A Review of Very Low Carbohydrate Diets for Weight Loss

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- *Background:* Many patients are asking about weight reduction diets publicized in the lay press, such as "Protein Power," "Sugar Busters," and "Dr. Atkins' New Diet Revolution." A common theme of these diets is the restriction of carbohydrate intake.
- *Objective:* To summarize the published medical literature regarding very low carbohydrate (< 40 g/day) diets.
- *Methods:* A MEDLINE search and hand-search of reference lists was performed.
- *Results:* The literature search yielded 329 citations; 32 contained primary data. Based on several small, short-term observational studies, very low carbohydrate diets can lead to ketosis, weight loss, and changes in carbohydrate and lipid metabolism. Most of these studies also included caloric restriction. The long-term risks are not documented.
- *Conclusions:* There is some evidence that very low carbohydrate diets can lead to significant metabolic changes including weight loss, but the long-term risks and benefits are not established. Due to the widespread popularity of these diets, further research is in order.

Many patients are asking their physicians about popular weight loss diets, yet most physicians are ill prepared to discuss them. These weight loss diets have a common theme of increasing the amount of protein and fat and limiting the amount of carbohydrate that is consumed. The strictest limitation of carbohydrate, to less than 40 g per day, results in the metabolic state of mild ketosis. Very low carbohydrate diets have been advocated for health conditions such as obesity, epilepsy, diabetes mellitus, and inborn errors of carbohydrate metabolism [1–4]. The use of a very low carbohydrate diet for treatment of epilepsy and obesity came from the clinical observations that starvation led to a reduction in seizures and a decrease in appetite. For epilepsy, the effectiveness of very low carbohydrate diets has recently been reconfirmed in a multicenter observational study [5].

When carbohydrate consumption is less than approximately 40 g per day, the body shifts into a metabolic state of using ketone bodies and fatty acids as its major metabolic fuels [6]. By doing so, the body mobilizes free fatty acids from adipose cells. The metabolic changes seen in starvation ketosis are as follows: after 1 to 2 days, glycogen stores are depleted, so the body changes into a mode of gluconeogenesis to supply tissues with glucose. After 3 to 4 days, the metabolism changes to using ketone bodies as a source of energy. After the second week, there is an increasing use of ketones and fatty acids as sources of metabolic energy for body tissues.

Because the most commercially successful very low carbohydrate diet book has sold over 12 million copies, the safety and efficacy of these types of diets is of importance to public health [7]. This paper summarizes the available data on very low carbohydrate diets for weight loss to allow clinicians to be more informed in their discussions of these diets with their patients.

Methods

The aim of the literature search was to review primary data on very low carbohydrate diets in humans using electronic databases and a manual search of reference lists of identified articles. A MEDLINE search from 1966 to May 1999 was performed using the text words "low carbohydrate diet," "ketogenic diet," and "Atkins' diet" in titles, abstracts, and MESH headings. Using these text words, 329 citations were retrieved, and 32 contained primary data relevant to very low carbohydrate diets (defined as fewer than 40 g of carbohydrate per day). The other 297 articles were excluded because they contained no primary data or abstractable data (eg, graphs only), were not relevant, were animal studies, or were in a non-English language. The data from the articles were abstracted by the author using a standardized form.

Results

Effect on Metabolism of Very Low Carbohydrate Diets

Several studies have documented that if the amount of carbohydrate grams is limited to fewer than approximately

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Table 1. Effect of Very Low Carbohydrate Diet or Starvation Ketosis on Carbohydrate Metabolism

Ref	Subjects and Body Type	CHO and Kcal per Day	Days	Timepoint	AcAc (mmol/L)	β-OH-B (mmol/L)	Glucose (mmol/L)	Insulin (mmol/L)
					Mean (SEM)			
Phinney	9	20 g	28	PRE		0.07 (0.02)	4.8 (0.12)	10.7 (0.8)
1983 [8]	Lean	30–50 kcal/kg		POST		1.6 (0.25)	4.1 (0.12)	9.0 (1.0)
Atkinson	7	0.5 g/kg	42	PRE			105 mg/dL (2.8)	29.2 (2.6)
1985 [9]	Obese	1800 kcal		POST			85 mg/dL (2.8)	15.4 (2.7)
Wing	10	"Ketogenic diet"	28	PRE		0.27 (0.08)		
1995 [10]	Obese	594 kcal		POST		2.64 (0.43)		
Langfort	8	< 5% CHO	3	PRE		0.28 (0.08)		23.0 (3.5)
1996 [11]	Lean	32 kcal/kg		POST		1.9 (0.27)		10.5 (3.5)
Hall	10	Starvation	12	PRE	0.15	0.27	5.0	21.4
1984 [12]	Obese			POST	1.04	3.97	3.82	

AcAc = acetoacetate; CHO = carbohydrate; β-OH-B = β-hydroxybutyrate; SEM = standard error of the mean.

