A Ketogenic Diet Favorably Affects Serum Biomarkers for Cardiovascular Disease in Normal-Weight Men


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ABSTRACT Very low-carbohydrate (ketogenic) diets are popular yet little is known regarding the effects on serum biomarkers for cardiovascular disease (CVD). This study examined the effects of a 6-wk ketogenic diet on fasting and postprandial serum biomarkers in 20 normal-weight, normolipidemic men. Twelve men switched from their habitual diet (17% protein, 47% carbohydrate and 32% fat) to a ketogenic diet (30% protein, 8% carbohydrate and 61% fat) and eight control subjects consumed their habitual diet for 6 wk. Fasting blood lipids, insulin, LDL particle size, oxidized LDL and postprandial triacylglycerol (TAG) and insulin responses to a fat-rich meal were determined before and after treatment. There were significant decreases in fasting serum TAG (−33%), postprandial lipemia after a fat-rich meal (−29%), and fasting serum insulin concentrations (−34%) after men consumed the ketogenic diet. Fasting serum total and LDL cholesterol and oxidized LDL were unaffected and HDL cholesterol tended to increase with the ketogenic diet (+11.5%; P = 0.066). In subjects with a predominance of small LDL particles pattern B, there were significant increases in mean and peak LDL particle diameter and the percentage of LDL-1 after the ketogenic diet. There were no significant changes in blood lipids in the control group. To our knowledge this is the first study to document the effects of a ketogenic diet on fasting and postprandial CVD biomarkers independent of weight loss. The results suggest that a short-term ketogenic diet does not have a deleterious effect on CVD risk profile and may improve the lipid disorders characteristic of atherogenic dyslipidemia. J. Nutr. 132: 1879–1885, 2002.

KEY WORDS: • triglycerides • postprandial lipemia • lipoprotein subclasses

Cardiovascular disease (CVD) is the leading cause of mortality in most industrialized countries including the United States (1). Diet is a major weapon used in the fight against CVD because of its influence on the myriad of CVD risk factors. Current dietary recommendations call for a low-fat (<30% of energy), low saturated fat (<7% total energy), low cholesterol (<300 mg/d) diet (2). However, high-carbohydrate diets are controversial (3,4), because they raise plasma triacylglycerols (TAG) (5) and may adversely affect LDL composition (6,7). There has been an alarming increase in the popularity of diets with the common theme of reducing carbohydrate, prompting concern regarding their safety (8). Despite the popularity of very low-carbohydrate diets, very few scientific studies have evaluated how these diets affect CVD risk factors (9) and no studies have examined the effect on recently identified CVD biomarkers (i.e., LDL particle size, postprandial lipemia, oxidized LDL, etc).

A recent meta-analysis of prospective studies indicated that elevated fasting TAG is an independent risk for CVD (10).

The atherogenicity of TAG-rich lipoproteins in the postprandial state may play a greater role than fasting TAG, prompting some authors to suggest that elevated postprandial lipemia is a better predictor of CVD than fasting TAG (11,12). Abnormal postprandial lipemia precipitates production of highly atherogenic small LDL particles and a reduction in HDL cholesterol (12), all of which contribute to the causal role for elevated postprandial lipemia in the pathogenesis and progression of CVD.

Individuals with a predominance of large buoyant LDL cholesterol have been classified as pattern A, whereas those with a predominance of small dense LDL particles are pattern B (10). Individuals exhibiting higher levels of small dense LDL have a greater than 3-fold risk of CVD (13,14). This is most likely a result of the longer half-life and increased susceptibility to oxidative modification (15). The fact that LDL is extremely susceptible to oxidative damage has been known for some time (16), with it now appearing that the oxidation of LDL plays an important role in atherogenesis (17).

