High-monounsaturated-fat diets for patients with diabetes mellitus: a meta-analysis

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ABSTRACT The most recent position statement on nutrition from the American Diabetes Association recommends an individualized approach to nutrition that is based on the nutritional assessment and desired outcomes of each patient and that takes into consideration patient preferences and control of hyperglycemia and dyslipidemia. To achieve these nutritional goals, either low-saturated-fat, high-carbohydrate diets or high-monounsaturated-fat diets can be advised. A meta-analysis of various studies comparing these two approaches to diet therapy in patients with type 2 diabetes revealed that high-monounsaturated-fat diets improve lipoprotein profiles as well as glycemic control. High-monounsaturated-fat diets reduce fasting plasma triacylglycerol and VLDL-cholesterol concentrations by 19% and 22%, respectively, and cause a modest increase in HDL-cholesterol concentrations. Furthermore, there is no evidence that high-monounsaturated-fat diets induce weight gain in patients with diabetes mellitus provided that energy intake is controlled. Therefore, a diet rich in cis-monounsaturated fat can be advantageous for both patients with type 1 or type 2 diabetes who are trying to maintain or lose weight.

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KEY WORDS Diabetes mellitus, dietary fat, dietary carbohydrate, monounsaturated fat, lipoproteins, hyperglycemia, obesity, diet therapy, glycemic control, high-monounsaturated-fat diet, humans

INTRODUCTION

The most recent American Diabetes Association (ADA) position statement on nutrition recommends that the diet composition for patients with diabetes mellitus be individualized based on nutritional assessment and desired outcomes (1). For example, obese patients with acceptable serum lipid concentrations are recommended to consume a high-carbohydrate diet with < 30% of energy from fat. Patients with elevated triacylglycerol and VLDL-cholesterol concentrations, however, are recommended to consume more energy from fat in the form of cis-monounsaturated fat (≤20%), < 10% of energy each from saturated and polyunsaturated fats, 10–15% of energy from protein, and a more moderate proportion of energy from carbohydrate. In fact, the ADA recommends dividing 60–70% of total energy between carbohydrate and monounsaturated fat depending on patient preference and nutritional goals.

Despite the recommendation of high-monounsaturated-fat diets as an alternative dietary therapy for patients with diabetes mellitus, several investigators still remain hesitant in recommending such diets to their patients. This paper thus critically reviews the literature comparing the two approaches to dietary therapy in patients with diabetes mellitus, ie, high-monounsaturated-fat diets and high-carbohydrate diets. A meta-analysis of the studies investigating the effect of diet composition on various metabolic indexes was conducted. The review is presented in three parts followed by a conclusion. In the first part, effects of diet composition on plasma lipids and lipoproteins are presented. The second part examines effects of diet composition on glycemic control and the third part reviews other metabolic effects of diet composition. Finally, conclusions are drawn from these studies and practical implications for dietary therapy for patients with diabetes mellitus are discussed.

SUBJECTS AND METHODS

Identification and selection of studies

The medical literature was searched for studies comparing the effects of high-monounsaturated-fat diets and high-carbohydrate diets in patients with type 2 diabetes; since the original report by my group comparing the two dietary approaches in type 2 diabetes patients (2), several other studies have been published (3–12). Only randomized, crossover trials using isoenergetic, weight-maintaining diets were included in the meta-analysis (2–10); the studies by Bonanome et al (11), Garg et al (12), and Neilsen et al (13) were excluded because the order of study diets was not randomized. In the following discussion, where possible, a meta-analysis of these trials is presented. The general characteristics of the studies, including number of subjects, study design, diet composition, and duration of each dietary intervention, are shown in Table 1.

Meta-analysis

The results of each study were tabulated by extracting the sample size, means, SD or SE of the mean, and, when available, the mean and variability of the difference or P values from diet comparisons.

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The primary outcome was the mean difference (Δ) between the two diets (the high-monounsaturated-fat diet — the high-carbohydrate diet). The variance used for each study was calculated in one of three ways: 1) directly from the paired differences when raw data were available, 2) imputed from the exact P value or the upper boundary of the P value where reported, or 3) imputed assuming a correlation coefficient of 0.5 between diets (14). The studies were then weighted by the reciprocal of the variance. The overall effect estimate and 95% CIs were then computed with these weights.

