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High or Low Carbohydrate Diets: Which is better for weight loss, insulin resistance and fatty livers?

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The recent increase in obesity and the health problems associated with it has grown into a huge public health burden (1). A plethora of diets continue to be promoted to help with weight reduction (2). Many of these diets are either low carbohydrate (LC) or high carbohydrate (HC) diets (2,3). There is continuing debate as to which of these two dietary approaches is best with respect to weight loss, reduction in cardiovascular risk including blood pressure and lipid levels and in patients with diabetes, improvement of blood glucose control.

The manuscript by Kirk et al. in this issue of Gastroenterology (4) addresses some of these issues. These authors studied 22 obese (BMI 36.5 ± 0.8) men and women, 14 of whom had impaired glucose tolerance but none had overt diabetes. These volunteers were admitted to the General Clinical Research Center (GCRC) at Washington University Medical Center and were randomized to either a HC (carbohydrate ≥ 180 g/d) or a LC (carbohydrate ≤ 60 g/d) diet. After 48 h on these diets, the patients were discharged from the GCRC and told to continue on their HC or LC diets at home until they reached a 7% weight loss, which occurred after ~ 6 weeks. At that time, their caloric intake was adjusted to maintain weight. After ~ 4 weeks on this new weight maintaining diet, all subjects were readmitted to the GCRC, where the clamps and body composition analyses were repeated.

What were the findings and what can we learn from them? Let us first look at weight loss. Both groups lost about 2 kg during the initial 48 h in the controlled environment of the GCRC, where their energy intake was ~ 1100 Kcal/day. Their pre-hospitalization energy intake is not known, but probably was at least 3000 Kcal/day, based upon a study with similarly obese subjects where energy intake was measured (6). Thus, assuming no change in energy expenditure, their estimated caloric deficit was ~ 4000 Kcal/48 h (~ 3000 − 1100 Kcal/day × 2 days).

More important than this initial ~ 2 kg weight loss, which was mostly a loss of body water (7), was the weight loss which occurred during the first ~ 6 weeks during which both LC and HC groups lost ~ 7 kg or 5250 g of fat (~ 75% of the weight loss was from fat). On average, therefore, they lost ~ 125 g of fat/day (5250 g/42 days) which translates into an energy deficit of ~ 1000 Kcal/day. This suggests that once out of the hospital, their average daily energy intake increased considerably, to perhaps as much as ~ 2000 Kcal/day. Interestingly, weight loss was similar in the LC and the HC group after 48 h and after ~11 weeks. Some studies have reported greater weight loss for several months with LC than HC diets (7–11); however, these differences disappeared during longer follow up (9,11). Moreover, a meta-analysis of several such studies came to the conclusion that there were no impressive differences in the effects on

weight loss between these diets (12). Thus, the study by Kirk supports the concept that over longer periods of time, the macronutrient composition of a calorie restricted diet is not very important for weight loss which depends primarily on the balance of calories ingested vs. calories expended (5).

Kirk et al. also found that insulin's effect to suppress hepatic glucose production (reflecting hepatic insulin sensitivity) improved more in the LC than the HC group, both after 48 h and after ~ 11 weeks. By contrast, insulin stimulation of glucose uptake, (reflecting peripheral, mostly skeletal muscle insulin sensitivity), improved only after ~ 11 weeks. What may explain the beneficial effect of the LC diet on the improvement in insulin sensitivity and why was it seen first in the liver and only later in the periphery? With respect to the first question, less insulin is secreted and needed to metabolize fatty acids or amino acids than glucose (13). A practical application of this is the calculation of insulin requirement by insulin pump users that is based exclusively on the carbohydrate contents of meals. Also, 63% of the subjects in the Kirk study were glucose intolerant, i.e., they had insufficient insulin secretion and therefore, can be anticipated to cope better with a less insulin requiring low LC diet than a more insulin requiring HC diet. Better glycemic control improves insulin resistance, perhaps by decreasing glucose toxicity (14). With respect to the second question, the liver is known to be several times more sensitive to insulin than skeletal muscle (15). Therefore, changes in insulin action can be detected first in the liver, particularly, if these changes are small, which was the case in the current study for both hepatic and peripheral insulin sensitivity.

Perhaps the most interesting observation made by Kirk and colleagues was that the LC diet decreased the excessive intrahepatic triglyceride (IHTG) content of these obese subjects within 48 h by 30% (compared to ~ 10% in the HC group) and that both the LC and HC calorie restricted diets reduced IHTG content by ~ 40% after ~ 11 weeks. The cause for the rapid clearance of IHTG with the LC diet is not known. One factor might be the early improvement of hepatic insulin sensitivity which was also ~ 3 times greater in the LC compared to the HC group. Several studies have shown that insulin resistance is an essential requirement for accumulation of hepatic fat (reviewed in reference 16). Insulin resistance driven hyperinsulinemia has been shown to markedly stimulate de novo lipogenesis (17) by upregulating the expression of the sterol regulatory element binding protein-1c (SREB-1c) in the liver which is followed by the activation of key lipogenic enzymes including fatty acid synthase and acetyl CoA carboxylase (18–20). Whatever the reason, the dramatic effect of LC diets on IHTG deserves further investigation in view of the clinical importance of hepatic steatosis, which can advance to steatohepatitis and cirrhosis (16), and because of our very limited pharmaceutical armentarium to combat this problem (21).

