A comparison of muscle glycogen metabolism in Type 2 diabetic and matched normal subjects

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To understand the basic pathophysiologic regulation of muscle glycogen metabolism in type 2 diabetes, the diurnal changes in calf muscle glycogen concentration were measured using carbon-13 magnetic resonance spectroscopy before and after two mixed meals of similar composition. Results showed that fasting muscle glycogen levels were lower in diabetic subjects compared to age-matched controls (57.1 ± 3.6 vs. 97.1 ± 7.0 mmol/l, p<0.05), that the postprandial increase in response to the first meal was less (65.9 ± 5.2 vs. 97.1 ± 7.0 mmol/l at 240 min, p<0.005). The induced response to the second meal observed in controls was even more attenuated in the type 2 diabetes.

Methods

Subjects (n=9) with diet controlled type 2 diabetes (early phase) and age matched controls (n=9) were studied by ¹³C MRS. They fasted for a 12 hours period overnight before the study, but were given unlimited access to drinking water. At the start of the experiment, a baseline spectrum was acquired together with an arterialised blood sample. Subjects were then given a standard breakfast (190.5g carbohydrate, 41.0g fat, 28.8g protein, 1253 kcal), and further MRS measurements and blood samples were taken at 1, 2 and 4 hours, after which they were provided with a meal of similar composition for lunch. Further measurements were made at 5, 6 and 8 hours.

The muscle glycogen measurements were conducted on a 3T magnet, using a RF probe consisting of a circular ¹³C surface coil and quadrature coil for 1H decoupling. Subjects were positioned supine inside the magnet with their calf muscle over the probe. To minimise the risk of movement and to reproduce the same positioning of the leg for each measurement, a vacuum pillow was used. ¹³C excitation was performed using hard pulse of 100µs duration with CYCLOPS phase cycling and proton decoupling used such that the power deposition was within the SAR limit. For each time point, a total of 3,000 acquisitions were acquired in a time of 18 minutes. A calf shaped glycogen phantom of known concentration was used to calculate the glycogen concentrations.

Results

The glycogen concentration time courses for each group are shown in Figure 1a. The concentration in normal subjects rises significantly from basal (68.9 ± 4.1 mmol/l) to 97.1 ± 7.0 mmol/l after 2 hours following breakfast. After lunch, this trend continues up to a concentration of 108.0 ± 11.6 mmol/l. In diabetic subjects, fasting levels were lower (57.1 ± 3.6 mmol/l) and rose only to 70.8 ± 6.7 mmol/l by the end of the study. This was so despite marked hyperinsulinemia in the diabetic subjects (68.1 ± 9.0 vs. 30.8 ± 2.5 mmol/l fasting; p<0.001 and 752.0 ± 109.0 vs. 372.3 ± 78.2 mmol/l at 300 min; p=0.013). In the diabetic subjects, blood glucose rose from 7.1 ± 0.3 to 14.1 ± 0.1 mmol/l and in control subjects from 4.6 ± 0.1 to 6.6 ± 0.3 mmol/l. After the second meal, the mean glucose level was over 10.0 mmol/l in the diabetic subjects and less than 6.0 mmol/l in the controls (Figure 1b).

Discussion

In control subjects blood glucose rises rapidly following the first meal, whereas there is a delay of approximately 2 hours before net muscle glycogen levels increase significantly. This suggests that the immediate postprandial fate of glucose taken up in the muscle of healthy subjects is oxidation. The second meal elicits a much smaller response, a phenomenon first described over 80 years ago and probably related to the suppression of hepatic glucose release for periods of about 4 hours after a meal. The subjects with type 2 diabetes have significantly lower fasting glycogen levels (almost 20% down) despite their elevated plasma glucose and insulin levels. Following breakfast, muscle glycogen levels increased by only 15% (compared to 40% in the control group), and the post-lunch increment was even more attenuated (about 10% of the increment following breakfast) than in the controls despite marked hyperinsulinemia.

References