Regional and intracellular lipid stores: Impact of a 12 week randomized cross over study of isonitrogenous low fat vs. low carbohydrate weight loss diets

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Introduction

Weight loss (WL) can have a potent effect to improve insulin sensitivity and reduce the risk for CVD in overweight individuals (1-3). Low fat vs. low carbohydrate weight loss diets have been widely debated for their effect on fat depots (3) and insulin sensitivity (4). Interactions in hepatic, intramyocellular lipid and abdominal fat (4-6) have been found in response to different diets. To our knowledge, no previous investigation has simultaneously assessed the effect of weight loss, in obese subjects due to low fat vs. low carbohydrate diets on the changes in fat storage on liver, muscle and adipose tissue and the relationship of such changes to insulin sensitivity improvement difference due to the low fat vs. low carbohydrate diets. Therefore, the current study was undertaken to study regional and intracellular lipid store changes as well as the insulin sensitivity after isonitrogenous low fat vs. low carbohydrate weight loss diets.

Methods

Subjects: Eight obese normoglucose tolerant subjects (7F/1M) (BMI: 35.0±1.5, range: 30.5 ~ 41.7. Age: 55.9±2.1, range: 48 ~ 66 yr) were studied.

Diet: Subjects were randomized to low carbohydrate (n=4) (LC: 5%CHO/65%Fat/30%Protein) vs. low fat (n=4) (LF: 50%CHO/20%Fat/30%Protein) diet with caloric intake pegged to their resting energy expenditure for 6 weeks. For the final 6 weeks, subjects crossed over to the other diet. Lunch and supper meals were provided, with breakfasts according to menu lists. Subjects were metabolically characterized 3 times: at baseline, after 6 weeks on one diet, and then after a further 6 weeks on the alternative diet.

MR: IMCL of right calf muscles in soleus (S) and tibialis anterior (TA) were measured by ^{1}H-MR spectroscopic imaging (^{1}H-MRSI) (TR/TE=1000/24 ms) in a 4 T Varian Inova whole body MR system with a TEM ^{1}H resonator. In-plane phase encoding (32x32) over 16.0-x16.0 cm^2 with a 1-cm slice thickness resulted in nominal voxel resolution of 0.25 mL. For internal reference purposes, water SI (TR/TE=5000/24 ms) on the same slice was also acquired with 16x16 phase encoding. For each muscle group (S and TA), all 32x32 MRSI spectra were inspected and the best resolved 3 ~ 4 voxels per muscle selected and processed. Intrahepatic lipid (IHL) content was obtained on a 1.5 T GE Signa scanner using water suppressed ^{1}H MRS via a single voxel PRESS (TR/TE=4000/28 ms) with a GE body coil. Typical voxel size was ~30 mL. Subcutaneous (SAT) and visceral fat (VAT) in the region from 6 cm above to 12 cm below of L2/L3 were assessed from T1-weighted axial images (TR/TE=400/14 ms; 18 slices) obtained on a 1.5 T GE Signa scanner using the body coil. The images were analyzed in Adobe Photoshop®.
Evaluation of insulin sensitivity: 3 Step (basal, 8, 40 mU/m^2/min) hyperinsulinmic-euglycemic pancreatic clamp with 6,6-d2 glucose tracers for measurement of insulin sensitivity within 48-hour of MR measurements.

Results and Discussion

Mean weight loss of the subjects was 10.2±0.9 kg after 12-week of dieting ($p<0.001$) and the BMI decreased to 31.2±1.6 from 35.0±1.5 ($p<0.001$). Subjects lost 4.4±0.7 kg after LF diet and 5.8±0.7 kg after LC diet while the BMI declined 1.6±0.2 after LF diet and 2.2±0.3 after LC diet (LF vs. LC: NS for both weight loss and BMI decline).

The IMCL increased significantly after LC diet and decreased after LF diet. Evans et al (7) demonstrated that all the fatty acids released by lipoprotein lipase (LPL) in skeletal muscle are taken up by this tissue. It is well known that LPL activity is increased by high fat diets thus LC diet may have similarly increased LPL activity resulting in increased FFA trapping in muscle and increase IMCL. The intrahepatic lipid decreased significantly from 160.8 to 59.5 mmol/kg wet wt ($p=0.003$) after the 1st 6-week diet and then slightly decreased to 39.3 mmol/kg wet wt after the 2nd 6-week diet (p=NS). The SAT and VAT decreased significantly in the 1st and 2nd 6-week diets although the subjects lost more VAT in the 1st 6-week ($p=0.03$). After the 12-weeks of weight loss, VAT decreased 34% from basal while SAT decreased 21% ($p=0.02$). There was no effect of diet *per se* on the decrement in IHL, SAT and VAT. The BMI loss in the period of LF diet strongly correlates with VAT loss ($R=0.769$, $p=0.026$) and IHL decline ($R=0.847$, $p=0.008$). Similar trends were seen after LC diet ($p=0.086$ vs.VAT loss and $p=0.050$ vs. IHL decline). Total glucose disposal (Rd) after both diets increased; the change was greater for LC ($p<0.05$). Rd after LC diet was negatively predicted by IHL ($R=-0.845$, $p=0.008$) and VAT ($R=-0.663$, $p=0.073$). EGP suppression decreased after LC diet (77.8±5.2% vs. 85.9±5.1%, $p=0.014$ post- vs. pre- LC diet); change was not significant for LF diet.

Table 1 Lipid stores, Rd and EGP suppression during weight loss diets (Mean±SE)

	IMCL-S	IMCL-TA	IHL	SAT	VAT	FFA	TG	Rd	%EGP Supp
Baseline	8.4±1.1	2.3±0.6	160.8±44.3	5.0±0.6	2.0±0.2	0.67±0.09	0.88±0.12	4.0±0.7	78.3±8.9
LF	5.1±0.7$^{++,\Theta}$	2.4±0.4^{+}	62.9±25.0**	4.1±0.5**$^{,\Theta\Theta}$	1.5±0.2**$^{,\Theta\Theta}$	0.60±0.11$^{+,\Theta}$	0.93±0.10$^{++,\Theta}$	4.3±0.5	83.8±4.4
LC	11.9±1.1$^{\Theta\Theta}$	4.9±1.0$^{\Theta}$	35.9±6.8*$^{,\Theta}$	4.2±0.6**$^{,\Theta}$	1.4±0.2**$^{,\Theta\Theta}$	0.75±0.09	0.47±0.03**$^{,\Theta\Theta}$	5.0±0.4*	77.8±5.2$^{\Theta}$

IMCL, IHL (mmol/kg wet wt); SAT, VAT (kg); FFA, TG (mM-basal); Rd (mg/kg-min-40mU/m2/min).
Pre- vs. Post- diet: $^{\Theta}p<0.05$, $^{\Theta\Theta}p<0.01$; LF or LC vs. Baseline: *$p<0.05$, **$p<0.01$; LF vs. LC: $^{+}p<0.05$, $^{++}p<0.01$

In conclusion, the intrahepatic lipid and abdominal region fat were decreased after substantial weight loss due to the LC and LF diets while IMCL increased after LC diet and decreased after LF diet. Increased FFA after LC diet (0.75±0.09 mM vs. 0.60±0.11, $p=0.11$) may be responsible for the decrease of EGP suppression after diet. The peripheral insulin sensitivity significantly improved only after the LC diet that was accompanied by lower plasma TG. This implies that IMCL is not the primary driving force for the improvement in peripheral insulin sensitivity associated with weight loss due to the LC diet.

References

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