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Direct nephrotoxic effect of Sri Lankan Russell's viper venom – an experimental study using *in vitro* models

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Abstract

Nephrotoxicity manifesting as acute renal failure is the principal cause of death in Russell's viper envenomation. The mechanisms responsible for nephrotoxicity are not clear and lack of experimental data in the Sri Lankan context prompted us to do this study. In the present experiments, the time related physiopathological changes in rabbits after injection of Russell's viper venom were studied using two *in vitro* models, *viz.* the isolated perfused kidney model and the kidney slice model. The isolated perfused kidney model experiments showed a significant time related reduction in renal function 4 hours after envenomation. This was associated with disturbances to the renal tubular cell integrity and renal pathology. Experiments using venom on kidney slices showed complete necrosis of the glomeruli and proximal convoluted tubular cells with the preservation of the basement membranes of tubular cells suggestive of direct damage caused by the venom. Data from these experiments are highly suggestive that Russell's viper venom causes renal damage mainly by a direct action on the kidney.

Key words: Russell's viper venom, renal failure, direct nephrotoxicity, isolated perfused kidney model, kidney slice model

Introduction

Russell's viper *(Vipera russelli pulchella)* contributes to the highest number of fatalities (40%) due to snake bite in Sri Lanka (1). Acute renal failure is the commonest cause of death in these patients and it can occur due to several mechanisms. These include direct nephrotoxicity, renal haemodynamic alterations, non specific effects of venom (such as hypotension, intravascular haemolysis, myoglobinuria, haemoglobinuria and disseminated intravascular coagulation) and immune mechanisms or due to the combined effect of several of these mechanisms (2, 3). Although death following the local viper bite is common hardly any experimental studies have been conducted here using the venom of the Sri Lankan Russell's viper. In the *in vivo* situation it is difficult to obtain evidence of a direct effect of venom on the kidney because of the difficulty in separating renal damage that can occur due to haemodynamic changes (4, 5). Therefore, the *in vitro* experiments described in this paper were carried out using the isolated perfused rabbit kidney (IPK) model and kidney slice model to elucidate the possible mechanisms for renal damage following envenomation by the local Russell's viper venom.

Material and Methods

Animals

Local cross-bred white male rabbits, approximately 9 months of age, weighing 1 to 2 kg were used in the experiments. Rabbits were kept in the animal house for 2 weeks prior to the experiments. They were fed a diet of carrot and green leaves. Ethical review for the experiments was obtained from the local institutional review body.

Source of venom

Russell's viper venom was obtained from the reptilium of the National Zoological Garden, Dehiwela, Sri Lanka. The snakes were identified

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