Activation of inward rectifier K^+channels by hypoxia in rabbit coronary arterial smooth muscle cells

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We examined the effects of acute hypoxia on Ba^{2+}-sensitive inwardly rectifying K^+ (Kir) current in rabbit coronary arterial smooth muscle cells. The amplitudes of Kir current were definitely higher in the cells from small-diameter (< 100 μm) coronary arteries (SCASMC, -12.8 1.3 pA pF^{-1} at 140 mV) than those in large-diameter (> 200 μm, LCASMC, -1.5 0.1 pA pF^{-1}). Western blot analysis confirmed that Kir2.1 protein was expressed in SCASMC but not LCASMC. Hypoxia activated much more Kir currents in symmetrical 140 K^+. This effect was blocked by the adenylyl cyclase inhibitor, SQ 22536 (10 μM) and mimicked by forskolin (10 M) and dibutyryl-cAMP (500 μM). The production of cAMP in SCASMC increased 5.7-fold following 6 minutes of hypoxia. Hypoxia-induced increase in Kir currents was abolished by the protein kinase A (PKA) inhibitors, Rp-8-CPT-cAMPs (10 μM) and KT 5720 (1 μM). The inhibition of G-protein with GDPs (1 mM) partially reduced (~50 %) the hypoxia-induced increase in Kir currents. In Langendorff-perfused rabbit hearts, hypoxia increased coronary blood flow, an effect that was inhibited by Ba^{2+}. In summary, the hypoxia augments the Kir currents in SCASMC via cAMP and protein kinase A-dependent signaling cascades, which might explain the hypoxia-induced coronary vasodilation.