

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	β -OH-B	Glucose	Insulin
					(mmol/L)	(mmol/L)	(mmol/L)	(mmol/L)
					Mean (SEM)			
Phinney 1983 [8]	9 Lean	20 g 30–50 kcal/kg	28	PRE		0.07 (0.02)	4.8 (0.12)	10.7 (0.8)
				POST		1.6 (0.25)	4.1 (0.12)	9.0 (1.0)
Atkinson 1985 [9]	7 Obese	0.5 g/kg 1800 kcal	42	PRE			105 mg/dL (2.8)	29.2 (2.6)
				POST			85 mg/dL (2.8)	15.4 (2.7)
Wing 1995 [10]	10 Obese	“Ketogenic diet” 594 kcal	28	PRE		0.27 (0.08)		
				POST		2.64 (0.43)		
Langfort 1996 [11]	8 Lean	< 5% CHO 32 kcal/kg	3	PRE		0.28 (0.08)		23.0 (3.5)
				POST		1.9 (0.27)		10.5 (3.5)
Hall 1984 [12]	10 Obese	Starvation	12	PRE	0.15	0.27	5.0	21.4
				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)
	Body Type		Kcal per Day								
Larosa 1980 [14]	24 Obese	0 g, 5-8 g ? kcal	2 mo	PRE POST	203.9 (4.0) 187.0 (6.2) P < 0.001*	205 (8) 217 (12) P = NS	138 (15) 93 (9) P < 0.01	51 (4) 49 (3) P = NS	127 (6) 151 (10) P < 0.01		
Grolay 1996 [15]	22 Obese	40 g, 1000 kcal	6 wk	PRE POST	235.4 (11) 217.6 (8.8) P < 0.001	220 (11.6) 173.7 (7.7) P < 0.001	150.5 (8.9) 123.9 (8.9) P < 0.01	42.7 (3.9) 34.9 (3.9) P < 0.001	—		
Willi 1998 [16]	6 Obese	25 g, 675 kcal	2 mo	PRE POST	147.8 (13.6) 132.4 P < 0.001	162 (12) 121 (8) P < 0.01	—	45 35 P < 0.05	100 90 P = NS		
Young 1971 [17]	3 Obese	30 g, 3666 kcal	9 wk	PRE POST	102.2 86.0	—	—	—	—		
Rabast 1981 [18]	14 Obese	40 g, 1340 kcal	28 d	PRE POST	240.5 (7.0) 214.1	—	—	—	—		
Rickman 1974 [19]	12 Lean	7 g, 1400 kcal	7-17 d	PRE POST	139.5 (SD = 19.9) 131.6 (SD = 20.0) P < 0.001	215 (SD = 32.8) 248 (SD = 31.6) P < 0.001	131 (SD = 40.7) 116 (SD = 36.8) P = NS	—	—		
Azar 1963 [20]	6 Lean	1 g, 2000 kcal	4 d	PRE POST	150.0 (SD = 22.8) 143.5 (SD = 23.2) P = 0.03	245.2 (SD = 35.2) 284.3 (SD = 53.5) P = 0.06	—	—	—		
Rabast 1978 [21]	25 Obese	25 g, 1000 kcal	1 mo	PRE POST	—	245 (SD = 78) 204 (SD = 43)	230 (SD = 256) 134 (SD = 61)	—	—		
Newbold 1988 [22]	7 ?	? g, ? kcal	3-18 mo	PRE POST	—	263.0 (SD = 39.3) 189.3 (SD = 19.9) P = 0.002	113.0 (SD = 35.6) 74.7 (SD = 8.3) P = 0.03	63.3 (SD = 25.2) 63.2 (SD = 24.5) P = NS	—		
Phinney 1983 [23]	9 Lean	20 g, ? kcal	28 d	PRE POST	—	169 (9) 208 (11) P = 0.001	91 (10) 79 (12) P = NS	40 (4.4) 40 (7.7)	—		

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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