Streptolysin O: a novel mediator of endothelial dysfunction

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Microbial imbalance (dysbiosis) is closely linked to several diseases including cardiovascular diseases. Gram-positive Streptococcus genus is reported to be increased in feces of spontaneous hypertensive rat (SHR) with increased intestinal permeability. However, the mechanisms of the dysbiosis induced high blood pressure remains unknown. In this study, we pharmacologically examined the effect of streptolysin O (SLO), a streptococcal pyrogenic exotoxin, on vascular functions (1. Relaxation 2. Contraction).

(1) Relaxation results: In aortas isolated from Wistar rat, in vitro treatment with SLO (1-100 ng/ml, 30 min) impaired acetylcholine (ACh)-induced endothelial dependent relaxation in a dose-dependent manner (n=6, p<0.05). In contrast, SLO did not change sodium nitroprusside-induced endothelial independent relaxation (n=4). Endothelial dysfunction caused by SLO was attenuated by pan protein kinase C (PKC) inhibitor (Ro 31-8222, n=6, p<0.05), PKCβ inhibitor (LY 333531, n=5, p<0.05) or selective PKCβ2 inhibitor (CGP53353, n=5, p<0.05). In vivo treatment of Wistar rat with SLO (0.1-10 ng/ml) blunted ACh-induced blood pressure reduction (n=4, p<0.05).

(2) Contraction results: In vitro treatment of aortas with SLO (1-100 ng/ml, 30 min) did not change contractile responses to noradrenaline (NA), serotonin (5-HT; n=4). Ex vivo treatment with SLO (10 ng/ml, 24 hr) did not change contractile response to NA or 5-HT (n=6).

We conclude that SLO causes endothelial dysfunction through PKCβ signaling and might contribute to the development of hypertension.