The therapeutic value of diet interventions aimed at improving CVD risk should take into account factors other than just fasting total cholesterol, LDL cholesterol, HDL cholesterol, and TAG. In this study, we evaluated the effect of a ketogenic diet on both fasting and postprandial lipoprotein metabolism including measures of postprandial lipemia, LDL size and LDL oxidation. As a first step, we studied a normal-
weight normolipidemic population to minimize the confounding
 effects of weight loss or metabolic abnormalities on the
 dependent variables. Based on our previous work showing a
 reduction in fasting TAG and postprandial lipemia after a
 ketogenic diet rich in monounsaturated fat and supplemented
 with (n-3) PUFA (9), we hypothesized that the ketogenic diet
 used in this study would result in a similar TAG response,
 which would in turn result in increased HDL cholesterol and an
 increase in the average size of LDL particles.

MATERIALS AND METHODS

Subjects. Twenty healthy white men free of metabolic and
endocrine disorders volunteered to participate in this investiga-
tion. To enhance compliance to the rigorous ketogenic dietary treatment, we initially asked subjects if they would
be willing to restrict carbohydrate intake to <10% of total energy for 6 wk. Twelve subjects volunteered to switch from their habitual diet to a ketogenic diet for 6 wk (mean ± SD; age: 36.7 ± 11.6 y; body mass: 79.2 ± 8.3 kg; fat: 20.5 ± 6.0%); the remaining 8 subjects consumed their habitual diet (control group) for 6 wk. Body weight was assessed and two 12-h fasting blood samples were collected at wk 0, 3 and 6. Postprandial TAG and insulin responses to a fat-rich test meal were measured at wk 0 and 6 only in the ketogenic group.

Dietary intervention. The aim of the intervention diet was to reduce carbohydrate intake to <10% of energy. The diet was designed so that fat comprised ~60% of energy with no restrictions on the type of fat from saturated and unsaturated sources or cholesterol levels. The actual diets consumed were mainly comprised of beef (e.g., hamburger and steak), poultry (e.g., chicken and turkey), fish, oils, various nuts/seeds and peanut butter, moderate amounts of vegetables, salads with low-carbohydrate dressing, moderate amounts of cheese, eggs, protein powder, and water or low-carbohydrate diet drinks. Foods avoided or consumed infrequently included fruits and fruit juices, most dairy products with the exception of hard cheeses, eggs, protein powder, and water or low-carbohydrate diet drinks. The remaining serum was analyzed for glucose, total cholesterol, HDL cholesterol, and TAG using automated techniques (Roche Modular; Roche Diagnostics, Indianapolis, IN) with calculated precision values < 3%. Concentrations of LDL and VLDL cholesterol were calculated from total cholesterol, HDL cholesterol, and TAG (18). Fasting serum β-hydroxybutyrate concentrations were enzymatically determined in duplicate using a commercially available kit (#310A; Sigma Diagnostics, St. Louis, MO) and spectrophotometric analysis (Spectronic 601; Milton Roy, Rochester, NY). The intra-assay CV was 0.9%. Fasting serum and postprandial plasma insulin concentrations were determined in duplicate using an ELISA kit with a sensitivity of 1.81 pmol/L (#10-1600; Diagnostic Systems Laboratory, Webster, TX) (19). Intra- and inter-assay CV were 5.5% and 3.2%, respectively. Fasting oxidized LDL were also determined in duplicate using an enzyme-linked immunoassorbent assay (American Laboratory Products Company, Windham, NH) with a solid two-site enzyme immunoassay that is based on the direct sandwich technique in which two monoclonal antibodies are directed against separate antigenic determinants on the oxidized apolipoprotein B molecule. Intra-assay CV was 7.9%. Absorptances were read on a multilabel counter (Wallac1420 Victor2; Wallac Oy, Turku, Finland).

