The Ketogenic Diet: Healthy or Harmful? A Review In Light Of Its Renewed Popularity

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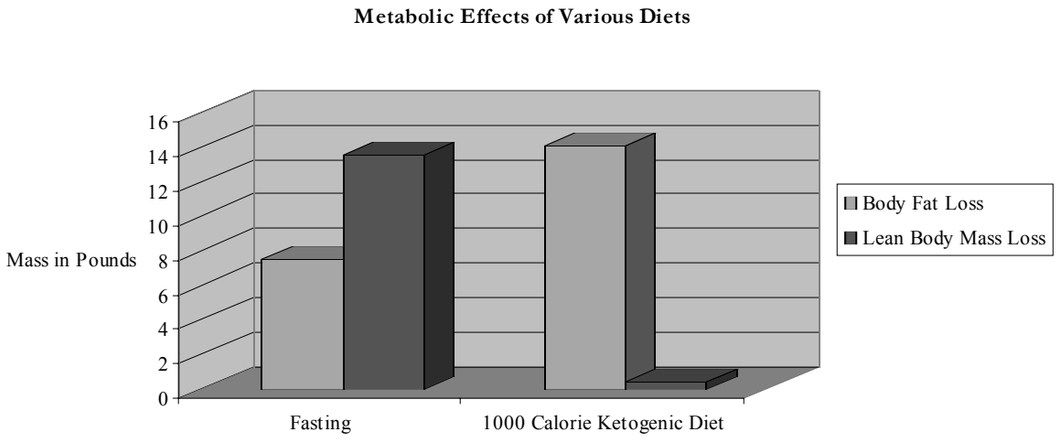
With obesity on the rise in the western world, there is increasingly strong medical and social pressure to lose weight. There is a vast array of diet plans and products that take advantage of this pressure; many of which have little scientific basis for their claims. Most diets fall under the three general categories of "do-it-yourself", non-clinical, and clinical regimes. Do-it-yourself diets rely on the motivation of the dieter and his or her willingness to investigate different options. These regimes usually employ diet books, special-purpose food products, and videos. The ketogenic Atkins diet is an example of this type of approach to weight loss. Non-clinical programs involve trained counselors who provide an educational and support service for clients, often after consultation with a health professional. Weight Watchers is a familiar example of a non-clinical program. Clinical programs involve direct interaction with health care professionals; often a group of specialists with training in nutrition, behaviour therapy, exercise, and counseling[1]. The goal of any diet is to maximise fat loss and minimise lean muscle breakdown. There is experimental evidence that ketogenic diets (a recently re-popularised group of weight loss regimes) are effective in reducing body fat, while maintaining lean muscle mass (see Figure 1).

The cornerstone of any ketogenic diet (so-called due to the production of ketones during lipolysis) involves the ingestion of significantly reduced amounts of complex carbohydrates, such as those found in pasta, rice, bread, and potatoes[3]. In place of these, diets rich in protein from foods such as meat, fish, and dairy as well as green leafy vegetables are recommended. A typical daily menu is given to illustrate what may be consumed on such a diet (see Figure 2). The ketogenic diet has been shown to minimise muscle loss during dieting while maintaining a steady loss of body fat stores[2]. This type of diet also allows for rapid weight loss, as demonstrated by one study in which patients were shown to lose 18-22kg in 12-15 weeks[4]. The ketogenic diet has also been utilised for applications outside of weight loss, including nutritional therapy for diabetics and for decreasing seizure frequency in children with medically refractory epilepsy[5]. Several examples of ketogenic diets include the currently popular Atkins Diet, the Banting Diet (introduced more than a century ago) and the Sippy diet (used for ulcer therapy)[6].

