EDHF Contribution To Microvascular Dilatation Is Not Linked To Endothelial Dysfunction In Morbidly Obese Qataris

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Abstract

Obesity is a growing health concern in Qatar because of the increased risk for type 2 diabetes, hypertension and other vascular disorders. One of the early adverse vascular events in obese individuals is an abnormal endothelial function which might alter the mechanism of vasodilatation. In particular, it is thought that loss of nitric oxide (NO)-mediated vasodilatation might be compensated by dilatation mediated by endothelium-derived hyperpolarizing factor (EDHF) in these individuals. It is however not clear whether such a switch in the contributions of these mediators would depend on the degree of loss of vascular endothelial function. Given that micro vessels in subcutaneous (SC) and omental (OM) fat depots of obese individuals might suffer different degrees of endothelial dysfunction [1], this study investigated whether the roles of NO and EDHF as mediators of vasodilatation of these vessels are altered in morbidly obese Qataris. Small arteries were isolated from SC and OM adipose tissues collected from consented morbidly obese Qatari patients (n=18) undergoing bariatric surgery at Hamad general hospital Doha. The vessels were studied by wire myography. Relaxation curves were generated for actetylcholine (Ach, the classical endothelium-dependent relaxant) in the absence or presence of Nω-Nitro-L-arginine methyl ester (L-NAME, 100 µM, inhibitor of nitric oxide synthase), apamin (0.5 µM) + charybdotoxin (0.1 µM) -combined blocker of EDHF, or BaCl2 (30 µM, blocker of inward rectifier potassium Kir channel ) on initial tone built with noradrenaline (1-5 µM). Curves were also generated for the NO donor and endothelium-independent relaxant, sodium nitroprusside (SNP). The patients had body mass index (BMI) of 46±2 Kg.m-2 and fasting plasma insulin of 17±2 mU/L [Mean±SEM]. Vessels from the SC depot were generally more responsive to Ach compared to OM vessels. Ach curves for both SC and OM vessels were significantly shifted to the right by L-NAME (n=5-7, p<0.05) and more so by apamine+charybdotoxin (n=6-7, p<0.01). The Emax for SC vessels dropped by 37 % in the presence of L-NAME and by 64 % in the presence of apamin+charybdotoxin. For OM vessels, the the reductions were 27 and 40 % respectively. BaCl2 caused a rightward shift in Ach response in both vessel types (n=4-5, p<0.05) although significant reduction in Emax was only recorded in OM vessels (p<0.05). When Ach and SNP responses were compared for each vessel type, only the OM vessels showed significant endothelial dysfunction (p<0.01). The results show that eventhough NO still plays a significant part in the endothelium-dependent dilator mechanisms of these vessels from morbidly obese Qataris, EDHF appears to play a greater role, particularly, in the SC vessels. The results also show that the increased role for EDHF is not due to loss of endothelial function since the substantially greater role in SC vessels was observed inspite of the relatively better endothelial function recorded in them compared with OM vessels. Furthermore, Kir channel involvement appears to be depot specific and largely in the OM vessels.

1. Farb MG et al., 2012 Arterioscler Thromb Vasc Biol. 32(2):467-73