Vascular endothelial dysfunction in type 2 diabetes: prenatal causes and effect of ACE-inhibition

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ABSTRACT

This PhD thesis is based on studies performed from March 2001 to March 2004 at the Department of Cardiology P, Gentofte Hospital, and the Department of Cardiology Y, Bispebjerg Hospital.

Patients with type 2 diabetes have an increased incidence of cardiovascular disease. Over the past decade there has been growing attention on the impact low birth weight on diabetes risk. Inhibition of angiotensin converting enzyme (ACE) may prevent the development of cardiovascular disease.

The purpose of this thesis was to: 1) Examine whether subjects with birth weight below the 10th percentile had simultaneously endothelial dysfunction, impaired insulin-stimulated endothelial function and impaired insulin-stimulated forearm glucose uptake (study I), 2) investigate whether endothelial function, insulin-stimulated endothelial function and glucose uptake was ameliorated by ACE inhibition in patients affected by type 2 diabetes (study II).

In study I 14 subjects with low birth weight and 16 matched subjects with normal birth weight subjects were included. Blood flow was measured by venous occlusion plethysmography. Endothelium-dependent vasodilation was stimulated by the infusion of acetylcholine. Endothelium-independent vasodilation was assessed by infusion of sodium nitroprusside. Insulin-stimulated endothelial function and insulin-stimulated glucose uptake was assessed. In study II, 24 patients with type 2 diabetes and 15 age matched healthy controls were studied. Endothelium-dependent and -independent vasodilation and a standard oral glucose tolerance test (75 g glucose) was performed before and after two months of quinapril treatment. Gene expression was measured by real time PCR.

In study I no difference was seen in insulin-stimulated endothelial function between the groups, while insulin-stimulated forearm glucose uptake was significant lower in the low birth weight group. In study II patients with type 2 diabetes both had endothelial dysfunction and impaired insulin-stimulated endothelial function, which was improved by two months quinapril treatment, while insulin-stimulated glucose uptake was unchanged.

Study I indicate that muscle specific defects in glucose uptake are present in early adulthood in low birth weight subjects. In study II ACE-inhibitor treatment was able to improve endothelial function and insulin-stimulated endothelial function, whereas no change was seen in forearm glucose uptake. Increased attention should be paid to maintain clinical control of subjects born with low birth weight.