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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 in normal and pathological conditions. In the present study the effects and underlying mechanisms of H2S donor, sodium hydrosulfide (NaHS), on isometric force of frog myocardium contraction were studied. NaHS in the concentration of 100 μM induced a negative inotropic effect and decreased the maximal velocity of contraction and relaxation of isolated ventricle strips. The substrate Of H2S synthesis L-cystein (200 μM and 1 mM) induced the same effect and the inhibitors of cystationin y-lyase, H2S-producing enzyme in heart, ß-cyanoalanin (500 μM) and propargylglycine (500 μM) increased the amplitude of contraction. Inhibition of cystationin y-lyase by ß-cyanoalanin prevented the negative inotropic effect of L-cystein. After inhibition of adenylate cyclase by MDL12,330A (3 μM) or phosphodiesterases by IBMX (200 μM) effect of NaHS was lesser than in control. In the presence of membrane-penetrating analogous of cAMP, 8Br-cAMP (100 μM) and pCPT-cAMP (100 μM), negative inotropic effect of NaHS completely retained. The effect of NaHS significantly decreased after preliminary application of the NO donor, SNAP (10 μM), and did not change after inhibition of NO-synthases by LNAME (100 μM). The obtained data suggest the possibility of endogenous synthesis of H2S in frog myocardium and regulation of its contractility by activation of phosphodiesterases hydrolyzing cAMP, which leads to a decrease of activation of cAM P-dependent protein kinases and phosphorylation of voltage-dependent L-type Ca-channels. As the result, a reduction of calcium entry into cardiomyocytes decreases the contractility of frog myocardium.