40 per day, then ketosis can be reliably induced. **Table 1** shows the effects of very low carbohydrate diets and starvation on ketone body levels, glucose, and insulin. Five studies involving a total of 44 subjects have shown that ketones will increase and insulin levels will decrease after the consumption of a ketogenic or starvation diet. For example, in 1 study of 9 lean subjects on a 20 g, 30 to 50 kcal/kg per day diet, the β-hydroxybutyrate levels increased from 0.07 to 1.6 mmol/L [8]. Ketone bodies (acetoacetate and β-hydroxybutyrate) increase to levels comparable to the ketosis that develops in starvation but are lower than the 15 to 20 mmol/L seen in diabetic ketoacidosis [13]. Although the long-term effects of mild ketosis are not known, there does not appear to be any serious adverse effect in up to 6 weeks as shown in these studies.

Effect on Weight of Very Low Carbohydrate Diets

Seven observational studies have shown that very low carbohydrate and low calorie diets can lead to significant weight loss from a pre-diet baseline (**Table 2**). In 6 studies evaluating very low carbohydrate diets for at least 1 month, the average amount of weight lost was approximately 10 lb per month [14–19]. Most of these studies restricted daily calories in addition to carbohydrates, so the weight loss seen in these studies reflects the combination of calorie and carbohydrate restriction. The 1 study that did not restrict calories (3666 kcal/day) but still restricted carbohydrate consumption to 30 g/day found a 16.2-lb weight loss on average after 9 weeks [17]. One controlled trial comparing 2 dietary interventions randomized 21 females to a 1182-calorie, low carbohydrate diet and found a weight loss of 12.0 lb over 2 weeks, superior to the 8.7-lb weight loss seen with the 1182-calorie balanced diet [24].

One study [14] evaluated a variation of the most commercially popular very low carbohydrate diet. In this study, 24 mildly overweight normocholesterolemic individuals were instructed to follow the low carbohydrate diet as described by Atkins [7] for 8 weeks. All but 3 subjects were confirmed to be restricting carbohydrate consumption based on urinary ketone measurement. After 8 weeks, subjects lost 16.9 lb on average, total cholesterol showed no significant change, but low-density lipoprotein (LDL) cholesterol increased 24 mg/dL on average ($P < 0.01$) and uric acid increased from 5.9 to 7.7 mg/dL on average ($P < 0.01$). There were no clinically serious adverse effects in this 8-week study.

Effect on Lipids of Very Low Carbohydrate Diets

Eight studies were found that document changes in lipid metabolism as a result of carbohydrate and calorie restriction (Table 2). For example, 1 study of 25 obese subjects restricted to 25 g of carbohydrate and 1000 kcal per day for 1 month had a reduction in total cholesterol of 41 mg/dL [21]. Another study of 24 obese subjects restricted to less than 8 g/day of carbohydrates for 2 months had an increase in LDL of 24 mg/dL, a reduction in triglycerides of 45 mg/dL, and a non–statistically significant change in total cholesterol and HDL [14]. Two of the 3 studies in obese subjects showed improvements in lipid parameters, while all 3 studies in lean subjects showed worsening of lipid parameters while on the diet (Table 2).

