Different channel modulation in arterial smooth muscle cells of diabetes

Eun A Ko[a], Won Sun Park[b], Sung Joon Kim[c], Insuk So[c], Ki Whan Kim[d] and Jin Han[a]

[a]Department of Physiology, College of Medicine, Inje University, Busan, 614-735, Republic of Korea.

[b]Department of Physiology, College of Medicine, Kwangwon National University, Chuncheon, 200-701, Republic of Korea.

[c]Department of Physiology, Seoul National University College of Medicine, Seoul, 110-799, South Korea.

[d]Department of Physiology, School of Medicine, Gachon University of Medicine and Science, Inchon, 405-835, Korea.

This study examined the mechanisms of hypertension in diabetes. We investigated the effects of serotonin (5-HT) on voltage-dependent K^+ (Kv) channel activity, vasoconstriction, 5-HT receptor expression levels, and the involvement of protein kinase C (PKC) in mesenteric arteries of Otsuka Long-Evans Tokushima fatty (OLETF) rats compared with Long-Evans Tokushima Otsuka (LETO) rats. Blood pressure, body weight, blood glucose level, and mesenteric arterial wall thickness were greater in OLETF rats. The 5-HT-induced vasoconstriction of mesenteric arteries was greater in OLETF rats than in LETO rats and inhibited by the $5\text{-}HT_{2A}$ inhibitor inhibitor, ketanserin. The Kv currents in mesenteric arterial smooth muscle cells (MASMCs), determined using a perforated patch clamp technique, was inhibited by 1 mM 4-AP (42.5 ± 4.1% vs. 63.5 ± 2.3% in LETO vs. OLETF rats at +40 mV), but was insensitive to 1 mM TEA and 100 nM iberiotoxin. The inhibition of Kv current by 1 μM 5-HT in MASMCs was greater in OLETF rats than in LETO rats (17.1 ± 2.2% vs. 33.2 ± 2.7% in LETO vs. OLETF rats at +40mV), and the inhibition was prevented by treatment with the PKCalpha- and beta- selective inhibitor, Gö6976. The expression level of $5\text{-}HT_{2A}$, but not $5\text{-}HT_{2B}$, receptor and the expression levels of total PKC, PKCbeta, and PKCepsilon, but not PKCalpha, were higher in the mesenteric arteries of OLETF rats compared with LETO rats. The enhanced expression of $5\text{-}HT_{2A}$ receptor together with PKCbeta may promote mesenteric vasoconstriction and increase vascular resistance in OLETF rats.