The physiological basis of the ketogenic diet relies on the reduction of insulin levels. Insulin is released in response to rising blood glucose. In the absence of glucose (either from digested carbohydrate or glycogen stores) certain hormonal changes occur leading to the use of stored fat for energy. When blood glucose decreases (<3.58mmol/L), growth hormone, epinephrine, and glucagon are released to maintain energy metabolism. Within the adipocyte, growth hormone and epinephrine activate the breakdown of triacylglycerol to fatty acids, which are transported to the liver and muscle. The oxidation of free fatty acids gives rise to acetyl-CoA, which can enter the Krebs cycle directly. However, in the liver, excess acetyl-CoA derived from fatty acid oxidation is converted to ketone bodies; namely acetoacetate, gamma-hydroxybutyrate, and acetone. This conversion occurs only in the liver, and the resultant ketone bodies are transported to peripheral tissues (such as muscle and brain) where they are converted back to acetyl-CoA for entry into the

Figure 1: Metabolic Effects of Various Diets[2]
(n=7 obese males. 10 days on each diet. Fast = No calorie Ketogenic diet = 4% carbohydrate, 14%Protein, 82% Fat)



Krebs cycle. Glucagon plays a major role in maintaining an adequate blood glucose level. Provided there is glycogen stored in the liver, glucagon can activate its degradation to glucose, which is then transported throughout the body for use as energy. However, as previously mentioned, this mechanism for stabilising blood glucose only functions in the presence of stored glycogen. Since the human body is unable to store more than a two-day supply of carbohydrate in the form of glycogen, restricting carbohydrate intake necessitates a conversion to fat as the primary fuel after glycogen has been depleted[7].

Figure 2: A typical daily menu of a ketogenic diet

Example of a 20 Gram Carbohydrate Daily Menu

Breakfast

Three egg omelette with avocado
Mozzarella cheese and tomato
Bacon (2 slices)

Lunch

Beef round (8 ounces)
Spinach and mixed leaf salad with mushrooms, onions, celery and Parmesan cheese
Seltzer water

Dinner

Broiled salmon
Kale topped with garlic, lemon and sesame seeds
Spring water

Opponents of the ketogenic diet suggest that increased fat and cholesterol intake leads to an increased risk of heart disease and stroke due to elevated levels of circulating Low Density Lipoprotein (LDL). While increased fat intake has been shown to increase the risk of myocardial infarction and strokes in those using carbohydrate as a primary fuel source, studies have demonstrated that the *opposite* is true when fat is the primary fuel source[8]. This study of 832 men aged 45 to 65 and free from cardiovascular disease at baseline indicated a decreased incidence of stroke with an increasing percentage of ingested dietary fat. Yet another study showed that the ketogenic diet actually lowers serum LDL and triglycerides, while simultaneously raising High Density Lipoprotein (HDL) (see Table 1)[9]. Therefore, ketogenic regimes requiring high fat intake may actually decrease morbidity and mortality associated with cardiovascular disease.

Hyperinsulinaemia, another known risk factor for the development of cardiovascular disease, was found to be caused by a reduction in hepatic insulin clearance in obese children and adolescents[10]. This may be ameliorated by the ketogenic diet which not only decreases the release of insulin from the pancreas but leads to the necessary weight loss ultimately leading to increased insulin clearance. Diabetic ketoacidosis (DKA) is known to cause atherosclerosis and cardiovascular disease through the oxidative modification of LDL, which results in deposition of cholesterol in arterial walls. The argument was proposed that the ketosis resulting from a ketogenic diet would have the same effect in non-diabetic patients. The ketogenic diet does not generate the comparable levels of ketones observed during DKA. The concentration of ketones during a typical episode of DKA rises above 25mmol/L; on the ketogenic diet it ranges between 1-3mmol/L. One study has shown that while the LDL of both normoketonaemic and hyperketonaemic diabetic individuals is more prone to oxidation, the same is not true for non-diabetic individuals with moderate ketonaemia. Normal individuals do not experience any increase in predisposition to LDL oxidation during moderate ketonaemia, such as that observed with ketogenic diets[11].