Table 2. Effect of Very Low Carbohydrate Diets on Weight and Lipids

Ref	Subjects and Body Type	CHO and Kcal per Day	Duration	Time	Weight (lb)	Cholesterol (mg/dL)	Triglycerides (mg/dL)	HDL (mg/dL)	LDL (mg/dL)
						Mean (SEM)			
Larosa	24	0 g, 5–8 g	2 mo	PRE	203.9 (4.0)	205 (8)	138 (15)	51 (4)	127 (6)
1980 [14]	Obese	? kcal		POST	187.0 (6.2)	217 (12)	93 (9)	49 (3)	151 (10)
					$P < 0.001$*	P = NS	$P < 0.01$	P = NS	$P < 0.01$
Golay	22	40 g	6 wk	PRE	235.4 (11)	220 (11.6)	150.5 (8.9)	42.7 (3.9)	—
1996 [15]	Obese	1000 kcal		POST	217.6 (8.8)	173.7 (7.7)	123.9 (8.9)	34.9 (3.9)	
					$P < 0.001$	$P < 0.001$	$P < 0.01$	$P < 0.001$	
Willi	6	25 g	2 mo	PRE	147.8 (13.6)	162 (12)	—	45	100
1998 [16]	Obese	675 kcal		POST	132.4	121 (8)		35	90
					$P < 0.001$	$P < 0.01$		$P < 0.05$	P = NS
Young	3	30 g	9 wk	PRE	102.2	—	—	—	—
1971 [17]	Obese	3666 kcal		POST	86.0				
Rabast	14	40 g	28 d	PRE	240.5 (7.0)	—	—	—	—
1981 [18]	Obese	1340 kcal		POST	214.1				
Rickman	12	7 g	7–17 d	PRE	139.5 (SD = 19.9)	215 (SD = 32.8)	131 (SD = 40.7)	—	—
1974 [19]	Lean	1400 kcal		POST	131.6 (SD = 20.0)	248 (SD = 31.6)	116 (SD = 36.8)		
					$P < 0.001$	$P < 0.001$	P = NS		
Azar	6	1 g	4 d	PRE	150.0 (SD = 22.8)	245.2 (SD = 35.2)	—	—	—
1963 [20]	Lean	2000 kcal		POST	143.5 (SD = 23.2)	284.3 (SD = 53.5)			
					P = 0.03	P = 0.06			
Rabast	25	25 g	1 mo	PRE	—	245 (SD = 78)	230 (SD = 256)	—	—
1978 [21]	Obese	1000 kcal		POST		204 (SD = 43)	134 (SD = 61)		
Newbold	7	? g	3–18 mo	PRE	—	263.0 (SD = 39.3)	113.0(SD = 35.6)	63.3(SD = 25.2)	—
1988 [22]	?	? kcal		POST		189.3 (SD = 19.9)	74.7(SD = 8.3)	63.2(SD = 24.5)	
						P = 0.002	P = 0.03	P = NS	
Phinney	9	20 g	28 d	PRE	—	169 (9)	91 (10)	40 (4.4)	—
1983 [23]	Lean	? kcal		POST		208 (11)	79 (12)	40 (7.7)	
						P = 0.001	P = NS		

CHO = carbohydrate; HDL = high-density lipoprotein; LDL = low-density lipoprotein; NS = not statistically significant; SD = standard deviation; SEM = standard error of the mean.

* Reflects statistical significance of the change between pre and post measurements.

Adverse Effects of Very Low Carbohydrate Diets

When beginning a very low carbohydrate diet, there may be a period of adjustment when side effects such as headache and fatigue occur [14]. Although major adverse effects have not been demonstrated with very low carbohydrate diets in adults, the appropriate studies to detect these adverse events have not been done. There is 1 case report that suggests a relationship between low carbohydrate diets and optic neuropathy [25]. One study of 6 adolescents following a low carbohydrate diet noted an increase in calcium excretion and a decrease in total bone mineral content [16]. The clinical relevance of this finding was not certain.

Adverse Effects of the Ketogenic Diet for Epilepsy

The "ketogenic diet" is a specific treatment for epilepsy that consists of a high fat, low carbohydrate, low protein diet to induce the state of ketosis [26–29]. Side effects of the chronic ketogenic diet in children have been calcium oxylate and urate kidney stones (from 0.5% to 5.0% incidence over 1 year), acidosis, persistent vomiting, amenorrhea (21%), hypercholesterolemia (unknown occurrence rate), and water-soluble vitamin deficiencies (unknown occurrence rate).

Discussion

Several small observational studies demonstrate that very low carbohydrate diets (< 40 g / day) can have significant effects on metabolism, including the induction of ketosis and weight loss. These ketosis-producing diets can also have significant effects on lipid metabolism, improving in some cases and worsening in other cases the cardiovascular risk profile. Although overall the results are encouraging, the studies of very low carbohydrate diets suffer from small sample sizes and possible selection biases that limit the generalizability of the findings.

