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ATP-BINDING CASSETTE TRANSPORTER G1 PROTECTS AGAINST ENDOTHELIAL DYSFUNCTION INDUCED BY HIGH GLUCOSE

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Introduction It is known that hyperglycaemia can contribute to defects in endothelial function, which is the early characteristic of atherosclerosis. ATP-binding cassette transporter G1 (ABCG1), a regulator of reversing cholesterol efflux, is highly expressed in endothelial cells. To gain further insight into the mechanism of endothelial dysfunction induced by high glucose, we strive to examine the effect of ABCG1 on endothelial function.

Methods Human umbilical vein endothelial cells (HUVECs) were incubated with D-glucose (5.6 and 30 mmol/l) for one to seven days in vitro. Expression of ABCG1 in HUVECs was measured by real-time PCR and Western blot. The rate of cholesterol efflux to HDL was measured by scintillation counting, and intracellular lipid content was measured by enzymatic fluorometric method. The level of IL-6 and TNFα were measured by ELISA, and eNOS expression and activity of NO were examined.

Results Compared with 5.6 mmol/l glucose, high glucose (30 mmol/l) decreased the mRNA and protein expressions of ABCG1 in HUVECs in a time-dependent manner. Consistent with downregulation of ABCG1, free cholesterol efflux to HDL was reduced. However, intracellular cholesterol levels were not changed. In addition, secretions of IL-6 and TNFα in HUVECs cultured in high glucose for seven days were increased three and four times respectively compared to normal glucose. In contrast, eNOS expression was downregulated for 20%, and activity of NO was inhibited. In addition, upregulation of ABCG1 gene expression by LXR agonist 22(R)-hydroxycholesterol reversed the levels of IL-6, TNFα in high glucose and upregulated the eNOS expression and NO activity.

Conclusions These results suggest that high glucose concentration decrease ABCG1 expression in ECs and that this effect is associated with endothelial dysfunction induced by high glucose. Upregulation of ABCG1 has an effective effect on protection of endothelial function.