; 300 μg/Kg); saline was injected in to control rats. Nitrite concentration was determined by Griess method after the arterial blood pressure assay. Systolic and diastolic arterial pressures, as well as mean arterial pressure decreased in a dose-dependent way after infusion of the venom. Increase of blood nitrite concentration has been noted, as well as, the involvement of Nitric Oxide in the hypotensive effect of the venom.

KEYWORDS: *Crotalus durissus cascavella* venom; mean arterial pressure; hypotensive effect.

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In Brazil, *Crotalus* genus is responsible for more than 1500 cases of snakebite annually (Santoro et al., 1999; Martins et al., 2003). The *C.d.cascavella* is usually found in scrublands of the Brazilian Northeast. Snake venoms are recognized as useful sources of bioactive substances with wide pharmacological activity. The crotalic venom presents neurotoxic, myotoxic (Beghini et al.,2004), renal (Martins et al, 1998) antithrombotic and analgesic effects (Zhang et al.,2006), as well as platelet aggregating activity. Snake venom components affect the vascular system (Yamazaki and Morita, 2007). de Mesquita et al.(1991) have demonstrated a hypotensive activity of *Crotalus atrox* venom. Martins et al. (1998) demonstrated the effects of the *Crotallus durissus cascavella* venom in isolated rat kidney, as increase in urinary flow and glomerular filtration rate. Previously, Martins et al. (2003) showed the renal effects of the supernatant of macrophages activated by *C.d.cascavella* venom. Envenoming by *C.d.cascavella* leads to systemic alterations, eventually responsible for primary cause of death after snakebite.

This study aims at the evaluation of the vascular potential of venom from *C.d.cascavella* on arterial blood pressure.

Male Wistar rats (250-300g; n=6 for each group experimental) were anesthetized with 50 mg/Kg pentobarbital and thereafter the right carotid artery was cannulated with a polyethylene tube (PE50) and the systemic blood pressure was recorded directly through a pressure transducer connected to a 4 channel-polygraph. The mean arterial blood pressure was recorded continuously and after a 30-minute equilibration period the venom was injected by a cannula implanted into the jugular vein. *C.d.cascavella* venom (100 and 300µg/Kg) was injected at 15min interval and compared with isovolumetric injection of saline. The nitrite concentrations were determined after the infusion of *C.d.cascavella* venom from in blood pressure assay. 50 ì L of non-diluted samples were incubated with the same volume of Griess reagent (1% sulphanilamide, 0.1% naphthylethylenediamine dihydrochloride in 5% phosphoric acid). A standard nitrite curve was obtained by incubating sodium nitrite (10 to 200 ì M) with the reductase buffer. Absorbance at 550nm was determined using a multiwell plate reader (ELx 800 Universal Multiplater). The results were reported as micromoles (ì M) of NO_2, comparing the optical density in samples with the standard curve. The data were analysed using Student's *t* test and analysis of variance

Table 1: Effects of the *Crotalus durissus cascavella* venom on arterial pressure (n=6 for each group experimental).

	Control	**100 µg/Kg**	**300 µg/ Kg**
Systolic arterial pressure (mmHg)	126.78 ± 1.34	91.56 ± 2.4	88.31± 2.06
Diastolic arterial pressure (mmHg)	83.88 ± 1.01	75.97± 2.68	65.62 ± 2.33
Mean arterial pressure (mmHg)	100 ± 1.85	70 ±1.84	55 ± 1.92
Respiratory frequency (mL/min)	40 ± 0.98	25 ± 2.04	15 ± 2.15
Cardiac frequency (bat/min)	150 ±1.20	100 ± 1.95	50 ± 2.01