Vessels and Endothelium

12.10 Role of Sympathetic Activation on Changes of Brachial Artery Endothelial Function During Hyperinsulinaemia in Healthy Subjects

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Introduction. It has been shown that hyperinsulinaemia worsens brachial artery endothelial function in healthy subjects, while other in vitro and in vivo evidences (in other vascular districts) show that insulin facilitated both nitric oxide release and endothelium-dependent dilatation.

Aim. To evaluate changes of conduit artery endothelial function during infusion of exogenous insulin and the possible role of sympathetic activity.

Methods. In 20 healthy male volunteers (age: 27 ± 5 years), endothelium-dependent (flow-mediated dilation, FMD) and -independent (sublingual administration of 25 microg of glyceryl trinitrate, GTN) dilation were evaluated by high-resolution ultrasound and computerized analysis of changes in brachial artery diameter. Measures were taken at times -60, -10, 120 and 240 minutes during euglycaemic hyperinsulinaemic clamp (insulin infusion at $0.25 \text{ mU} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$ and 20% glucose solution at variable rates), in absence ($n=10$) or presence ($n=5$) of intravenous infusion of clonidine ($0.0052 \text{ microg/min/kg}$). In 5 subjects the protocol was assessed during infusion of saline.

Results. FMD nor GTN were affected by saline infusion. Insulin infusion raised plasma hormone concentrations from 63 ± 4 to $210 \pm 22 \text{ pmol/l}$, without changes in blood pressure or heart rate. Insulin infusion elicited a raise in plasma noradrenaline (from 260 ± 40 to $333 \pm 62 \text{ pg/ml}$, $p < 0.05$) which was not observed during parallel clonidine infusion. No change in FMD was observed during insulin infusion (from 7.2 ± 0.7 to $7.2 \pm 0.5\%$), while response to GTN was decreased (from 9.1 ± 1.0 to $6.8 \pm 0.8\%$; $p < 0.05$). Infusion of clonidine alone did not modify blood pressure, heart rate, FMD and response to GTN. During parallel insulin and clonidine infusion, FMD did not change (from 7.4 ± 1.8 to $6.7 \pm 2.9\%$, $p = \text{n.s.}$), while response to GTN was increased (from 9.4 ± 1.0 to 12.2 ± 0.8 , $p < 0.05$).

Conclusion. In healthy subjects, a mild 4-hour hyperinsulinaemia does not alter brachial artery endothelial function, but impairs endothelium-independent response. This effects disappears by sympathetic nervous system blockade.