Hypoxic pHi and function modulation by Na+/H+ exchange and alpha-adrenoreceptor inhibition in heart in vivo.

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Regulation of intracellular pH (pHi) may contribute to maintenance of cardiac contractile function during graded hypoxia in vivo. To test this hypothesis, we disturbed pHi regulation in vivo using two approaches: alpha-adrenoreceptor antagonism with phentolamine (1 mg/kg) (Phen; n = 9); and Na+/H+ exchange inhibition with HOE-642 (2 mg/kg; n = 6) before graded hypoxia in open-chest sheep. Hemodynamic parameters including left ventricular maximal pressure development (dP/dtmax) cardiac index (CI), and left ventricular power were monitored continuously and simultaneously with high-energy phosphate levels and pHi, measured with 31P nuclear magnetic resonance spectroscopy in Phen, HOE-642, and control (Con; n = 9). In subgroups (n = 6) in Con and Phen, coronary flow, myocardial oxygen consumption (MVO2), and lactate uptake were also measured. During hypoxia, the functional parameters left ventricular dP/dtmax, CI, and left ventricular power decreased significantly compared with baseline and Con values. These decreases were preceded by a significant drop ($P < 0.05$) in pHi from 7.10 +/- 0.04 to 6.69 +/- 0.05 in Phen and corresponded temporally to a pHi drop from 7.10 +/- 0.02 to 6.77 +/- 0.03 in HOE-642. Decreases in pHi in Phen were not preceded by decreases in cardiac function or MVO2. In contrast, cardiac function parameters increased significantly in Con, whereas no significant pHi decrease occurred (7.07 +/- 0.03 to 6.98 +/- 0.04). We conclude that these data indicate that pHi regulation can be disrupted through alpha-adrenergic antagonism or Na+/H(+)-exchange inhibition in vivo. These studies demonstrate that pHi regulation performs a role in the modulation of cardiac function during hypoxia in vivo.