The contribution of ATP-dependent potassium channels (K_{ATP}) to renal vascular tone regulation

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Objective: Sympathectomy raises norepinephrine (NE) sensitivity in renal resistance arteries. This effect is partly mediated through a depolarized vascular smooth muscle cell (VSMC) membrane potential and facilitated L-type Ca^{2+} channel activation. Preliminary data suggest that altered K_{ATP} channel function contributes to these effects. We investigated the role of K_{ATP} channels for the maintenance of VSMC membrane potential and agonist-induced vasoconstriction in renal resistance arteries by testing if K_{ATP} channel blockade or activation have greater effects on NE-induced vasoconstriction in arteries from sympathectomized or denervated kidneys than in control vessels.

Methods: Renal resistance arteries were obtained from humans and rats. Rats underwent sympathectomy, renal denervation or sham-treatment. Vessels were investigated by wire-myography. Cumulative concentration-response curves (CRCs) were obtained for the L-type Ca^{2+} channel activator S-(-)-BayK8644 and NE in the absence or presence of glibenclamide (K_{ATP} channel blocker) or levcromakalim (K_{ATP} channel activator).

Results: S-(-)-BayK8644 did not induce vasoconstrictions in arteries of untreated rats. Glibenclamide slightly facilitated S-(-)-BayK8644-induced vasoconstriction (10% of K^+-induced vasoconstriction). S-(-)-BayK8644 caused strong vasoconstrictions (60% of K^+-induced vasoconstriction) in human arteries, which were prevented by levcromakalim. Arteries from sympathectomized and renal denervated rats showed a leftward shift of the NE CRCs. Glibenclamide did not affect NE CRCs in rats but shifted the NE CRC in human arteries to the left. Levcromakalim caused similar rightward shifts of the NE CRCs in all groups of rats (ΔlogEC50 -0.58 – -0.41 mol/l) and induced a rightward shift of the NE CRCs in human arteries.

Conclusions: K_{ATP} channels play a minor role for the maintenance of VSMC membrane potential and NE-induced changes in renal vascular tone in rats. The effects of K_{ATP} channel blockade or activation are unaffected by sympathectomy or renal denervation. In humans K_{ATP} channels appear to contribute more to the regulation of renal resistance artery tone than in rats.