LDL subclasses. Separation of LDL subclasses was performed using nongradient polycrylamide gel electrophoresis (Lipoprint LDL System; Quantimetrix, Redondo Beach, CA) previously described in detail (20,21). High-resolution 3% polycrylamide gel tubes were used for electrophoresis. Seven bands of LDL were quantitatively determined using computer software (NIH imaging software, utilizing the Lipoprint LDL macro; Quantimetrix), which divides the scanned gel image at designated RI values identified by their relative mobility.
This is based on differences in particle size (smaller particles migrate further) and calculates the area under the curve for each fraction. We report the relative percentage of LDL cholesterol in each band and the mean and peak particle diameter. The peak particle diameter for phenotype A is generally $>25.5$ nm, in contrast the major peak for phenotype B is usually $<25.5$ nm (22). The determination of a sample being characterized as either phenotype A or B is based on LDL migration rates and is described in detail in Hoefner et al. (20).

**Insulin sensitivity.** Because high-fat diets have been associated with insulin resistance, we estimated insulin sensitivity using the homeostasis model analysis using fasting glucose and insulin concentrations (23). Assuming that normal-weight subjects aged $<35$ y have an insulin resistance of 1, the values for a subject can be assessed from the insulin and glucose concentrations by the formula: insulin resistance (near approximation) $= \text{insulin}(22.5e^{-\ln \text{glucose}})$.

**Statistical analyses.** Means and sd were calculated for all variables using conventional methods. Two fasting samples were obtained for each blood variable and the mean of these two values used for statistical analysis. A two-way repeated-measures ANOVA was used for each blood variable and the mean of these two values used for statistical analysis. A two-way repeated-measures ANOVA was used to evaluate changes over time in the ketogenic and control groups. When a significant F value was achieved, Fisher’s least significant difference test was used to locate the pair-wise differences between means. The total area (serum concentration × time) under the line connecting the postprandial TAG and insulin responses was calculated using the trapezoidal method. The change in body weight was used as a covariate in all analyses. Relationships between variables were examined using Pearson’s product-moment correlation coefficient. A criterion α-level of $P \leq 0.05$ was used for all statistical comparisons.

**RESULTS**

**Body mass and dietary intake.** All dietary nutrients were significantly different when men consumed the ketogenic diet compared with their habitual diet with the exception of dietary carbohydrate was significantly lower (8% of total energy) during the ketogenic diet period. There were no significant changes in dietary nutrient intake in the control group after the ketogenic diet was consumed (Table 1). Dietary protein, fat and cholesterol were significantly greater and dietary carbohydrate was significantly lower (8% of total energy) during the ketogenic diet period. There were no significant changes in dietary nutrient intake in the control group after the ketogenic diet was consumed (Table 1). Dietary protein, fat and cholesterol were significantly greater and dietary carbohydrate was significantly lower (8% of total energy) during the ketogenic diet period. There were no significant changes in dietary nutrient intake in the control group after the ketogenic diet was consumed (Table 1).

**TABLE 1**

| Daily intake of dietary energy and nutrients in men who switched from their habitual diet to a ketogenic diet for 6 wk and in a control group who continued to consume their habitual diet for 6 wk$^1$ |
|-------------------------------|-----------------|-----------------|-----------------|-----------------|
|                               | Ketogenic diet  | Ketogenic diet  | Habitual diet   | Habitual diet   |
|                               | (wk 0)          | (wk 6)          | (wk 0)          | (wk 6)          |
| Energy, kJ                    | 10627 ± 2469    | 9770 ± 1569     | 8489 ± 1962     | 7594 ± 816      |
| Protein, g                    | 113 ± 40b       | 176 ± 45a       | 82 ± 16b        | 70 ± 10b        |
| Protein, %$^2$                | 17 ± 4b         | 30 ± 5a         | 16 ± 2b         | 15 ± 1b         |
| Carbohydrate, g               | 306 ± 100a      | 46 ± 10b        | 287 ± 79a       | 271 ± 47a       |
| Carbohydrate, %               | 48 ± 10a        | 8 ± 3b          | 55 ± 5a         | 59 ± 7a         |
| Total fat, g                  | 91 ± 31b        | 157 ± 27a       | 65 ± 18b        | 50 ± 14b        |
| Total fat, %                  | 32 ± 6b         | 61 ± 4a         | 29 ± 5b         | 25 ± 8b         |
| Saturated fat, g              | 31 ± 12b        | 56 ± 11a        | 21 ± 6b         | 16 ± 6b         |
| Saturated fat, %              | 14 ± 4b         | 25 ± 2a         | 14 ± 4b         | 12 ± 4b         |
| Monounsaturated fat, g        | 27 ± 11b        | 57 ± 12a        | 14 ± 5c         | 12 ± 8c         |
| Monounsaturated fat, %        | 12 ± 4b         | 25 ± 3a         | 9 ± 2b          | 9 ± 5b          |
| Polyunsaturated fat, g        | 12 ± 6b         | 24 ± 5a         | 9 ± 3b          | 6 ± 3b          |
| Polyunsaturated fat, %        | 6 ± 2b          | 11 ± 2a         | 6 ± 1b          | 4 ± 2b          |
| Cholesterol, mg               | 332 ± 126b      | 741 ± 254a      | 130 ± 14c       | 118 ± 7c        |
| Alcohol, %                    | 3 ± 3           | 1 ± 2           | 0 ± 0           | 0 ± 1           |