Any diet that produces such dramatic changes in weight and metabolism has side effects [24]. Minor symptoms can be expected during the first 2 weeks and can be reduced by sufficient fluid intake. Possible serious adverse effects of long-term very low carbohydrate dieting include hyperuricemia, kidney stones, and hyperlipidemia. Hyperuricemia can be reduced by using uricosuric agents such as allopurinol. Nephrolithiasis can be reduced with adequate hydration and treated with urinary alkalinization in affected patients [27]. A conservative approach would be to measure the lipid profile, kidney function, and uric acid before and a few months after initiating the diet to monitor any changes that may occur.

Many overweight patients are unable to follow diets that require exercise due to morbid obesity, disability, and arthritis. Although the very low carbohydrate diets may work better if dieters exercise, they still may work without any exercise at all. Should these diets prove safe and effective for obesity, there would be an immediate clinical usefulness for patients who are unable to exercise to lose weight.

Several important questions remain to be answered: How do very low carbohydrate diets work? Do these diets work in some individuals and not in others? What factors are related to a positive response from the diet? Because morbidly obese patients may have to follow the diet for several years, what are the risks of long-term diet adherence?

In summary, very low carbohydrate diets can lead to ketosis, weight loss, and a variable effect on lipid parameters. Because the long-term risks of these diets are not known, further research into the long-term clinical and quality of life outcomes should be conducted before widespread implementation in the health care setting. In patients who choose to follow a very low carbohydrate diet, periodic measurement of lipid profiles, uric acid, and kidney function may be prudent.

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References

1. Harvey W. On corpulence in relation to disease. London: Henry Renshaw; 1872:109–22.
2. Bernstein RK. Dr. Bernstein's diabetes solution: a complete guide to achieving normal blood sugars. Boston: Little, Brown; 1997.
3. Lennox WG. Ketogenic diet in the treatment of epilepsy. N Engl J Med 1928;199:744–75.
4. Wexler ID, Hemalatha SG, McConnell J, Buist NR, Dahl HH, Berry SA, et al. Outcome of pyruvate dehydrogenase deficiency treated with ketogenic diets. Studies in patients with identical mutations. Neurology 1997;49:1655–61.
5. Vining EP, Freeman JM, Ballaban-Gil K, Camfield CS, Camfield PR, Holmes GL, et al. A multicenter study of the efficacy of the ketogenic diet. Arch Neurol 1998;55:1433–7.
6. Devlin TM, editor. Textbook of biochemistry: with clinical correlations. 3rd ed. New York: Wiley-Liss; 1992.
7. Atkins RC. Dr. Atkins' new diet revolution. New York: Avon Books; 1992.
8. Phinney SD, Bistrian BR, Wolfe RR, Blackburn GL. The human metabolic response to chronic ketosis without caloric restriction: physical and biochemical adaptation. Metabolism 1983;32:757–68.
9. Atkinson RL, Kaiser DL. Effects of calorie restriction and weight loss on glucose and insulin levels in obese humans. J Am Coll Nutr 1985;4:411–9.
10. Wing RR, Vazquez JA, Ryan CM. Cognitive effects of ketogenic weight-reducing diets. Int J Obes Relat Metab Disord 1995;19:811–6.
11. Langfort J, Pilis W, Zarzeczny R, Nazar K, Kaciuba-Uscilko H. Effect of low-carbohydrate-ketogenic diet on metabolic and hormonal responses to graded exercise in men. J Physiol Pharmacol 1996;47:361–71.

