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Oral Sessions

Atrial natriuretic peptide exerts hypotensive effect via regulator of G-protein signaling 2-mediated endothelial hyperpolarization

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Objective: Atrial natriuretic peptide (ANP) functions via guanylyl cyclase (GC)-A, a single transmembrane receptor, resulting in diuresis, natriuresis, and lowering of blood pressure. However, molecular mechanism of hypotensive effect of ANP is not well understood. **Results:** Immunohistochemistry indicated that GC-A is abundantly expressed in endothelial cells. Intravenous infusion of ANP in wild-type mice significantly lowered systolic blood pressure. ANP failed to lowering systolic blood pressure in endothelial cell-specific GC-A knockout mice. In endothelial nitric oxide synthase knockout mice, ANP also significantly lowered systolic blood pressure. In in vitro study, ANP treatment significantly hyperpolarized cultured human umbilical vein endothelial cells (HUVECs), but not changed intracellular Ca^{2+} concentration in HUVECs. ANP-induced hyperpolarization of HUVECs was dependent of cyclic GMP-Protein Kinase G and regulator of G-protein signaling2 (RGS2) pathway but not dependent of Ca^{2+} -activated K^{+} channels. **Conclusions:** These results suggest that hypotensive effect of acute ANP administration can be caused by endothelial GC-A-mediated RGS2 pathway-dependent endothelial hyperpolarization.