$^1$ Values are means ± so. Ketogenic diet group, n = 12. Control group, n = 8. Means in a row with different superscripts differ ($P \leq 0.05$).

$^2$ Percentage of total energy intake.
pattern B subjects had significantly smaller mean and peak LDL particle diameters, a significantly greater percentage of LDL-3 and LDL-4, and a significantly smaller percentage of LDL-1 compared with pattern A subjects. There were no significant changes in the percentage of any LDL subclasses or the mean and peak particle size in pattern A subjects. There was a significant increase in peak LDL particle diameter from 25.28 nm to 26.16 nm after the ketogenic diet in pattern B subjects (Fig. 2), and also a significant increase in mean LDL particle diameter. There was a significant increase in the percentage of LDL-1 and a significant decrease in the percentages of LDL-3 and LDL-4 after the ketogenic diet in pattern B subjects. There were no changes from 0 to 6 wk in the concentrations of oxidized LDL in either the ketogenic group (44.38 ± 33.7 U/L → 46.45 ± 15.6 U/L) or control group (36.49 ± 10.9 U/L → 39.56 ± 16.9 U/L).

**Postprandial TAG and insulin responses.** Postprandial TAG concentrations peaked 3 h after the meal and started to decline toward fasting values ~5 h after the meal (Fig. 3). Compared with wk 0, peak postprandial TAG concentrations were significantly lower (~24%) after the ketogenic diet (2.57 ± 1.4 to 1.96 ± 0.7 mmol/L). The area under the postprandial TAG curve was also significantly lower (~29%) after the ketogenic diet (17.47 ± 9.3 to 12.39 ± 4.2 mmol/L × h). Postprandial insulin concentrations peaked immediately after the meal at wk 0 and 1 h after the meal at wk 6. Compared with wk 0, the area under the postprandial insulin curve was unaffected at wk 6 (339 ± 168 to 283 ± 140 pmol/L × h).

**DISCUSSION**

The primary objective of this study was to examine how healthy normolipidemic, normal-weight men respond to a ketogenic diet in terms of fasting and postprandial CVD biomarkers. Ketogenic diets have been criticized on the grounds that they jeopardize health (8); however, very few studies have directly evaluated the effects of a ketogenic diet on fasting and postprandial risk factors for CVD. Subjects consumed a diet that consisted of 8% carbohydrate (<50 g/d), 61% fat, and 30% protein. Adaptation to this ketogenic diet resulted in significant reductions in fasting TAG (~33%), postprandial lipemia after a fat-rich meal (~29%), and fasting insulin concentrations (~34%). There were significant increases in LDL particle size, and no change in the oxidative LDL concentrations. There was a significant increase in HDL cholesterol at wk 3 after the ketogenic diet. Collectively, the responses in serum lipids, insulin and lipid subclasses to the ketogenic diet were favorable in terms of overall CVD risk profile.