### DIET COMPOSITION AND PLASMA LIPOPROTEINS

#### Plasma lipoproteins

Diets rich in monounsaturated fat, compared with diets rich in carbohydrate, were accompanied by a significant lowering of fasting plasma triacylglycerol, total cholesterol, and VLDL-cholesterol concentrations; no change in LDL-cholesterol concentrations; and an increase in HDL-cholesterol concentrations (Table 2). The net change in fasting plasma triacylglycerol concentrations with consumption of a high-monounsaturated-fat diet was a reduction of 0.36 mmol/L (32 mg/dL), or 19%. Of the nine studies, a high-monounsaturated-fat diet was a reduction of 0.2 mmol/L (8 mg/dL), or 22.5%. Changes in HDL-cholesterol concentrations, however, were not consistent. Five studies reported increases and four reported no change in HDL-cholesterol concentrations with consumption of a high-monounsaturated-fat diet compared with a high-carbohydrate diet. Overall, a net increase of only 0.05 mmol/L (2 mg/dL), or 4%, in HDL-cholesterol concentrations was observed (Figure 1).

Plasma total cholesterol concentrations were modestly reduced by 0.15 mmol/L (6 mg/dL) with ingestion of high-monounsaturated-fat diets, a 3% reduction overall (Figure 2). High-monounsaturated-fat diets, however, had no effect on plasma LDL-cholesterol concentrations (net change: 0%). Of the seven studies from which adequate data were available for meta-analysis, two showed an increase, three showed a decrease, and two showed no change in LDL-cholesterol concentrations with consumption of a high-monounsaturated-fat diet compared with a high-carbohydrate diet. Calculated LDL-cholesterol concentrations in two other studies showed slight increases with a high-monounsaturated-fat diet (Figure 2).

#### Plasma apolipoproteins

Only two of the nine studies included measurements of apolipoprotein (apo) concentrations. Garg et al (2) reported a 9% increase in apo A-I concentrations with consumption of a high-monounsaturated-fat diet, which was statistically significant, but noted no changes in concentrations of apo A-II or apo B. Rivellese et al (3) reported no changes in concentrations of apo B, C-I, C-III, or E with dietary interventions, but a significant 15% increase in apo C-II concentrations with consumption of a high-carbohydrate diet.

### DIET COMPOSITION AND GLYCEMIC CONTROL

#### Fasting plasma glucose and insulin

The meta-analysis revealed a significant net lowering of fasting plasma glucose concentrations by 0.23 mmol/L (95% CI: −0.39,


<table>
<thead>
<tr>
<th>Number of studies</th>
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<th>Change</th>
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<tr>
<td></td>
<td></td>
<td>mmol/L</td>
<td>%</td>
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<tr>
<td>Total cholesterol</td>
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<td>−0.15</td>
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<tr>
<td>Triacylglycerol</td>
<td>9</td>
<td>−0.36</td>
<td>−19.0</td>
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<tr>
<td>VLDL cholesterol</td>
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<td>−0.20</td>
<td>−22.5</td>
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<td>0.0</td>
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<tr>
<td>HDL cholesterol</td>
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<td>0.05</td>
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*Net and percentage change are expressed as the concentration during the high-monounsaturated-fat diet minus that during the high-carbohydrate diet. 95% CI in parentheses.*

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Mean preprandial plasma glucose

Garg et al. (2) measured preprandial plasma glucose concentrations at 0300, 0700, 1100, 1600, and 2000 h each day during the last week of each dietary period in type 2 diabetes patients receiving insulin therapy. These authors reported significant lowering of mean (± SEM) glucose values with consumption of a high-monounsaturated-fat diet compared with a high-carbohydrate diet (8.8 ± 0.2 compared with 10.1 ± 0.3 mmol/L, respectively; *P* < 0.05). In another study in diet-treated type 2 diabetes patients, however, mean preprandial plasma glucose values during the last 4 days of each dietary period remained essentially unchanged [7.7 ± 0.8 compared with 7.6 ± 0.8 mmol/L, respectively (4)].

Postprandial plasma glucose

Parillo et al. (5) reported lower 2-h postprandial (after lunch and dinner) plasma glucose concentrations (mean ± SEM) with consumption of a high-monounsaturated-fat diet than with a high-carbohydrate diet (8.8 ± 2.1 compared with 10.1 ± 2.8 mmol/L, respectively; *P* < 0.05). Recently, the same group (10) noted improvement in 2-h postprandial plasma glucose concentrations with consumption of a high-monounsaturated-fat diet compared with a high-carbohydrate diet in type 2 diabetes patients treated with diet and oral medications (11.0 ± 1.8 compared with 13.6 ± 1.4 mmol/L, respectively; *P* < 0.05), but not in those treated with diet alone (8.9 ± 0.6 compared with 9.7 ± 0.9 mmol/L, respectively). Rasmussen et al. (6) also noted reductions in peak blood glucose concentrations with consumption of a high-monounsaturated-fat diet compared with a high-carbohydrate diet (8.9 ± 0.5 compared with 11.3 ± 0.7 mmol/L, respectively; *P* < 0.01). Lerman-Garber et al. (8) reported a trend toward lower postprandial plasma glucose values determined 1, 2, and 6 h after meals when subjects consumed a high-monounsaturated-fat diet. The exact data, however, were not reported. In the Multicenter Study (9), the improvement in overall daylong glycemic profile with consumption of a high-monounsaturated-fat diet was most evident during the postprandial periods.

