MR Assessment of the Effect of a Low Carbohydrate Diet on Hepatic Fat Content

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Introduction

Diets which involve restricting the intake of carbohydrates have been widely used for weight loss, but their influence on hepatic fat is not fully understood although the liver is responsible for much of the related ketone production caused by the diet. We are unaware of any previous studies analysing the effect of such a diet on the liver. The result of severe carbohydrate restriction is initially the depletion of glucose and glycogen stores and subsequently mobilisation of fat stores which are converted into ketones by the liver [1]. The increased utilisation of body fat stores is thought to be one of the major contributors to weight loss along with decreased calorie intake due to appetite suppression [2,3]. Hepatic steatosis is relatively widespread and increasingly thought to relate to carbohydrate metabolism and insulin resistance: recent studies provide evidence that insulin resistance and steatosis may be ameliorated by weight loss [4]. Several MR chemical shift methods of hepatic fat estimation have been described [5], including a well validated method that allows absolute fat estimation through correction for $T2^*$ variations [6]. These are thought to detect mainly hepatic triglyceride. The purpose of this study is to measure any hepatic fat change in healthy volunteers when following a low-carbohydrate diet by using MRI rather than established liver biopsy methods [7].

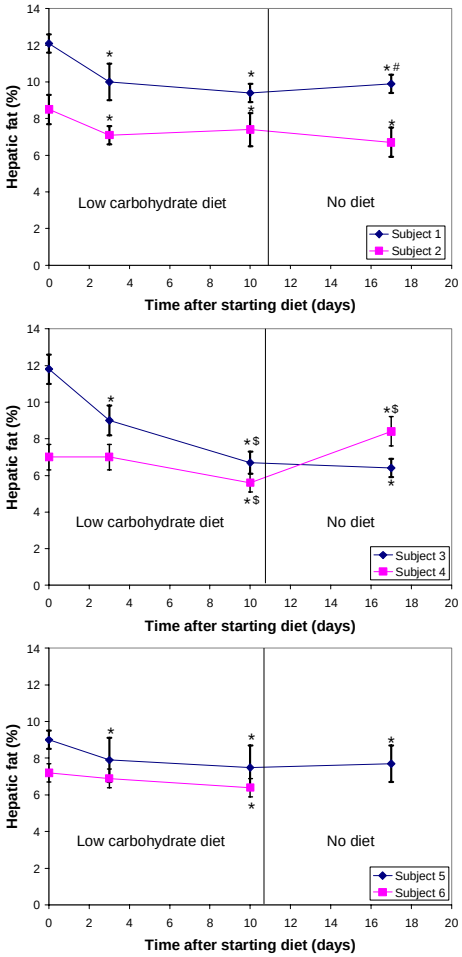

Figure 1 : Plot of hepatic fat content for 6 healthy volunteers during and after the low carbohydrate diet
* $p < 0.01$ compared to initial point
$ $p < 0.01$ compared to previous point
# $p < 0.05$ compared to previous point

Methods

The study was approved by the Local Ethical committee and informed consent obtained. Healthy volunteers were studied using the MR protocol below and their hepatic fat content percentage was calculated using the method in [6]. Using an arbitrary limit based on previous work those with a hepatic fat estimate of 7% or above were invited to enter the study. Six volunteers (3 male, 3 female, age 32-56) followed a low carbohydrate diet for ten days (keeping a diet diary and also abstaining from alcohol) and were studied at 4 time points; three days and ten days after commencing the diet and one week after returning to their normal diet.

MR protocol: Examinations were performed on a 1.5T whole body MRI (Excite, GEHT, Milwaukee) with an 8-channel body array. In and out of phase gradient echo scans were acquired axially during 20 second breath holds (matrix 256 x 128, 4 sections, section thickness 10mm, gap 1.5mm, TR/TE/NEX = 180/2.2 (out of phase), 4.4 (in phase)/1, flip angles 20^o and 70^o). A T2* map of the liver was obtained using a location-matched, multi-slice, multi-echo gradient sequence (TR = 120, 16 equally spaced echoes, TE1 = 2.2 ms, TE2 = 4.4 ms) and used to correct the in and out of phase images for $T2^*$ relaxation [6]. 4 slices were analysed and 3 ROIs were selected within each slice, giving 12 ROIs for each individual for each time point, which were averaged at that time point.

Results

Figure 1 shows the changes in hepatic fat content for the 6 individuals. 4 of the subjects experienced a significant ($p < 0.01$) decrease in hepatic fat in the first three days of dieting. Three of these subjects displayed no further significant change between day 3 and day 10 of the diet. Subjects 4 and 6, who had the lowest initial fat concentrations (7.2% and 7% respectively), showed no significant decrease within the first three days of dieting: in both cases a significant decrease ($p<0.01$) was demonstrated after 10 days of dieting. Two subjects (1 and 4) experienced an increase ($p<0.05$) one week after returning to normal dietary habits, in one case to a level exceeding the initial fat content. Several trends are suggested by the data: those individuals with the greatest initial fat content had the greatest percentage decrease during the first three days of the diet ($\kappa = 0.87$) and over the full 10 days of the diet ($\kappa = 0.70$). Weight loss during the diet was also found to be weakly correlated with hepatic fat loss: the weight loss and hepatic fat loss both measured at day 3 are correlated ($\kappa = 0.64$), and more weakly correlated at day 10 ($\kappa = 0.51$). There was no correlation between the Body Mass Index (BMI) and the percentage hepatic fat loss by day 10 ($\kappa = 0.08$). One week after ceasing the diet, two subjects gained weight, two lost weight and one remained the same (one was lost to follow up). This variability may be due to changed dietary habits following successful weight loss.

Conclusions

The onset of the hepatic fat reduction appears to be related to the initial fat concentration. These effects will be studied further with a larger number of volunteers. One effect not accounted for here is the effect of cessation of alcohol consumption during the diet: this effect alone will be studied in a second leg of the trial. To the best of our knowledge this is the first study to use MR fat measurement to track a longitudinal change in hepatic fat during dietary manipulation. This study shows that a low carbohydrate diet produced a reduction of hepatic fat content in all 6 participants.

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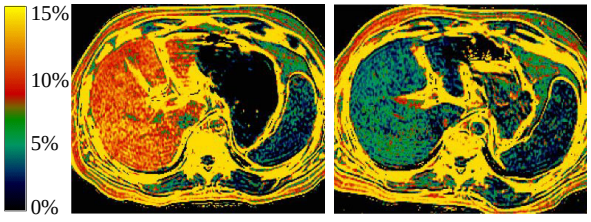

Figure 2 : Liver fat concentration maps shown for subject 3 before the diet (left) and 10 days after commencing the diet.

Subject	Initial BMI (kg/m^2)	Initial hepatic fat conc^n (%)	Total weight loss: day 3 (kg)	Total weight loss by day 10 (kg)	Total weight loss by day 17 (kg)	% Hepatic Fat Loss by Day 10
1	30	12.1	2	4	3.5	22
2	32	8.5	2	4	2	13
3	29	11.8	3	4.5	6	43
4	27	7.0	1	2	3.5	20
5	23	9.0	4	3	3	17
6	28	7.2	0	3	-	11

Table 1 : Initial BMI, hepatic fat and weight data for the volunteers.