12. Hall SE, Wastney ME, Bolton TM, Braaten JT, Berman M. Ketone body kinetics in humans: the effects of insulin-dependent diabetes, obesity, and starvation. J Lipid Res 1984;25:1184–94.
13. Degroot LJ, editor. Endocrinology. 3rd ed. Philadelphia: WB Saunders; 1995:1511.
14. Larosa JC, Fry AG, Muesing R, Rosing DR. Effects of high-protein, low-carbohydrate dieting on plasma lipoproteins and body weight. J Am Diet Assoc 1980;77:264–70.
15. Golay A, Allaz AF, Morel Y, de Tonnac N, Tankova S, Reaven G. Similar weight loss with low- or high-carbohydrate diets. Am J Clin Nutr 1996;63:174–8.
16. Willi SM, Oexmann MJ, Wright NM, Collop NA, Key LL Jr. The effects of a high-protein, low-fat, ketogenic diet on adolescents with morbid obesity: body composition, blood chemistries, and sleep abnormalities. Pediatrics 1998;101:61–7.
17. Young CM, Scanlan SS, Im HS, Lutwak L. Effect of body composition and other parameters in obese young men of carbohydrate level of reduction diet. Am J Clin Nutr 1971;24:290–6.
18. Rabast U, Vornberger KH, Ehl M. Loss of weight, sodium and water in obese persons consuming a high- or low-carbohydrate diet. Ann Nutr Metab 1981;25:341–9.
19. Rickman F, Mitchell N, Dingman J, Dalen JE. Changes in serum cholesterol during the Stillman diet. JAMA 1974;228: 54–8.
20. Azar GJ, Bloom WL. Similarities of carbohydrate deficiency and fasting. II. Ketones, nonesterified fatty acids and nitrogen excretion. Arch Int Med 1963;112:338–43.
21. Rabast U, Kasper H, Schonborn J. Comparative studies in obese subjects fed carbohydrate-restricted and high carbohydrate 1,000-calorie formula diets. Nutr Metab 1978;22: 269–77.
22. Newbold HL. Reducing the serum cholesterol level with a diet high in animal fat. South Med J 1988;81:61–3.
23. Phinney SD, Bistrian BR, Evans WJ, Gervino E, Blackburn GL. The human metabolic response to chronic ketosis without caloric restriction: preservation of submaximal exercise capability with reduced carbohydrate oxidation. Metabolism 1983;32:769–76.
24. Worthington BS, Taylor LE. Balanced low-calorie vs. high-protein-low-carbohydrate reducing diets. I. Weight loss, nutrient intake, and subjective evaluation. J Am Diet Assoc 1974;64:47–51.
25. Hoyt CS III, Billson FA. Low-carbohydrate diet optic neuropathy. Med J Aust 1977;1:65–6.
26. Freeman JM, Vining EP, Pillas DJ, Pyzik PL, Casey JC, Kelly LM. The efficacy of the ketogenic diet-1998: a prospective evaluation of intervention in 150 children. Pediatrics 1998;102:1358–63.
27. Edelstein SF, Chisholm M. Management of intractable childhood seizures using the non-MCT oil ketogenic diet in 20 patients. J Am Diet Assoc 1996;96:1181–2.
28. Ballaban-Gil K, Callahan C, O'Dell C, Pappo M, Moshe S, Shinnar S. Complications of the ketogenic diet. Epilepsia 1998;39:744–8.
29. Herzberg GZ, Fivush BA, Kinsman SL, Gearhart JP. Urolithiasis associated with the ketogenic diet. J Pediatr 1990;117:743–5.

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Very-low-carbohydrate diets or ketogenic diets have been in use since the 1920s as a therapy for epilepsy and can, in some cases, completely remove the need for medication. From the 1960s onwards they have become widely known as one of the most common methods for obesity treatment. Recent work over the last decade or so has provided evidence of the therapeutic potential of ketogenic diets in many pathological conditions, such as diabetes, polycystic ovary syndrome, acne, neurological diseases, cancer and the amelioration of respiratory and cardiovascular disease risk factors. Recent reports showing a greater weight loss with a free-living very low-carbohydrate ketogenic (VLCK) than a low-fat diet after 3 and 6 months [1â€“5] has generated interest in mechanisms that may account for these responses. Earlier work that involved comparison of isocaloric formula VLCK and low-fat (LF) diets [6], indicated that weight loss was greater with a VLCK, suggesting a metabolic advantage (i.e., a greater weight loss with one diet over another with different macronutrient distribution but the same energy content) [7, 8].Â Volek and Westman [16] have reviewed the potential favorable effects of VLCK diets while other reviews that have focused on the potential adverse effects of VLCK diets caution to avoid or limit their use [17â€“19]. Very-low-carbohydrate diets or ketogenic diets have been in use since the 1920s as a therapy for epilepsy and can, in some cases, completely remove the need for medication. From the 1960s onwards they have become widely known as one of the most common methods for obesity treatment. Recent work over the last decade or so has provided evidence of the therapeutic potential of ketogenic diets in many pathological conditions, such as diabetes, polycystic ovary syndrome, acne, neurological diseases, cancer and the amelioration of respiratory and cardiovascular disease risk factors.Â This review revisits the meaning of physiological ketosis in the light of this evidence and considers possible mechanisms for the therapeutic actions of the ketogenic diet on different diseases.