Twenty-four-hour plasma glucose and insulin profiles

Garg et al. (2, 9) measured plasma glucose and insulin concentrations at 2-h intervals for 24 h on the last day of each dietary period. The high-monounsaturated-fat diet produced lower daylong concentrations (mean ± SEM) of plasma glucose [143 ± 3 compared with 160 ± 4 mmol·h/L⁻¹ (area under the curve), respectively; *P* < 0.01] and insulin [5221 ± 316 compared with 6499 ± 365 mmol·h/L⁻¹, respectively; *P* < 0.01] than did the high-carbohydrate diet (2). In fact, in the Multicenter Study (9), the lowering of daylong plasma glucose concentrations with a high-monounsaturated-fat diet was even more impressive (205 ± 49 compared with 229 ± 57 mmol·h/L⁻¹, respectively; *P* < 0.0001), and a significant reduction in daylong plasma insulin concentrations was also noted [7778 ± 3831 compared with 8467 ± 3961 pmol·h/L⁻¹, respectively; *P* < 0.02]. Rasmussen et al. (6) conducted profiles from 0800 to 1600 h and also reported lowering of mean plasma glucose (7.0 ± 0.4 compared with 8.2 ± 0.6 mmol/L, respectively; *P* < 0.01) and insulin (173 ± 26 compared with 205 ± 28 pmol/L, respectively; *P* < 0.05) concentrations with a high-monounsaturated-fat diet. Significant lowering of mean plasma glucose concentrations with the high-monounsaturated-fat diet (10.4 ± 1.0 compared with 11.7 ± 1.3 mmol/L, respectively; *P* < 0.01) was also noted by Campbell et al. (7) for 6-h profiles.

Urinary glucose excretion

Only three studies reported data on urinary glucose excretion and, in general, consumption of high-monounsaturated-fat diets.
Insulin sensitivity
To investigate the mechanisms of improved glycemic control with consumption of high-monounsaturated-fat diets, insulin sensitivity was measured by using the euglycemic, hyperinsulinemic, glucose clamp technique. Garg et al (4) reported no change in insulin-mediated glucose disposal (mean ± SEM) after 3 wk of feeding a high-monounsaturated-fat diet and a high-carbohydrate diet (16.5 ± 2.3 compared with 14.7 ± 1.4 μmol·kg⁻¹·min⁻¹, respectively; \( P = 0.18 \)) to eight patients with mild type 2 diabetes receiving diet therapy alone. Fasting and residual hepatic glucose output during the hyperinsulinemic phase of the clamp study also did not change. Parillo et al (5) reported improvement in insulin-mediated glucose disposal (mean ± SD) with consumption of a high-monounsaturated-fat diet compared with a high-carbohydrate diet (5.8 ± 2.1 compared with 4.6 ± 1.8 mg·kg⁻¹·min⁻¹, respectively; \( P = 0.02 \)) but no effects on hepatic insulin sensitivity. Therefore, the notion that high-carbohydrate diets improve insulin sensitivity is not supported by these studies. Further studies, however, are needed to confirm whether high-monounsaturated-fat diets improve insulin sensitivity in patients with diabetes mellitus.

DIET COMPOSITION AND OTHER METABOLIC EFFECTS

Lipoprotein oxidation
Recently, oxidative and other modifications of lipoproteins, particularly of LDL, have been proposed to play an essential role in the atherogenic process (16). Of interest, the susceptibility of LDL particles to oxidation is determined not only by concentrations of antioxidants such as β-carotene and α-tocopherol in LDL but also by the ratio of oleic acid to linoleic acid (17, 18). Reaven et al (19) showed that LDL from subjects fed diets rich in oleic acid was less susceptible to oxidation than that from subjects fed diets rich in linoleic acid. Whether LDL particles during high-carbohydrate or high-monounsaturated-fat diet feeding have different susceptibilities to oxidation has not been well studied. In a preliminary study, Berry et al (20) reported reduced thiobarbituric acid–reactive substances in plasma and LDL from six subjects fed a high-monounsaturated-fat diet compared with that in five subjects fed a high-carbohydrate diet. The high-monounsaturated-fat diet, however, was ≥27 mg/d higher in α-tocopherol than the high-carbohydrate diet, which may have confounded the results. The diets were also not matched for ascorbate and β-carotene contents. Therefore, whether diets rich in monounsaturated fat have any advantages over high-carbohydrate diets concerning LDL oxidation potential, independent of antioxidants, is unclear.

