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Determining the sub-lethal nephrotoxic dose of Russell's Viper (*Daboia russelii)* venom in Wistar rats

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Objective: This study was designed to develop a rat model to determine if serum and urinary biomarkers could detect early acute kidney injury following Russell's viper envenomation. An initial dosing study was performed in order to determine the sub-lethal nephrotoxic dose for Russell's viper venom in rats.

Methods: Healthy male Wistar rats weighing 150-250 g were used. During the first phase groups of three rats at a time were injected with a known dose of venom intra-peritoneally. The injected venom dose was increased until the majority of rats in the group developed nephrotoxicity. In the second phase the rats were injected with an identified sub-lethal dose and were monitored for development of nephrotoxicity. The calculated venom dose was injected using a 1 ml syringe and a 27G needle into the right lower quadrant of the abdomen of each rat. Each animal was kept in a metabolic cage for 72 hours after the venom injection. Blood samples were obtained for serum creatinine from the tail vein of each animal before the venom injection and at 8, 24, 48 and 72 hours after the venom injection. Each rat was euthanized at the end of 72 hours and the left kidney was removed for histological analysis.

Results: Except in one rat at the initial venom dose of 2.5 µg/100 g, no rats died until a dose of 25 µg/100 g was administered. Of the rats that were alive at 24 hours, an elevated creatinine was only observed at an injected venom dose of 40 µg/100 g, except for two animals that developed AKI at doses of 2.5 µg/100 g and 25 µg/100 g. Histological evidence of nephrotoxicity was seen only at a venom dose ≥25 µg/100 g except for four animals that developed changes at a dose of 2.5 µg/100 g and one animal that developed changes at a dose of 5 µg/100 g. Of the 13 rats that developed histological evidence of nephrotoxicity and survived for 24 hours, only five had a significant rise in serum creatinine. Of the seven rats that developed biochemically confirmed AKI only five had histological evidence of nephrotoxicity. Of the rats that received a venom dose of ≥25 µg/100 g and developed histological evidence of nephrotoxicity, only a quarter were alive at 48 hours.

Conclusion: Early mortality of rats that develop nephrotoxicity makes the Wistar rat a poor animal model to develop early biomarkers of acute kidney injury following Russell's viper venom injection