P123

Indomethacin Decreases the Particulate Guanylyl Cyclase Activity in the Kidney in Rats

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Background: Whether an altered regulation of local hormonal systems involved in the sodium transport is associated with the non-steroidal anti-inflammatory drug (NSAID)-induced fluid retention was investigated.

Methods: Male Sprague-Dawley rats were treated with indomethacin (5 mg/kg, every 12 h, intraperitoneally) for two days. The control group was treated with solvent. The mRNA expression of atrial natriuretic peptide (ANP) and natriuretic peptide receptor-A (NPR-A) and the protein expression of endothelial nitric oxide synthases (NOS) were determined in the kidney. The particulate and soluble guanylyl cyclase activities were measured. The protein expression of $\alpha 1$ and $\beta 1$ subunits and the catalytic activity of Na,K-ATPase were also determined.

Results: Following the treatment with indomethacin, the urinary total and fractional excretion of sodium was decreased. The plasma level of ANP significantly altered. However, the expression of NPR-A was significantly decreased, although that of ANP was not significantly altered. The protein expression of endothelial NOS was increased. The catalytic activity of Na,K-ATPase was increased, although no significant changes were noted in its expression of $\alpha 1$ and $\beta 1$ subunits. The particulate guanylyl cyclase activity evoked by ANP was significantly decreased, while the soluble guanylyl cyclase activity evoked by SNP was increased.

Conclusions: It is suggested that indomethacin decreases the urinary sodium excretion in part through a decreased activity of ANP system. The increased activity of NO system may then play a compensatory role in dissipating the fluid volume retention.