Abstract

Calcium sensitization represents a mechanism that enables vascular smooth muscle cells to change the sensitivity of the contractile apparatus to intracellular calcium The aim of this study was to determine to what extent is calcium sensitization modulated by the renin-angiotensin system (RAS), sympathetic nervous system (SNS), nitric oxide (NO) and prostanoids produced by cyclooxygenase (COX). For this purpose we studied the effects of acute and chronic blockade of particular systems on blood pressure changes elicited in conscious normotensive rats by administration of Rho-kinase inhibitor fasudil. Adult male chronically cannulated Wistar rats were used in all experiments. Main findings of this study are as follow: 1) Decrease of blood pressure elicited by Rho-kinase inhibition was enhanced under the conditions of acute NOS inhibition. Inhibition of NOS was shown to have a bigger effect than COX inhibition (this was confirmed under the conditions of acute RAS and SNS inhibition as well). These findings are in agreement with the hypothesis that NO exerts a suppressive effect on calcium sensitization. 2) Chronic NOS inhibition caused hypertension characterized by a more pronounced blood pressure lowering after Rho-kinase inhibition in comparison with control. NO chronically suppresses the calcium sensitization. 3) In contrast chronic inhibition of RAS by captopril led to lowering of the response to fasudil. Thus RAS enhances calcium sensitization through its long-term effects. 4) Chronic administration of inhibitor of catecholamine release guanethidine did not change the blood pressor response to fasudil. Long-term effect of the SNS on calcium sensitization was not found. The results collectively show that balance between RAS and NO is important in maintenance of normal blood pressure.