



Lack of endothelium-derived hyperpolarizing factor (EDHF) up-regulation in endothelial dysfunction in aorta in diabetic rats

Gabor Csanyi¹, Istvan Lepran², Timea Flesch¹, Gyula Telegdy¹, Gyula Szabo¹, Zsafia Mezei¹

¹Department of Pathophysiology, Albert Szent-Gyorgyi Medical and Pharmaceutical Center, University of Szeged, Semmelweis 1, 6725 Szeged, Hungary

²Department of Pharmacology and Pharmacotherapy, University of Szeged, Dom square 12, 6720 Szeged, Hungary

Correspondence: Zsafia Mezei, e-mail: mezei@patph.szote.u-szeged.hu

Abstract:

It is not known whether the impairment of nitric oxide (NO)-dependent vasodilation of the aorta of diabetic rats is associated with any changes in the endothelial production of vasoactive prostanoids and endothelium-derived hyperpolarizing factor (EDHF). Therefore, we analyzed the contribution of NO, vasoactive prostanoids and EDHF to the decreased endothelium-dependent vasorelaxation in Sprague-Dawley rats at 4 and 8 weeks after diabetes mellitus induced by streptozotocin (STZ).

The acetylcholine-induced (ACh) endothelium-dependent relaxation was significantly decreased in the thoracic aorta 8 weeks after the STZ-injection (ACh 10^{-6} M: $73.1 \pm 7.4\%$ and $56.7 \pm 7.9\%$ for control and diabetic rats, respectively). The sodium nitroprusside-induced (NaNP) endothelium-independent vasodilation was also impaired in the diabetic rats (8 weeks after STZ) (NaNP 10^{-8} M: $74.2 \pm 11.4\%$ and $35.9 \pm 9.4\%$ for control and diabetic rats, respectively). In contrast, the basal NO production, as assessed by the N_{ω} -nitro-L-arginine methyl ester (L-NAME)-induced vasoconstriction was not modified in diabetes. Moreover, the amount of 6-keto-PGF_{1 α} (stable metabolite of prostacyclin / prostaglandin I₂ / PGI₂), 12-L-hydroxy-5,8,10-heptadecatrienoic acid (12-HHT) and thromboxane B₂ (TxB₂) (stable metabolite of thromboxane A₂ – TxA₂) were significantly increased in the 8 weeks diabetic rat aorta. The EDHF-pathway did not change in the aortic endothelium during the development of STZ-induced diabetes.

Our results indicate that STZ-induced diabetes mellitus did not modify the basal NO production, but induced the impairment of acetylcholine- and sodium nitroprusside-induced vasodilation in the thoracic aorta. In parallel with the impairment of NO-dependent vasodilation, the basal PGI₂, 12-HHT and TxA₂ synthesis were increased. The EDHF-pathway did not contribute to the endothelium-dependent relaxation either in control or diabetic aorta. The above alterations in the endothelial function may play an important role in the development of endothelial dysfunction and vascular complications of diabetes.

Key words:

nitric oxide, prostaglandins, eicosanoids, EDHF, diabetes, aorta