Another concern about the ketogenic diet is its possible effect on bone density. One study showed that bone mineral density decreased during ketogenic dieting, even with calcium and vitamin D supplementation. This was thought to be due to increased urinary calcium excretion resulting from ketosis[12]. Another group studying premenopausal women reported a smaller decrease in bone density with high dietary fat intake, relative to a control group with lower percentage of daily fat consumption[13]. Still another study found that high protein, low carbohydrate, high fat diets had no measurable effect on bone density[14]. According to these conflicting results (which involve different study populations) bone density loss may decrease with increasing percentages of ingested carbohydrates or fats, so the effect of the ketogenic diet on calcium homeostasis remains unclear. If ketonaemia does indeed result in decreased bone mineral density, this would be a serious concern for those undertaking a ketogenic dieting regime. More research will be necessary to confirm or refute the findings of these studies.

Despite the possible pitfalls of adhering to a ketogenic diet, there are clear health advantages to weight loss in general, particularly for those who are obese (Body Mass Index >30). Obese individuals suffer from increased incidences of cardiovascular disease, diabetes, hyperlipidaemia, gout, osteoarthritis, gallstones, and bowel, breast, and genitourinary cancers[15]. Additionally, conditions such as obstructive sleep apnoea represent a potentially fatal complication of obesity[16]. Weight loss significantly improves this condition and is much more attractive than surgery as a long-term solution[17]. Unfortunately, many individuals who are overweight complain of feeling too fat to involve themselves in any form of physical activity. For this reason, the rapid reduction in weight afforded by ketogenic diets (and its association with increased self-esteem) may encourage the adoption of a healthy, more active lifestyle[18]. In addition to the health consequences of obesity, there are also significant financial consequences. In the United States, for example, more than 33 billion dollars are spent annually on weight reduction products and services. Even more significant are the associated health care costs of obesity, which are estimated to exceed 70 billion dollars per year[19]. With effective manage-

Table 1: The effect of a ketogenic diet on serum lipids[9]

Variable (mg/dL)	Baseline *mean (SD)*	Week 16 *mean (SD)*	Percentage Change
Cholesterol	212.0 (34.4)	201.4 (40.5)	-5.6%*
LDL	132.9 (28.8)	129.8 (37.5)	NS
HDL	53.4 (13.6)	55.9 (12.4)	+8.8%*
Cholesterol/HDL ratio	4.2 (1.3)	3.7 (1.6)	-16.7%*
Triglycerides	122.3 (59.6)	78.6 (35.1)	-42.6%*

* $p<0.05$, comparing change from baseline to week 16

ment of obesity, the average expenditure required for pharmacotherapy of hypertension, diabetes, hyperlipidaemia, and osteoarthritis would fall dramatically[15]. In diabetics on ketogenic regimes, lowered blood glucose levels and a decreased need for insulin may decrease the complications associated with this disease. Another unforeseen benefit of the ketogenic diet is its effect on breast cancer risk. One study reported that women who had been treated for breast cancer and had hyperinsulinaemia were eight times more likely to develop recurrence than those with normal insulin levels[20]. As already mentioned, the ketogenic diet also has a role in the management of epilepsy in children[5].

Although there are numerous advantages to the ketogenic regime, this type of diet is not for everyone. Rapid weight loss and/or increased fat content may aggravate existing gout, kidney stones and gall-bladder colic. Also, pregnant women should not be in ketosis due to the potential harm it may have on a developing foetus[21]. The limited choices of food required by ketogenic diets may also be difficult (or even unacceptable) for some people. Furthermore, because the body requires time to switch from the carbohydrate burning state to the fat utilisation state, those just beginning the diet may experience transient fatigue, headache, dizziness, and irritability. What a ketogenic diet does do is deliver rapid weight loss, together with all of its associated benefits. The question remains as to whether or not the health benefits of weight loss outweigh the potential ill effects of the ketogenic diet. The dogma of human nutrition for the past fifty years has vilified fat and cholesterol and embraced low fat, high carbohydrate, and high fiber. However, research has shown some very surprising advantages of ketogenic diets and their high fat content. Controversial among medical professionals yet very popular with diet enthusiasts, ketogenic regimes are heavily underrepresented in nutritional research. The majority of existing studies tend to focus on diabetics and the obese, and the world of nutritional research needs to explore the possible benefits of these diets in healthy individuals. The authors of this article are unaware of any current research on this topic but eagerly look forward to future developments.

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