Dutch Association for Diabetes Research (NVDO)

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Insulin secretion and insulin sensitivity were assessed in 20 first-degree NIDDM family members and compared with 20 controls matched for gender, body mass index, waist/hip ratio, and aerobic capacity ($\mathrm{VO}_{2\text{max}}$). All subjects had a normal glucose tolerance (OGTT, 75 g glucose). $\mathrm{VO}_{2\text{max}}$ was assessed by endurance exercise-test on a bicycle ergometer. A hyperglycemic clamp (10 mmol/l, 180 min) was performed. Glucose infusion rates (GIR) during the second and third hour of the clamp were measured; the relation between GIR and mean plasma insulin was used for assessment of insulin sensitivity. First-phase insulin secretion (plasma insulin 0–10 min, logarithmic transformation) showed a trend towards lower values in NIDDM family members ($\text{MANOVA, } P = 0.091$). Second-phase insulin secretion (2nd and 3rd hour) was lower in family members ($\text{MANOVA, } P = 0.042$). ANOVA showed lower insulin levels at all time-points after 100 min (all $P < 0.05$); at 180 min the geometric mean was 56 (range 27–152) vs 79 (range 32–230) mU/l. GIR of 2nd and 3rd hour were significantly lower in family members (5.7 ± 2.4 vs 8.3 ± 3.4, and 8.3 ± 3.7 vs 12.0 ± 4.0 mg/kg/min, both $P < 0.01$). After correction for the mean insulin level, insulin sensitivity (2nd and 3rd hour) was not significantly different (0.140 ± 0.054 vs 0.165 ± 0.075; and 0.165 ± 0.066 vs 0.180 ± 0.087 mg/kg/min/mU/l, both $P > 0.20$).

Conclusions: Glucose-tolerant first-degree NIDDM family members have decreased insulin secretion as compared to matched controls; their insulin sensitivity does not appear to be markedly decreased.


Insulin resistance is a prominent common pathogenetic trait of disorders such as non-insulin-dependent diabetes mellitus. It has been shown previously that under conditions of insulin resistance, glucose uptake in skeletal muscle is decreased as is glycogenesis. The rate of glycogen formation in response to insulin, however, is difficult to assess, and requires sequential muscle biopsies. $^{13}$C-MR spectroscopy offers an attractive non-invasive alternative. In 2 male insulin-sensitive healthy volunteers (age 23 and 27 yr, body mass index (BMI) 23.3 and 22.4 kg m$^{-2}$), glucose infusion rate (GIR) 14.0 and 16.1 mg kg$^{-1}$ min$^{-1}$, and 2 male insulin-resistant obese subjects (age 28 and 39 yr, BMI 31.0 and 33.6 kg m$^{-2}$, GIR 6.32 and 5.37 mg kg$^{-1}$ min$^{-1}$) hyperinsulinemic (60 mU m$^{-2}$ min$^{-1}$) euglycemic clamps with infusion of glucose 20% solution (30% enriched with $[1-^{13}]$C glucose) were combined with $^{13}$C-MR-spectroscopy of the gastrocnemius muscle. Proton-decoupled $^{13}$C-MR spectra were acquired with a time resolution of 15 min. Signals of creatine, glycogen and glucose were analyzed. Glycogen concentrations were calculated using creatine as an internal concentration standard. Plasma glucose enrichment levels were measured using high-resolution NMR. Resonances from glycogen and the glucose anomers were clearly visible. During the clamp glucose levels in spectra showed a steady state within 60 min after infusion. A strong linear increase was observed in $[1-^{13}]$C glycogen formation until the end of glucose infusion. Insulin-resistant subjects showed a much slower glucose incorporation rate in glycogen than the insulin-sensitive subjects (10.5 and 19.4 mM/h for the insulin-sensitive subjects, 4.3 and 3.9 mM/h for the insulin-resistant subjects, respectively).

Conclusion: $^{13}$C-MR spectroscopy in combination with euglycemic hyperinsulinemic clamping with infusion of $^{13}$C-enriched glucose offers a powerful tool to study glucose metabolism in vivo.

3. Effects of acarbose on glycaemic control in subjects with IDDM. J.P.J.E. Sels, H.E.R. Verdonk, B.H.R. Wollenhaupt, on behalf of the Dutch IDDM Acarbose Study Group. Department of Endocrinology, University Hospital, Maastricht; Bayer NV, Mijdrecht, Netherlands.