Metabolic Effects of High-Protein, Low-Carbohydrate Diets

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Weight-losing diets appeal to the growing population of overweight Americans. Fad diets promise rapid weight loss, easy weight loss, limited restrictions on portion sizes of favorite foods, and above all an enhanced sense of well being. The popularity of fad diets points out the honest promises of traditional weight loss diets. Traditional weight loss diets promise slow weight loss of 0.45 to 0.9 kg/week. The weight loss is nothing but easy, because portion sizes of nearly all foods except low-calorie "free foods" must be continuously evaluated and tracked. Claiming an enhanced sense of well being is hardly appropriate for a traditional diet—most patients report dissatisfaction from the constant vigilance over dietary intake. Through discipline and perseverance, traditional weight loss programs try to teach a patient a new lifestyle of healthy eating. Unfortunately, 70% of successful weight losers return to their old habits and within 2 years regain at least half of the weight lost. These patients typically have little insight into the reasons why the weight was regained, and consider themselves "failures" to traditional diet programs. They become prime targets for diets promising rapid and easy weight loss.

PROTOTYPES OF THE HIGH-PROTEIN, LOW-CARBOHYDRATE DIETS

High-protein, low-carbohydrate diets have a long history of cyclic popularity. Greek Olympians ate high meat, low vegetable diets >2,000 years ago to improve athletic performance. Dr. William Harvey recommended a diet prohibiting sweet and starchy foods and permitting ad lib consumption of meats for patients who needed diuresis. As the basic understanding of nutrition and essential vitamins developed, these diets fell out of favor. They regained popularity in the late 1960s and early 1970s with the publication of the Atkins' Diet, Stillman's Diet, The Drinking Man's Diet, the Scarsdale Diet, and the Air Force Diet. The American Medical Association strongly criticized these diets,[1] leading to their submergence on the popular diet trend.

Resurgence of low carbohydrate diets has been fueled by rising obesity and insulin resistance in the general population. Although the Atkins' Diet is the prototype of the low carbohydrate diet, The Sugar Busters Diet, Carbohydrate Addicts Diet, Protein Power Diet, and the Zone Diet are all variations on this common theme.

Several diets promise that, as long as you restrict carbohydrates, you will lose weight and you can eat as much food as you want. There may be a kernel of truth to this claim. For some patients, high-protein intake suppresses appetite.[2] For other patients, ketosis from carbohydrate restriction suppresses appetite. Restricting carbohydrate eliminates some popular foods that are often consumed in excess such as bread, cereal, soft drinks, french fries, and pizza. By simply excluding carbohydrate foods, patients following the Atkins diet typically consume 500 fewer calories a day.[3]

HOW LOW-CARBOHYDRATE DIETS PRODUCE INITIALLY GREATER WEIGHT LOSS

Reducing caloric intake by 500 kcal/day should result in a 0.45- to 0.9-kg weight loss each week. However, low-carbohydrate, high-protein diets typically produce a 2- to 3-kg weight loss in the first week. This added weight loss is not due to the miracle of "switching the body's metabolism over to burning fat stores." It is due to a diet-induced diuresis. When carbohydrate intake is restricted, 2 metabolic processes occur, both of which simultaneously reduce total body water content. The first process is mobilization of glycogen stores in liver and muscle. Each gram of glycogen is mobilized with approximately 2 g of water. The liver stores approximately 100 g of glycogen and muscle has 400 g of glycogen. Mobilization glycogen stores result in a weight loss of approximately 1 kg. Patients notice this change as a reduction in symptoms of "bloating" and are very pleased with the effect. The second process is generation of ketone bodies from catabolism of dietary and endogenous fat. Ketone bodies are filtered by the kidney as nonreabsorbable anions.[4] Their presence in renal lumenal fluids increase distal sodium delivery to the lumen, and therefore increase renal sodium and water loss.

In a study comparing an 800-calorie mixed diet with an 800-calorie low-carbohydrate, high fat diet,[5] 10-day weight loss was 4.6 kg on the ketogenic diet and 2.8 kg on the mixed diet. Energy-nitrogen balanced studies documented that the difference in weight lost was all accounted for by losses in total body water.

