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Evaluation of L-arginine on Kidney Function and Vascular Reactivity Following Ischemic Injury in Rats: Protective Effects and Potential Interactions

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There is an interaction between many cell types involved in the pathophysiology of ischemic acute renal failure. Nitric oxide (NO) plays a major role in renal hemodynamics and tubular sodium transport [1,2] and participates in the pathophysiology of acute renal failure. [3] NO precursors, especially L-arginine, may have protective effects on tissue ischemia–reperfusion injury; however, their molecular mechanisms are unclear with many controversies reported.

This study was designed to evaluate the protective use of L-arginine in ischemic reperfusion injury and to investigate the possible interaction between NO availability, changes in COX-2 activity and oxidative stress in the pathogenesis of renal dysfunction secondary to IRI in kidney and vascular beds in rats.

Ischemic/reperfusion injury (IRI) model in male albino Sprague-Dawley rats, weighing 250-300 gm, was used and various biochemical parameters examined. The rat isolated aortic rings served as model for hypoxia/reoxygenation where endothelium dependent and independent relaxations were exerted. Study protocols comply with the guidelines for the proper conduct of animal experiments and are approved by institutional ACUC. Results are expressed as mean ± SEM of 7 experiments. Criteria for significance was set at $p<0.05$.

Pre-treatment of rats subjected to IRI with L-arginine (125 mg/kg) significantly reduced kidney malonaldehyde levelselevated kidney superoxide dismutase activity, reduced glutathione level and total nitric oxide levels at 24 & 48 hours after reperfusion. For example, at 48 hours, malonaldehyde levels changed from 1.80±0.11 nmole/mg protein for IRI group to 0.95±0.05 for L-arginine-treated group), Kidney COX-2 level was only different in the L-arginine-treated group 48 hours after reperfusion (2.08±0.12 ng/mg protein) compared to the IRI group (3.01±0.12 ng/mg protein). Pre-treatment with L-arginine (10^{-2}M) alone or in combination with celexocib (2x10-7 M) significantly potentiated the ACh (1-4 µM) -induced relaxations in control and ischemic rings. The effect of the combination was synergistic only in ischemic rings. Addition of ascorbic acid (10 µM) to the celexocib+L-arginine combination did not produce further potentiation. Sodium nitroprusside (10^{-9}-10^{-7} M)-induced relaxations in control and ischemic rings were potentiated by L-arginine or celexocib+L-arginine combination but not by ascorbic acid.

The protective effect of L-arginine may result from the interaction between NO and ROS and increased NO bioavailability. The protective effects of combined celecoxib and L-arginine against IRI could be attributed to their antioxidant activity which

surpassed that of ascorbic acid.

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