Only a few studies have examined the effects of a diet with very low amounts of carbohydrate on blood lipids (9,24). Our laboratory recently examined the effects of a ketogenic diet rich in monounsaturated fat and supplemented with (n-3) PUFA on blood lipids in normolipidemic men (9). Fasting TAG, total cholesterol, LDL cholesterol, and HDL cholesterol changed −55%, +2%, +10%, and +10%, respectively (9).

**TABLE 2**

<table>
<thead>
<tr>
<th></th>
<th>Ketogenic group (n = 12)</th>
<th>Control group (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wk 0</td>
<td>Wk 3</td>
</tr>
<tr>
<td>TC, mmol/L</td>
<td>4.27</td>
<td>4.78</td>
</tr>
<tr>
<td>TAG, mmol/L</td>
<td>1.09</td>
<td>0.75</td>
</tr>
<tr>
<td>HDL-C, mmol/L</td>
<td>1.22</td>
<td>1.43</td>
</tr>
<tr>
<td>LDL-C, mmol/L</td>
<td>2.87</td>
<td>3.22</td>
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<tr>
<td>VLDL-C, mmol/L</td>
<td>0.17</td>
<td>0.12</td>
</tr>
<tr>
<td>TC/HDL</td>
<td>3.60</td>
<td>3.45</td>
</tr>
<tr>
<td>Insulin, pmol/L</td>
<td>23.7</td>
<td>19.1</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>5.00</td>
<td>4.84</td>
</tr>
<tr>
<td>β-HBA, mmol/L</td>
<td>0.08</td>
<td>0.40</td>
</tr>
</tbody>
</table>

1 Values are means ± so. Data were analyzed with a two-way ANOVA using body weight as a covariate. Ketogenic Diet group, n = 12. Control group, n = 8. Means in a row with different superscripts differ (P ≤ 0.05). TC, total cholesterol; TAG, triacylglycerol; β-HBA, β-hydroxybutyrate.

2 Percent change from wk 0 to wk 6.
TABLE 3

Serum LDL subclass responses in 12 men who consumed a ketogenic diet who started as either pattern A or pattern B1,2

<table>
<thead>
<tr>
<th>Ketogenic group (n = 12)</th>
<th>% LDL-1, 27.7 nm</th>
<th>% LDL-2, 26.1 nm</th>
<th>% LDL-3, 24.5 nm</th>
<th>% LDL-4, 23.0 nm</th>
<th>Peak LDL size, nm</th>
<th>Mean LDL size, nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wk 0</td>
<td>13.9 ± 6.4b</td>
<td>16.6 ± 5.0</td>
<td>6.1 ± 5.2</td>
<td>2.0 ± 3.9</td>
<td>26.19 ± 10.7b</td>
<td>26.28 ± 7.8</td>
</tr>
<tr>
<td>Wk 3</td>
<td>18.4 ± 6.8a</td>
<td>19.2 ± 5.5</td>
<td>5.9 ± 3.7</td>
<td>0.8 ± 1.0</td>
<td>26.76 ± 7.8a</td>
<td>26.54 ± 4.3</td>
</tr>
<tr>
<td>Wk 6</td>
<td>18.2 ± 6.2a</td>
<td>19.4 ± 5.7</td>
<td>4.7 ± 3.6</td>
<td>0.6 ± 1.3</td>
<td>26.71 ± 7.9b</td>
<td>26.57 ± 4.5</td>
</tr>
</tbody>
</table>

Pattern A subjects (n = 7)

| Wk 0                    | 18.2 ± 4.1       | 17.0 ± 4.9       | 2.0 ± 1.6        | 0.1 ± 0.2        | 26.83 ± 5.1      | 26.80 ± 1.6      |
| Wk 3                    | 21.8 ± 6.4       | 19.1 ± 5.5       | 4.2 ± 2.7        | 0.4 ± 0.5        | 27.04 ± 7.8      | 26.70 ± 3.0      |
| Wk 6                    | 22.2 ± 4.1       | 19.0 ± 7.1       | 2.8 ± 1.8        | 0.1 ± 0.3        | 27.10 ± 7.2      | 26.81 ± 2.5      |

