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Pathophysiological Roles of ANP in Hypertrophied Heart

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Cardiac atrium is now well-known as an endocrine organ which secretes atrial natriuretic peptide (ANP), participating in the regulation of body fluid and blood pressure. ANP is released mainly from cardiac muscle cells in response to various physiological and pathological conditions to induce atrial stretch. Ca^{2+} may be one of the most important factors affecting ANP secretion even though controversy still persists. The aim of the present study is to investigate the effect of lysophosphatidylcholines (LPCs) and moxonidine on atrial hemodynamics and ANP secretion in hypertrophied atria. LPC is an endogenous phospholipid released from cell membrane during ischemia, and moxonidine is a imidazoline 1 (I1) receptor agonoist.

LPC (10 and 30 μM) caused decreases in ANP secretion in a dose-dependent manner with slightly increases in intra-atrial pressure and extracellular fluid (ECF) translocation. Therefore, the ANP secretion in terms of ECF translocation was markedly decreased by LPC. The order of suppressive effect of ANP release was S-LPC > LPC= P-LPC > M-LPC = L-LPC = O-LPC. Staurosporine and wortmannin significantly attenuated the suppression of ANP release and an increase in intra-atrial pressure by LPC. High extracellular Mg^{2+} also attenuated LPC-induced suppression of ANP release. However, other protein kinase C inhibitors such as chelerythrine, GF109203X, and tamoxifen citrate did not affect LPC-induced suppression of ANP release. The suppression of ANP release by LPC, S-LPC, P-LPC or O-LPC was markedly attenuated in hypertrophied atria. The degree of hypertrophy positively correlated to relative changes in ANP release by LPC but not to changes in pulse pressure by LPC. Increases in intracellular Ca^{2+} by LPC and S-LPC were attenuated in hypertrophied atrial myocytes. On the other hand, moxonidine caused accentuation of ANP release, which was pronounced in hypertrophied atria. The degree of hypertrophy also positively correlated to relative changes in ANP release by moxonidine.

These results suggest that LPC-induced suppression of ANP release may mediate through protein kinase C-Ca^{2+} and phosphoinositol 3-kinase and moxonidine-induced accentuation of ANP release may mediate through I1 and α2 receptors with different mechanism from clonidine. Attenuation of LPC-induced suppression and moxonidine-induced accentuation of ANP release in hypertrophied atria may be considered as a compensatory adaptation to reduce cardiac load.

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