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Gentamicin Decreases Guanylyl Cyclase Activity in Rat Glomerulus

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Background : Gentamicin (GM)-induced urinary concentration defect is associated with reduced abundance of aquaporin water channels and major sodium transporters in the kidney. Natriuretic peptides (NP) and nitric oxides (NO) have been implicated in the regulation of urinary sodium excretion. We examined whether an altered regulation of local NP and NO systems contributes to GM-induced nephropathy.

Methods : Male Sprague-Dawley rats (180-200 g) were injected with GM (100 mg/kg per day, IM) for 5 days. The expression of nitric oxide synthase (NOS) isozymes was determined by Western blot analysis, and that of NPs by real-time polymerase chain reaction. The activity of guanylyl cyclase was determined by the amount of guanosine 3', 5'-cyclic monophosphate (cGMP) generated in responses to atrial natriuretic peptide (ANP) or sodium nitroprusside (SNP).

Results : GM treatment resulted in renal failure in association with increases of urinary flow rate and fractional excretion of sodium. Accordingly, the expression of iNOS was increased in the cortex, while that of eNOS remained unchanged. The urinary excretion of NO metabolites was increased. The expression of ANP, brain natriuretic peptide and C-type natriuretic peptide mRNA was increased in the kidney. The cGMP production provoked by either ANP or SNP was decreased in the glomerulus, but not in the papilla.

Conclusion : GM-induced nephropathy may be causally related with decreased guanylyl cyclase activities in the glomerulus, which in turn results in compensatory upregulation of NOS and NPs.