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Hydrogen sulfide in regulation of frog myocardium contractility

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Abstract

Hydrogen sulfide (H2S) is an endogenously synthesized gaseous molecule which, along with nitric oxide and carbon monoxide, induces a number of effects in cardiovascular system under normal and pathological conditions. In the present work, the effects and underlying mechanisms of the H2S donor sodium hydrosulfide (NaHS) on the isometric force of frog myocardium contraction have been studied. NaHS at the concentration of 100 μM induced negative inotropic effect and reduced the maximum velocity of the contraction and relaxation of the isolated ventricle strips. The substrate of H2S synthesis, L-cysteine (200 μM and 1 mM), induced the same effect, while the inhibitors of cystathionin-γ-lyase, the H2S-producing enzyme in heart, β-cyanoalanine (500 μM) and propargylglycine (500 μM), increased the amplitude of contraction. Inhibition of cystathionin-γ-lyase by β-cyanoalanine prevented the negative inotropic effect of L-cysteine. After the inhibition of adenylate cyclase by MDL-12,330A (3 μM) or phosphodiesterases by IBMX (200 μM), the effect of NaHS was less than that in the control. In the presence of membrane-penetrating analogous of cAMP, 8Br-cAMP (100 μM) and pCPT-cAMP (100 μM), the negative inotropic effect of NaHS was completely retained. The effect of NaHS significantly decreased after preliminary application of the NO donor, SNAP (10 μM), and did not change after the inhibition of NO synthases by L-NAME (100 μM). The results suggest the possibility of endogenous synthesis of H2S in frog myocardium and regulation of its contractility by the activation of phosphodiesterases hydrolyzing cAMP, which leads to a decrease in the activation of cAMP-dependent protein kinases and phosphorylation of voltage-dependent L-type Ca channels. As a result, the reduction of calcium entry into cardiomyocytes decreases the contractility of frog myocardium. © 2013 Pleiades Publishing, Ltd.

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Keywords

adenylate cyclase, hydrogen sulfide, myocardial contractility, nitric oxide