Diminished insulin secretory response to glucose but normal insulin and glucagon secretory responses to arginine in a family with maternally inherited diabetes and deafness caused by mitochondrial tRNA(LEU(UUR)) gene mutation

Michael Brändle, R Lehmann, F E Maly, C Schmid & G A Spinas

OBJECTIVE: The effects of glucose, arginine, and glucagon on beta-cell function as well as alpha-cell response to arginine were studied in a family with mitochondrial diabetes. RESEARCH DESIGN AND METHODS: The function of alpha- and beta-cells was assessed in all five siblings carrying the mitochondrial tRNA Leu(UUR) gene mutation at position 3243 and compared with six sex-, age-, and weight-matched control subjects. Insulin and C-peptide responses were evaluated by intravenous glucagon application, intravenous arginine stimulation test, and intravenous glucose tolerance test. Glucagon secretion was assessed during the arginine stimulation test. RESULTS: The glucose disappearance constant (K(g)) value (mean +/- SEM 0.61 +/- 0.04 vs. 1.1 +/- 0.04, P = 0.0002) as well as the acute insulin response to glucose (area under the curve [AUC] 0-10 min, 77.7 +/- 50.7 vs. 1,352.3 +/- 191.5 pmol/l, P = 0.0004) were decreased in all patients. Similarly, glucagon-stimulated C-peptide response was also impaired (728 +/- 111.4 vs. 1,526.7 +/- 157.7 pmol/l, P = 0.005), whereas the insulin response to arginine (AUC) was normal (1,346.9 +/- 710.8 vs. 1,083.2 +/- 132.5 pmol/l, P = 0.699). Acute glucagon response to arginine (AUC) was normal but tended to be higher in the patients than in the control subjects (181.7 +/- 47.5 vs. 90.0 +/- 21.1 pmol/l, P = 0.099). CONCLUSIONS: This study shows impaired insulin and C-peptide secretion in response to a glucose challenge and to glucagon stimulation in diabetic patients with mitochondrial tRNA Leu(UUR) gene mutation, although insulin and glucagon secretory responses to arginine were normal.