

Endothelial Function and Arterial Stiffness in Uncomplicated Type 1 Diabetes and Healthy Controls and the Impact of Insulin on These Parameters during an Euglycemic Clamp

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Abstract

Background:

In addition to its role in glucose metabolism, insulin has shown to exert numerous vascular effects, and an impaired vascular function of insulin is assumed to be a major contributor in the development of vascular complications. Arterial augmentation (AP) and the augmentation index (Aix) are surrogate parameters of arterial stiffness and are commonly used as predictors for cardiovascular risk. The aim of this study is to investigate the effect of insulin on arterial stiffness and parameters of endothelial function in patients with type 1 diabetes and healthy control subjects.

Methods:

Fourteen patients with type 1 diabetes (six male, eight female) with a mean age of 36.6 ± 11.8 years and 14 healthy subjects (seven male, seven female) with a mean age of 27.3 ± 5.5 years were randomized to an euglycemic clamp with either a low (0.25 mU/kg/min) or a high (1.0 mU/kg/min) insulin dose on two different days. The mean HbA1c in the diabetic subjects was $7.3 \pm 0.7\%$. In these subjects, arterial stiffness was measured by pulse wave analysis (SphygmoCor, AtCor Medical, Australia). AP was calculated as the difference between the second and the first systolic shoulders of the central pressure wave curve, and the Aix was expressed as the percentage of AP from total pulse pressure. As parameters of endothelial function, cyclic guanosine monophosphate, nitrotyrosine, and asymmetric dimethylarginine were determined at baseline and after 120 minutes.

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Abbreviations: (ADMA) asymmetric dimethylarginine, (Aix) augmentation index, (AP) augmentation, (cGMP) cyclic guanosine monophosphate, (DM) diabetes mellitus, (NO) nitric oxide, (PWA) pulse waveform analysis

Keywords: ADMA, augmentation, augmentation index, endothelial function, diabetes mellitus type 1, nitrotyrosine

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Abstract (continued)

Results:

Patients with type 1 diabetes showed increased values for AP with 3.5 ± 3.1 mm Hg and Aix with $12.5 \pm 12.5\%$ compared to healthy controls with -0.7 ± 2.6 mm Hg for AP and $-4.2 \pm 10.6\%$ for Aix. This difference was statistically significant ($p < 0.01$). During the euglycemic clamp, insulin improved, but did not normalize the increased values for AP and Aix in patients with type 1 diabetes. Concerning parameters of endothelial function, patients with type 1 diabetes showed statistically significant increased values for nitrotyrosine compared to healthy controls at baseline [low insulin: diabetes mellitus (DM) 1993.12 ± 1330.85 nmol/liter vs healthy controls 803.7 ± 726.91 ; high insulin DM: 2208.02 ± 1736.57 nmol/liter vs healthy controls: 750.83 ± 426.03 nmol/liter] ($p < 0.05$).

Conclusion:

Patients with type 1 diabetes mellitus revealed an increased arterial stiffness measured as augmentation and augmentation index and increased nitrotyrosine levels as a marker of oxidative stress compared to healthy control subjects at baseline. Application of insulin improves the arterial elastic properties, but was not able to normalize the vascular function in patients with type 1 diabetes.

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