Role of VPAC2 receptor in monocrotaline-induced pulmonary hypertension in rats

(モノクロタリン誘発肺高血圧ラットにおけるVPAC2受容体の役割)

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(http://jap.physiology.org/content/117/4/383)

<Introduction> Pulmonary hypertension (PH) is associated with significant morbidity and mortality. Vasoactive intestinal peptide (VIP) and pituitary adenyl cyclase activating peptide (PACAP) have pulmonary vasodilatory and positive inotropic effects via receptors VPAC1 and VPAC2, which possess a similar affinity for both peptides, and PAC1, a PACAP-preferring receptor. VIP is a promising option for PH treatment; however, various physiological effects of VIP have limited its clinical use. We investigated the effects of VPAC1 and VPAC2 selective agonists VIP and PACAP to explore more appropriate means of treatment for PH.

<Materials and Methods> We examined hemodynamic changes in right ventricular systolic pressure (RVSP), systemic blood pressure (SBP), total pulmonary resistance index (TPRI), total systemic resistance index, and cardiac index (CI) in response to their agonists with monocrotaline (MCT)-induced PH and explored involvement of VIP/PACAP expression and receptors in PH. Sprague-Dawley rats were divided into the MCT group (administered MCT 60 mg/kg) and control group.

<Results> In MCT-induced PH, decreased VIP and PACAP were associated with upregulation of VPAC1, VPAC2, and PAC1 in lung tissues. Intravenous injection of VPAC2-selective agonist BAY 55–9837 and VIP, but not [Ala11,22,28]VIP, improved the CI. The decrease in SBP with VPAC2 agonist was significantly less than that in the control. Although they decreased SBP, these agonists hardly affected RVSP in the control.

<Conclusion> Activation of VPAC2 receptor with BAY 55–9837 effectively improved RVSP, TPRI, and CI in MCT-induced PH, suggesting a VPAC2 agonist as a possible promising treatment for PH.
I 主論文
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