LONG-TERM WEIGHT LOSS IS INFLUENCED BY CALORIC RESTRICTION, NOT CARBOHYDRATE RESTRICTION

The diuretic effect of low-carbohydrate intake is limited to the first week of the diet. The remaining

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weight loss is a function of the laws of energy balance. Calories from any source determine the success of additional weight loss.

In the only published study of Atkins diet, patients following the diet reduced caloric intake by 500 kcal/day. The average weight loss was 7.7 kg at 8 weeks, which is no greater than that expected from caloric restriction alone.[6] The ability of low carbohydrate intake to generate ketones has been touted as a relative advantage for losing weight. However, this advantage was not confirmed in a 1-month study comparing ketogenic with nonketogenic hypocaloric diets.[7] Most comparison studies have evaluated the relative advantages of either a low carbohydrate or low fat hypocaloric diets; some studies found a slight 1- to 3-kg greater weight loss on a low-carbohydrate diet,[8,9,10,11] others a slight advantage with a high-carbohydrate diet,[12] but most studies have observed no statistical advantage of a low-carbohydrate diet.[13–18] The preponderance of evidence suggests that as long as caloric intake remains constant,[19] there is no intrinsic advantage to cutting carbohydrate intake.[20]

UNTOWARD METABOLIC EFFECTS

Complications from ketosis: Eucaloric ketogenic diets have been prescribed as part of an antiepileptic regimen in children with refractory seizure disorders. Children following these ketogenic diets have higher rates of dehydration, constipation, and kidney stones. Other reported adverse effects include hyperlipidemia, impaired neutrophil function, optic neuropathy, osteoporosis, and protein deficiency.[21]

Because ketogenic diets effect the central nervous system, it has been suspected that ketogenic diets may alter cognitive function. In a randomized weight loss study comparing a ketogenic with a nonketogenic hypocaloric diet, subjects consuming the ketogenic diet had impairments in higher order mental processing and flexibility than those following the nonketogenic diet.[7]

Complications from high saturated fat intake: Despite the beneficial effects of weight loss, diets that promote liberal intake of high fat meats and dairy products raise cholesterol levels. In a study 24 subjects following the Atkins'-type 4-week induction diet, then 4 weeks maintenance diet,[6] low-density lipoprotein cholesterol levels increased significantly from 127 to 151 mg/dl. Similar increases in total cholesterol (13%) were reported in a study of patients following the Stillman diet.[22]

Complications from high fat intake: High fat diets increase free fatty acid flux and circulating free fatty acids. Fasting plasma free fatty acids may have a pro-arrhythmic effect in cardiac muscle. A number of mechanisms have been suggested including a possible detergent effect of circulating free fatty acids on cell membranes and direct effects of acylcarnitine on cellular ion channels and exchangers.

Complications from exclusion of fruits, vegetables, and grains: Because they exclude fruits, vegetables, and grains, low-carbohydrate, high-protein diets are deficient in micronutrients. Children consuming low-carbohydrate ketogenic diets have reduced intakes of calcium, magnesium, and iron.[21] Two sailors following a low-carbohydrate, high-protein hypocaloric diet during an extended voyage developed optic neuropathy from thiamine deficiency.[23] Although vitamin deficiencies can be circumvented by supplemental multivitamins, even supplemented low-carbohydrate diets will still be deficient in a growing number of important, biologically active phytochemicals present in fruits, vegetables, and grains.

Complications from high-protein intake: Increasing the protein content of a diet significantly increases glomerular filtration rate.[24,25] Increases in glomerular filtration rate are likely explained by increased renal capillary permeability. Unfortunately, this compensatory response to the greater production of nitrogen is insufficient to clear protein by-products, and blood urea nitrogen levels increase. High protein diets significantly lower urinary pH by increasing titratable acid concentrations.[25,26] High protein intakes provide a greater uric acid load to the kidney. Despite increases in urinary uric acid excretion, increases in serum uric acid are observed.[6,26]

UNTOWARD LONG-TERM EFFECTS

Development of nephrolithiasis: Hypercalciuria is a risk factor for nephrolithiasis. High-protein diets induce hypercalciuria by several different mechanisms. High-protein diets increase glomerular filtration rate and decrease renal tubular reabsorption of calcium. The relation between dietary protein intake and calcium excretion (Table 1) is clearly linear.[27]

The stone-forming propensity of the hypercalciuria induced by high-protein diets is aggravated by other changes in urine composition. A high animal protein diet reduces gastrointestinal alkali absorption, leading to reduced urinary citrate.[28] Hyperuricemia and hyperuricosuria are also associated with excess intake of animal protein. Animal protein is a rich source of sulfur-containing amino acids; amino acids have a greater propensity to lower urinary pH.