Pattern B subjects (n = 5)

| Wk 0                    | 7.9 ± 3.1b       | 16.0 ± 6.1       | 11.7 ± 2.3b      | 4.7 ± 5.5a       | 25.28 ± 9.9b     | 25.54 ± 7.0b     |
| Wk 3                    | 13.7 ± 4.2a      | 19.2 ± 6.1       | 7.2 ± 4.6a       | 1.3 ± 1.2b       | 26.37 ± 6.6a     | 26.32 ± 5.3a     |
| Wk 6                    | 12.6 ± 3.8a      | 19.9 ± 3.7       | 7.3 ± 4.0a       | 1.4 ± 1.9b       | 26.16 ± 5.1a     | 26.22 ± 4.6a     |

1 Values are means ± so. Means in a column within a group with different superscripts differ (P = 0.05).
2 Individuals with pattern A have a predominance of large LDL particles and those with pattern B have a predominance of smaller LDL particles.

Larosa et al. (24) examined the effects of a hypocaloric ketogenic diet on blood lipids in moderately overweight normolipidemic subjects. Fasting TAG, total cholesterol, LDL cholesterol and HDL cholesterol changed −33%, +6%, +18% and −6%, respectively. Corresponding changes in serum lipids in this study for fasting TAG, total cholesterol, LDL cholesterol, and HDL cholesterol were −33%, +4%, +4%, and +11%, respectively. Confounding variables in these studies include varying degrees of weight loss (−2.2 to −7.7 kg) and slight differences in the type of fat consumed. Nevertheless, these studies collectively indicate that carbohydrate restriction result in significant decreases in serum TAG, small increases in total and LDL cholesterol, and moderate increases in HDL cholesterol in normolipidemic individuals. The small but significant weight loss (−2.2 kg) could have partially explained the HDL and TAG responses in this study. A meta-analysis by Dattilo and Kris-Etherton (25), showed that for every kilogram decrease in body weight during weight loss, HDL-C increases 0.009 and TAG decreases 0.015 mmol/L. Using these estimates, the −2.2 kg weight loss would have been predicted to increase HDL by 0.198 mmol/L and decrease TAG by 0.033 mmol/L, which amounts to only 14% and 9% of the observed changes in these parameters. Thus, dietary composition most likely contributed to the changes in blood lipids in this study.

There was a significant decrease in postprandial lipemia after the fat-rich meal (−29%), which was significant but somewhat lower than the decrease (−50%) we observed in response to a ketogenic diet rich in monounsaturated fat and supplemented with (n-3) polyunsaturated fatty acids (9). In contrast to our results, Miller et al. (26) reported that a low-fat (19% of total energy)/high-carbohydrate (64% of total energy) diet significantly reduced postprandial lipemia compared with a diet higher in fat (41% of total energy) in normolipidemic men. The high-fat diet in the study by Miller et al. (26) still contained significant amounts of carbohydrate (42% of total energy), which likely explains the conflicting results with our postprandial TAG response in men that consumed a very low carbohydrate (8% of total energy) diet.

The significant reduction in fasting TAG was probably due to the combination of a reduced VLDL production rate, which has been shown to increase on a high-carbohydrate diet (27), and an increase in TAG removal because high-fat diets (46–65% of total energy) significantly increase postheparin plasma LPL activity and skeletal muscle LPL activity in humans (28–30). A greater VLDL-TAG pool size would also compete...
with TAG from intestinal origin for removal during the post-prandial period. Thus, elevated fasting TAG (primarily VLDL-TAG) is associated with enhanced postprandial TAG (primarily chylomicron-TAG) due to competition for removal (31). It follows then that a reduction in fasting TAG should be directly related to a reduction in TAG responses to a fat-rich meal, which was the case in this study (r = 0.59; P < 0.05).