In the study by Garg et al (2), a high ratio of oleic acid to linoleic acid was noted to reduce glucosuria. Garg et al (2) reported reductions in daily urinary glucose excretion from a median value of 142 mg/d with a high-carbohydrate diet to 0 mg/d with a high-monounsaturated-fat diet (0.05 < \( P < 0.1 \)). In another report (4), five of eight patients studied had no glucosuria while consuming either diet but in three glucosuria was reduced with consumption of a high-monounsaturated-fat diet minus the values for the high-carbohydrate diet. The weighted mean of all studies with 95% CIs was calculated from the meta-analysis.

Glycated hemoglobin and fructosamine concentrations
Of all the studies reviewed, glycated hemoglobin concentrations were measured in three (2, 4, 9) and fructosamine concentrations in another three (6–8). In none of the studies, however, were changes in these indexes significant. It must be kept in mind that concentrations of glycated hemoglobin and fructosamine reflect long-term changes in glycemic control; therefore, the reasons for lack of change in these indexes could be that the studies were of short duration (2–6 wk) and that the high-monounsaturated-fat diet caused only modest reductions in hyperglycemia, not sufficient to affect these indexes significantly.

Dose of insulin and oral hypoglycemic drugs
In most of the studies, the dose and time of administration of oral hypoglycemic drugs was kept constant (3, 5, 6, 10). However, in two studies, changes in dose of insulin or glipizide were made if needed (2, 9). In the study by Garg et al (2), the insulin dose was reduced or increased by 2–4 units/d to prevent symptomatic hypoglycemia and persistent hyperglycemia, respectively. A reduction in daily insulin requirements from an average of 81 units with consumption of a high-carbohydrate diet to 70 units with a high-monounsaturated-fat diet was reported. The insulin dose was reduced in six patients by 5–34 units, increased in one patient by 3 units, and remained unchanged in three patients. In the Multicenter Study (9), however, the dose of glipizide remained unchanged.
concentrations were also significantly lower with consumption of the high-monounsaturated-fat diet but no changes were noted in concentrations of HDL or LDL cholesterol.

Another recent study from Australia (30) compared isonergic high-carbohydrate and high-monounsaturated-fat diets for 3 mo each and observed similar amounts of spontaneous weight loss in 16 patients with type 2 diabetes during a randomized, crossover study. With use of dual-energy X-ray absorptiometry, however, a disproportionate loss of lower body fat was observed with the high-carbohydrate diet.

CONCLUSIONS

The main goal of therapy in patients with diabetes mellitus is improving metabolic control (1). The specific goals of therapy are 1) maintaining normal or near-normal blood glucose concentrations by synchronizing hypoglycemic drugs with food intake and physical activity, 2) optimizing serum lipid and lipoprotein concentrations, 3) helping patients attain desirable body weights, 4) preventing and treating complications of diabetes, and 5) improving overall health (1). Physicians and nutritionists should assess a patient’s ability and willingness to accept nutrition intervention, taking into consideration the patient’s cultural, ethnic, and financial background.

On the basis of the meta-analysis of several studies, it is clear that compared with high-carbohydrate diets, high-monounsaturated-fat diets improve lipoprotein profiles as well as the glycemic profile. Overall, high-monounsaturated-fat diets reduce fasting plasma triacylglycerol and VLDL-cholesterol concentrations by 19% and 22%, respectively, and cause modest increases in HDL-cholesterol concentrations without adversely affecting LDL-cholesterol concentrations. The improvement in the glycemic profile with high-monounsaturated-fat diets may not be related to changes in insulin sensitivity but to a reduction in the carbohydrate load, which patients with type 2 diabetes may not be able to handle readily because of severe insulin resistance and β cell defects. High-monounsaturated-fat diets may also reduce the susceptibility of LDL particles to oxidation and thereby reduce their atherogenic potential. Whether high-monounsaturated-fat diets can improve blood pressure needs to be investigated further. Furthermore, a high-monounsaturated-fat diet should not induce weight gain in patients provided that energy intake is controlled. Therefore, this dietary approach can be recommended to type 2 diabetes patients who are trying to maintain or lose weight. In conclusion, diets rich in cis-monounsaturated fats may be advantageous for improving lipoprotein and glycemic profiles in patients with diabetes mellitus.

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REFERENCES