Adding a carbohydrate restriction to a high-protein diet exacerbates many of these parameters. Low-carbohydrate intake further reduces urinary pH by inducing ketosis. Limiting the intake of vegetables and fruits further reduces urinary citrate by reducing dietary sources of alkali. Thus, high-protein, low-carbohydrate diets are associated with hypercalciuria, hyperuricosuria, and hypocitraturia, which can all contribute to renal calculi formation.

Development of osteoporosis: High-protein, low-carbohydrate diets generate a high acid load, resulting in a subclinical chronic metabolic acidosis. Metabolic acidosis promotes calcium mobilization from bone.[29] Osteoclasts and osteoblasts respond to small changes in pH in cell culture; thus, a small decrease in pH results in a large burst of bone resorption.

The effects of varying dietary protein intakes on

TABLE 1 Graded Effects of High-Protein Diets on Urinary Calcium Excretion

Diet Duration	% Calories from Protein*	No.	Creatinine Clearance (ml/min) Low	Medium	High	Urinary Calcium Excretion (mg/24 h) Low	Medium	High
15 d	1%/12%/25%	6	98	105	122	51	99	161
4 d	8%/12%/25%	16	85	95	107	108	129†	196†
15 d	8%/16%/24%	33				168	240†	301†
15 d	8%/16%/24%	9				217	303†	426†
15 d	8%/16%/24%	9				168	240†	301†

*Percent calories calculated assuming 70-kg average subject weight, 2,400-calorie diet.
†Significantly different from low-protein diet.

bone turnover has been carefully documented in young women consuming metabolic diets. High-protein diets increase renal calcium excretion, raised parathyroid hormone levels, and raise urinary N-telopeptide concentrations. Markers of bone formation (alkaline phosphatase and osteocalcin) remain steady, suggesting that high-protein diets increase bone resorption without affecting the rate of bone formation.[27] These effects may be exaggerated in older persons who tend to have decrements in renal clearance of acid and higher serum parathyroid hormone concentrations.[29]

Progression of chronic renal insufficiency: In several small, randomized, controlled dietary trials, dietary protein restriction retarded the progression of diabetic nephropathy to end-stage renal disease.[30] High-protein, low-carbohydrate diets have a weak effect at reducing creatinine clearance over time, and could potentially hasten renal failure in patients with baseline renal insufficiency.

Patients are inherently attracted to the simple, permissive dietary instructions: eat as much as you want of foods containing fat and protein, but don't eat foods containing carbohydrate. As promised, almost everyone loses weight during the first week. Low-carbohydrate diets cause a greater initial weight loss from a physiologic diuresis accompanying the obligate loss of glycogen stores and renal clearance of ketone bodies. Once glycogen stores have been liberated, and a new steady state for total body sodium has been achieved, these diets hold no greater promise for weight loss than any other caloric restricted diet. High-fat, low-carbohydrate diets can be harmful. The diet plan is deficient in micronutrients. Consuming ad libitum fatty meats raises total and low-density lipoprotein cholesterol levels. High-protein, low-carbohydrate intakes create a subclinical metabolic acidosis, and increase blood urea nitrogen and uric acid levels. Resultant urine acidification, hyperuricosuria, and hypercalciuria increase urine lithogenicity. Trying to convince a devotee to stop the diet uncovers yet another deleterious effect; ketogenic diets impair higher order cognitive function. High-protein, low-carbohydrate diets have untoward clinical consequences for patients with coronary artery disease, including progression of diabetic nephropathy, exacerbation of gouty diathesis, increases in circulating free fatty acids, and increases in low-density lipoprotein cholesterol levels. High-protein, low-carbohydrate diets are not superior weight-losing diets and should not be recommended.

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