Although the majority of studies have reported significant correlations between changes in fasting and postprandial TAG (9), a recent study demonstrated that a dietary regimen that lowered fasting TAG did not result in a reduction in postprandial TAG (32), emphasizing the importance of measuring postprandial TAG to assess overall CVD risk.

Dietary cholesterol intake increased >100% (332–741 mg/d) when subjects switched to the ketogenic diet, which would be predicted to result in significant increases in total cholesterol and LDL cholesterol, although these were not significantly elevated after 6 wk of the ketogenic diet. There is great variability in the responsiveness of blood cholesterol after increases in dietary cholesterol, which may be due to differences in hormonal factors, obesity, and genetic predisposition (33). There were changes in the distribution of the LDL subfractions that would be considered favorable in terms of CVD. We observed general increases in the mean and peak LDL particle sizes during the ketogenic diet, which were more pronounced in subjects that exhibited a pattern B distribution at the start of the study. Individuals with pattern B exhibit a pronounced in subjects that exhibited a pattern B distribution (33). There were changes in the distribution of the LDL subfractions that would be considered favorable in terms of CVD. We observed general increases in the mean and peak LDL particle sizes during the ketogenic diet, which were more pronounced in subjects that exhibited a pattern B distribution at the start of the study. Individuals with pattern B exhibit a pronounced increase in LDL subclasses. For example, switching to a fat-rich diet (46% vs. 24% of total energy) was shown to increase mean particle diameter and large LDL-1 mass and decrease small dense LDL-III cholesterol (28), while reductions in dietary fat have the opposite effect (6,7). Despite the changes in LDL size, we did not observe any significant changes in oxidized LDL concentrations. Collectively these studies indicate that when dietary fat is reduced, the distribution of LDL moves toward a smaller more dense particle and when dietary fat is increased the distribution of LDL moves toward a larger less dense particle. The reason some individuals are more stable in their LDL subclass distribution in response to changes in diet is unknown but is likely to reflect complex interactions between metabolic and genetic traits that are influenced to varying extents depending on the level of dietary fat (1,7).

We observed a significant decrease in fasting and postprandial insulin responses after the ketogenic diet. Decreases in resting insulin concentrations have been reported in response to 3–4 d of a low-carbohydrate diet high in fat (34–38). The mechanism for such a response probably resides in the greater reliance on fat oxidation induced by dietary carbohydrate restriction (39) and subsequent reduced requirement for insulin to assist in glucose uptake. To our knowledge, the reduced postprandial insulin response to a fat-rich meal observed after a ketogenic diet has not been reported in the literature. According to our estimate of insulin resistance using fasting levels of glucose and insulin, subjects in this study were not insulin resistant and there was no adverse effect of the ketogenic diet on insulin sensitivity. This is in agreement with other studies showing no adverse effects on glucose metabolism or insulin resistance after ketogenic diets using the insulin clamp technique (40,41).

Numerous studies now suggest that high-carbohydrate diets can raise TAG levels, create small, dense LDL particles, and reduce HDL cholesterol (i.e., atherogenic dyslipidemia) — a combination along with insulin resistance, that has been termed syndrome X (42,43). Syndrome X is postulated to be resistance to insulin-mediated glucose disposal by muscle (44), 30% of adult males and 10% to 15% of postmenopausal women have this particular syndrome X profile, which is associated with several-fold increase in heart disease risk. Replacing saturated fat with carbohydrate appears to accentuate insulin concentrations and the atherogenic dyslipidemia associated with syndrome X (44,45). The ketogenic diet in this study resulted in favorable responses in fasting TAG, postprandial lipemia, HDL-C, LDL particle size, and insulin levels in healthy normolipidemic men. Although the duration of the diet was short (6 wk), these data suggest that a ketogenic diet does not have an adverse effect on accepted biochemical risk factors for CVD and improves those associated with syndrome X.

**LITERATURE CITED**