In summary, for non-diabetic individuals who desire weight loss, long term compliance with a calorie restricted diet is important. There is presently no convincing evidence that over the long term, LC calorie restricted diets are better than HC calorie restricted diets. Similarly, to mobilize fat from fatty livers in individuals with NAFLD, reduction of excessive nutrient intake is most important. Thus, any calorie restricted diet, whether LC or HC to which individuals are able to adhere for years rather than weeks, should be effective to improve weight, insulin resistance and cardiovascular risk factors (22). By contrast, for glycemic control in diabetic patients LC diets are better than HC diets.

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References

1. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999–2000. JAMA 2002;288:1723–1727. [PubMed: 12365955]
2. Freedman MR, King J, Kennedy E. Popular diets: a scientific review. Obes Res 2001;9(Suppl 1):1S–40S. [PubMed: 11374180]
3. Atkins, RC. Dr. Atkins' new diet revolution. New York: Avon Books; 1992.
4. Kirk E, Reeds DN, Finck BN, Mayurranjan MS, Klein S. Dietary fat and carbohydrates differentially alter insulin sensitivity during caloric restriction. Gastroenterology. 2008in press
5. Kinsell LW, Gunning B, Michaels GD, Richardson J, Cox SE, Lemon C. Calories do count. Metabolism 1964;13:195–204. [PubMed: 14127686]
6. Boden G, Sargrad K, Homko C, Mozzoli M, Stein TP. Effect of a low-carbohydrate diet on appetite, blood glucose levels and insulin resistance in obese patients with type 2 diabetes. Ann Intern Med 2005;142:403–411. [PubMed: 15767618]
7. Yang M-U, Van Itallie TB. Composition of weight lost during short-term weight reduction. Metabolic responses of obese subjects to starvation and low-calorie ketogenic and nonketogenic diets. J Clin Invest 1976;58:722–730. [PubMed: 956398]
8. Samaha FF, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, Williams T, Williams M, Gracely EJ, Stern L. A low-carbohydrate as compared with a low-fat diet in severe obesity. N Engl J Med 2003;348:2074–2081. [PubMed: 12761364]
9. Foster GD, Wyatt HR, Hill JO, McGuckin BG, Brill C, Mohammed BS, et al. Randomized trial of a low-carbohydrate diet for obesity. N Engl J Med 2003;348:2082–2090. [PubMed: 12761365]
10. Brehm BJ, Seeley RJ, Daniels SR, D'Alessio DA. A randomized trial comparing very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. J Clin Endocrinol Metab 2003;88:1617–1623. [PubMed: 12679447]
11. Stern L, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, et al. The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. Ann Intern Med 2004;140:778–785. [PubMed: 15148064]
12. Malik VS, Hu FB. Popular weight-loss diets; from evidence to practice. Nat Clin Pract Cardiovasc Med 2007;4:34–41. [PubMed: 17180148]
13. Fajans SS, Floyd JC, Knopf RF, Conn JW. Effect of amino acids and protein on insulin secretion in man. Rec Prog Horm Res 1967;23:617–656. [PubMed: 4876487]
14. Boden G, Ruiz J, Kim C-J, Chen X. Effects of prolonged glucose infusion on insulin secretion, clearance, and action in normal subjects. Am J Physiol 1996;270:E251–E258. [PubMed: 8779946]
15. Rizza RA, Mandarino LJ, Gerich JE. Dose-response characteristics for effects of insulin on production and utilization of glucose in man. Am J Physiol 1981;240:E630. [PubMed: 7018254]
16. Angulo PA. Nonalcoholic fatty liver disease. N Engl J Med 2002;346:1221–1231. [PubMed: 11961152]
17. Tamura S, Shimomura I. Contribution of adipose tissue and de novo lipogenesis to nonalcoholic fatty liver disease. J Clin Invest 2005;115:1139–1142. [PubMed: 15864343]
18. Browning JD, Horton JD. Molecular mediators of hepatic steatosis and liver injury. J Clin Invest 2004;114:147–152. [PubMed: 15254578]
19. Shimomura I, Matsuda M, Hammer RE, et al. Decreased IRS-2 and increased SREBP-1 lead to mixed insulin resistance and sensitivity in livers and lipodystrophic and ob/ob mice. Mol Cell 2000;6:77–86. [PubMed: 10949029]
20. Koo SH, Dutcher AK, Towle HC. Glucose and insulin function through two distinct transcription factors to stimulate expression of lipogenic enzyme genes in liver. J Biol Chem 2001;276:9437–9554. [PubMed: 11112788]
21. Boden G, Zhang M. Recent findings concerning thiazolidinediones in the treatment of diabetes. Expert Opin Investig Drugs 2006;15:243–250.
22. Fontana L, Meyer TE, Klein S, Holloszy JO. Long-term calorie restriction is highly effective in reducing the risk for atherosclerosis in humans. PNAS 2004;101:6659–6663. [PubMed: 15096581]