Cyclic AMP-dependent protein kinase and mechanical heart function in ventricular hypertrophy induced by pressure overload or secondary to myocardial infarction

Piddo, A. M., Sánchez, M. I., Sapag-Hagar, M., Corbalán, R., Foncea, R., Ebensperger, R., ... & Lavandero, S. (1996). Cyclic AMP-dependent protein kinase and mechanical heart function in ventricular hypertrophy induced by pressure overload or secondary to myocardial infarction. Journal of molecular and cellular cardiology, 28(5), 1073-1083.

Abstract

The role of cyclic AMP-dependent protein kinase (PKA) and systolic function during the development of left ventricular hypertrophy (LVH) still remain uncertain. The aim of this work is to study PKA activity and mechanical heart function in two experimental heart hypertrophy models: specifically, one induced by pressure overload (Goldblatt model: two kidneys, one clamped, Gb); and another secondary to myocardial infarction (MI) generated by ligation of the left coronary artery. Hypertension in the Gb group becomes evident by the third and fourth week after surgery without any significant change in the corresponding sham group. The myocardial infarction group did not show any change in systolic pressure. Different degrees of LVH for the two experimental models were observed. Relative cardiac mass (RCM) and relative ventricular mass (RVM) increased 23 and 16%, respectively, above the sham-operated rats in MI group ($P<0.05$). For the pressure overload model, the increase values were 42 and 44%, respectively ($P<0.05$). Left ventricular hypertrophy was also evaluated through quantitative changes in cardiacβ-myosin heavy chain which agreed with morphometric studies in Goldblatt rats. Ventricular PKA activity did not show any significant difference with respect to the sham-operated group after induction of pressure overload. For the MI model, ventricular PKA activity changed only at day 7 post-infarction with a 289% increase above the sham-operated group ($P<0.05$). The absence of activation of ventricular PKA after constriction of renal artery or myocardial infarction was also corroborated by the patterns of PKA-dependent phosphorylated proteins. While force-generating capacity was increased, there was no change in ventricular PKA activity, indicating that there is no relation between this enzyme and systolic stress–strain regression lines in either pressure overload or myocardial infarction conditions. Cyclic AMP-dependent protein kinase activity had no relation with development of cardiac hypertrophy in the two experimental models of LVH. These findings contribute to the hypothesis for a multifactorial interaction of different intracellular biochemical and molecular mechanisms in the genesis of cardiac hypertrophy.

Keywords

Heart hypertrophy, Protein kinases, Systolic function, Protein phosphorylation, Myocardial infarction.