A COMPARISON OF HEPATIC LIPID AND GLYCOGEN LEVELS IN TYPE II DIABETICS USING ^{1}H AND ^{13}C MRS

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Background:

Metabolic disturbances in diabetes are thought may include an increase in hepatic lipid content, which has been suggested to contribute to the level of insulin resistance[1]. The purpose of this study was (i) to compare basal liver lipid concentrations in patients with type II diabetes and matched healthy controls, and (ii) to use ^{13}C MRS to compare liver glycogen concentrations in the same subject groups.

Method:

11 healthy subjects (mean ± SD: age = 53±10 years, Body Mass Index (BMI) = 27.9±3.4 kg/m^2, HbAlC = 5.3±0.2%) and 12 type II diabetic subjects (age = 62±9 years, BMI = 30.9±3.0 kg/m^2, duration of diabetes =8.2±5.0 years, HbAlC = 7.4±1.3%) were recruited for the study. Three measurements were taken over a 28 day period, on days 1, 5-8 and 21-28. All subjects were requested to record their dietary intake for 3 days prior to each scan and abstain from alcohol and exercise. The evening before each scan subjects were requested to eat the same meal, followed by a 12h overnight fast. On each visit, measurements of blood glucose, plasma insulin and HbA1C were also taken. All MR measurements were acquired on a Philips Achieva 3T system using a transmit/receive body coil for ^{1}H MRS and a ^{13}C surface probe with quadrature proton decouple coils for ^{13}C MRS and accompanying ^{1}H images.

Lipid measurements: T_1-weighted TFE images (flip angle=15º, resolution = 1.76x1.76x15mm^3, with 60 slices in the transverse plane and 10 sagittal slices) were acquired to allow positioning of the volume within the right lobe of the liver and for calculation of total liver volume. ^{1}H MR spectra were then acquired using a PRESS sequence and the following parameters: TE/TR = 40/5000ms, VOI = 30x30x30mm, N_{ave} = 8, BW = 2000Hz, 1024 samples. Proton spectra were post-processed using jMRUI and peak areas were calculated using in-house software built in Matlab. Liver lipid values are given as lipid/water ratios, assuming basal water concentrations to be constant.

Glycogen measurements: After acquisition of an initial survey to check positioning of the coil over the liver, ^{13}C spectra were acquired using a proton-decoupled pulse acquire sequence with the following parameters: TR = 1s, N_{ave} = 896, BW = 7000Hz, samples = 512 and CYCLOPS phase cycling. Decoupling was achieved using a WALTZ sequence. The ^{13}C pulse was optimised to give a 90º flip angle ~6cm from the coil. ^{13}C spectra were analysed using the Matlab version of MRUI with spectral peaks selected using the AMARES algorithm, fitted to Lorentzian lineshapes. Peak areas were calculated relative to a formate peak derived from a marker positioned at the centre of the ^{13}C coil and glycogen concentrations were calculated using a phantom replacement method in which scaling factors for the phantoms were calculated using the images to measure distance of the glycogen containing volume (hepatic tissue) from the coil.

Glycogen concentrations and lipid measurements were averaged across the three visits for each of the subjects.

Results:

Values of hepatic lipid/water were approximately 3-fold higher ($p < 0.05$) in diabetic subjects than in healthy subjects (Fig. 1a) whereas hepatic glycogen concentrations were not significantly different between the two groups (Fig. 1b). The absolute variation in liver lipid concentration was substantially greater in the diabetic group. Dividing the diabetic subjects into poor control (HbA1C ≥ 7.5%) and good control enabled a better understanding of the likely source of the increased variation. The poor control diabetics had higher values of lipid/water than the good control group, although this was not significant ($p = 0.22$). There were no differences in liver glycogen between the poor control, good control and healthy groups. When the liver lipid contents were considered in relation to BMI (i.e. level of obesity where BMI>30 is taken to be obese) the values tended to be greater in the obese diabetics than the non-obese diabetics, and similarly for the non-diabetic group. No differences in liver glycogen were measured due to differences in BMI.

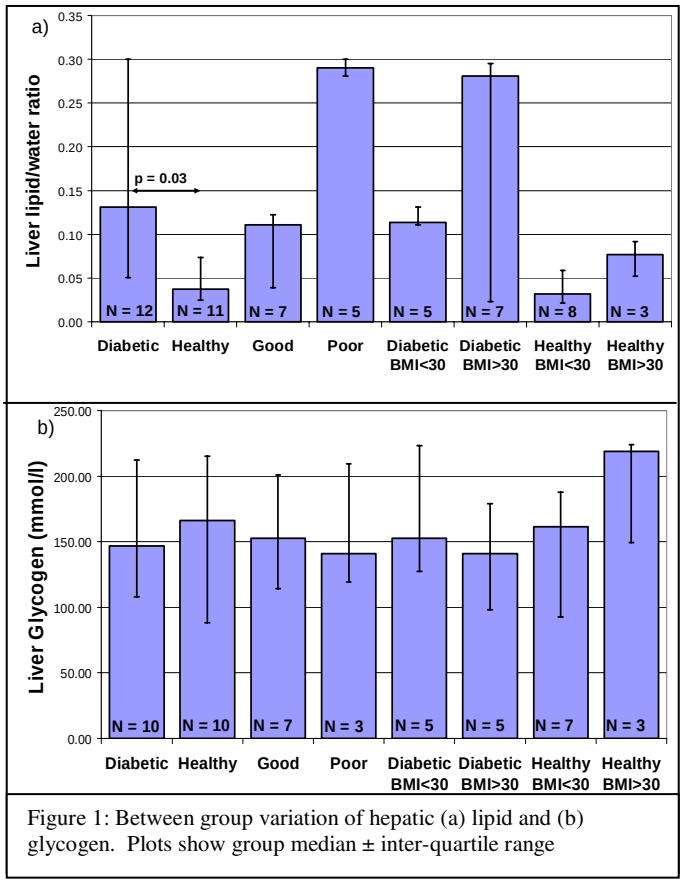

Figure 1: Between group variation of hepatic (a) lipid and (b) glycogen. Plots show group median ± inter-quartile range

Discussion:

Our findings, that patients with type II diabetes have higher liver lipid contents than age and BMI matched controls is in agreement with previous measurements obtained from biopsy[2]. However, this difference in liver lipid levels not reflected in differences in liver glycogen concentration in contrast to earlier studies in which the level of control was poorer[3] (HbAlc = 12±1%) than in our 'poorly controlled' subjects (HbAlc = 8.5±0.9%). Although there was insufficient power to achieve significance our results also suggest that the degree of diabetic control and level of obesity are major contributing factors to the increased liver lipid levels observed in type II diabetes subjects. The present study also provided some indication that the degree of diabetic control and level of obesity may affect liver lipid concentration however there was insufficient power to give significant results.

References:

1. Anderwald. C, Diabetes (2002), 51(10), pp3025. **2**. Knobler, H, Q J Med (1999), 92, pp73. **3**. Magnusson, I. J Clin Invest. (1992), 90(4) pp1323.