Pathophysiological Mechanisms in an Experimental Model of Acute Kidney Injury induced by Lonomia obliqua Venom: The Role of Kinin Receptors, Coagulation System and Inflammation

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Purpose. The Lonomia obliqua caterpillar envenomation is considered a common and serious occupational disease, especially in rural areas of southern Brazil regions. L. obliqua venom is highly nephrotoxic and acute kidney injury (AKI) is the main cause of death among envenomed victims. This study evaluates the pathophysiological mechanisms involved in renal dysfunction.

Procedures. Here we use an in vivo model to characterize the L. obliqua-induced AKI. A multidisciplinary approach was employed including methods of renal biochemistry, pharmacology, morphology and a global proteomic analysis to identify the molecular pathways of kidney injury.

Findings. According to our results, the pathophysiological mechanism of venom-induced AKI, it seems to be complex involving three main issues: the heme-derived tubular cytotoxicity; vascular alterations, including systemic hypotension, increase in vascular permeability and glomerular fibrin deposition; and the activation of renal kinin system. Acting together these mechanisms are directly related to the functional alterations observed in envenomed animals such as renal hypoperfusion, inflammation, tubular necrosis and the sudden loss of basic renal functions, including filtration and excretion capacities, urinary concentration and maintenance of body fluid homeostasis. The activation of renal kallikrein and the bradykinin receptor B1 (B1R) play a crucial role in L. obliqua-induced AKI, because both the pharmacological blockade of B1R or systemic kallikrein inhibition are able to prevent the renal functional and histopathological alterations and also ameliorates the venom-induced blood incoagulability observed in envenomed animals. The main mechanisms underlying these beneficial effects are associated with a decrease in renal inflammatory response (reduction of pro-inflammatory cell migration and pro-inflammatory cytokine levels) and tubular degeneration.

Conclusions. Thus, our findings show a consistent evidence linking kinin system with the L. obliqua-induced AKI and indicate that the inhibition of kinin components, mainly kallikrein inhibition or B1R antagonism, could be a therapeutic alternative to control the progression of renal injury.

Keywords: Venom, Lonomia, Kinin.