4-aminopyridine contracts pulmonary artery in voltage-dependent and voltage-independent manner
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Voltage-gated K⁺ (Kᵥ) channels are predominantly expressed in pulmonary vasculature and have been thought to play an important role in regulation of membrane potential (Vm) and vessel contractility. The main aim of this project was to investigate the role of Kᵥ channels in intrapulmonary arteries (PAs) isolated from male Wister rats (200-250 gm) using small vessel wire myography. Mesenteric arteries (MAs) were used as a representative of systemic circulation. Our results demonstrate that the effect of 4-AP, a specific inhibitor of the Kᵥ channels, was significantly potentiated by 20 mM KCl that causes membrane depolarization. 4-AP-induced contraction of PAs was only partly (35.0±4%, n=6) blocked by the inhibitor of L-type Ca²⁺ channels diltiazem (10 µM), whereas in MAs contraction was nearly completely blocked (94.0±2%, n=6). Similar partial block by diltiazem was observed in PAs but not in MAs for contraction induced by 80 mM KCl. 4-AP induced contraction in PAs was also blocked by Rho-kinase inhibitor Y-27632 (10 µM). The effects of diltiazem and Y-27632 were additive in PAs. The role of Rho-kinase in 4-AP-induced contraction was confirmed with Western blot analysis.

Pretreatment with 4-AP (10 µM) increased the levels of phosphorylated myosin light chain (p-MLC) in PAs. This effect was reversed by pretreatment of tissues with Y-27632 (10 µM). These results suggest that 4-AP induced contraction involves voltage-dependent and voltage-independent mechanisms and that Rho-kinase signalling pathway contributes, at least in part, to 4-AP-induced pulmonary vasoconstriction.