Effect of Fat-Free Diet on Insulin Requirements in Type I Diabetes Controlled With Artificial β-Cell

Fredrick L. Dunn, MD
Patricia B. Carroll, MD

We investigated the effect of eliminating calories derived from fat sources on postprandial and basal insulin requirements in five patients with type I (insulin-dependent) diabetes mellitus. The patients were studied on a metabolic ward on two solid-food diets with similar quantities of carbohydrate and protein with or without the addition of fat. Diet A was isocaloric (weight maintenance) with calories distributed as 45% carbohydrate, 15% protein, and 40% fat. Diet B contained the same carbohydrate and protein content as diet A but was virtually fat free and therefore hypocaloric (1233 ± 106 vs. 1830 ± 99 cal, mean ± SE). The diets were given as five equal meals each day on consecutive days. Insulin requirements and blood glucose measurements were determined by use of the artificial β-cell. During the study, mean (± SE) preprandial blood glucose levels were maintained at 85 ± 11 mg/dl, and peak postprandial blood glucose levels were <180 mg/dl. The elimination of fat calories had no effect on total (68.9 ± 10.3 vs. 69.3 ± 4.9 U/day), postprandial (9.8 ± 3.8 vs. 10.3 ± 3.7 U/meal), or basal (1.9 ± 0.2 vs. 1.8 ± 0.2 U/h) insulin requirements. Thus, despite a hypocaloric diet, no change in insulin requirements was noted when fat-derived calories were deleted from the diet. We conclude that fat-derived calories do not alter short-term basal or postprandial insulin requirements in type I diabetes. *Diabetes Care* 11:225–29, 1988

The importance of restricting dietary fat versus carbohydrate for optimal diabetic therapy remains controversial (1–4). Although traditional diabetic diets were high in fat and emphasized carbohydrate restriction, recent studies have suggested that high-carbohydrate, low-fat diets may improve diabetic control and often decrease insulin requirements (5–9). In addition, because of a concern for the effect of high-fat diets on hypercholesterolemia and atherosclerosis, current recommendations are to decrease the fat content and liberalize the carbohydrate content of the diabetic diet (10,11).

These changes have prompted renewed interest in the effect of changes in carbohydrate and fat content on insulin requirements in type I (insulin-dependent) diabetes (12–14). This study was designed to determine the effect of the deletion of calories derived from fat on insulin requirements in patients with type I diabetes mellitus. Insulin requirements were determined by use of the artificial β-cell to maintain euglycemia. The study examined the short-term effect of deletion of calories derived from fat on insulin requirements while carbohydrate and protein content of the diet remained constant.

MATERIALS AND METHODS

Subjects. Five patients with type I diabetes were studied (3 men, 2 women). Their clinical data are given in Table 1. For all subjects, diabetes was relatively well controlled before the study, as demonstrated by their average hemoglobin A_{1c} (HbA_{1c}) level of 8.5 ± 0.9%. Two patients had retinopathy, and one had peripheral neuropathy. None of the patients had nephropathy. All of the patients had undetectable fasting C-peptide levels and normal fasting plasma lipid levels.

Before entering the study, each patient was treated with the diet recommended by the American Diabetes

From the Joslin Diabetes Center, New England Deaconess Hospital, and Brigham and Women's Hospital, Boston, Massachusetts.
Address correspondence and reprint requests to Fredrick L. Dunn, MD, Duke University Medical Center, Box 3939, Durham, NC 27514.

TABLE 1
Clinical characteristics of 5 type I diabetic patients controlled with artificial β-cell

	Mean ± SE	Range
Age (yr)	42 ± 4	32–56
Duration of diabetes (yr)	20 ± 4	8–31
Ideal body weight (%)	107 ± 8	31–130
HbA_{1c} (%)	8.5 ± 0.9	5.8–10.6
Insulin (U/day)	43 ± 6	24–60

Values are means ± SE.

Association and two to three subcutaneous insulin injections per day. Intermediate-acting insulin was discontinued 48–72 h before the study. All studies were carried out at the Clinical Research Center of Brigham and Women's Hospital (Boston, MA). The protocol for this study was approved by the Committee on Human Studies, Joslin Diabetes Center, and the Committee for Protection of Human Subjects from Research Risks, Brigham and Women's Hospital. Informed consent was obtained from each patient.

Experimental diets. Both diets examined in the study were solid food and consisted of five meals with similar quantities of carbohydrate and protein with or without additional fat. Meals were given every 4 h from 0800 to 2400 h, and the size of each of the five meals was the same. Diet A was isocaloric and was calculated to provide sufficient calories to maintain a stable body weight. Diet A (total cal 1830 ± 99) consisted of 45% of calories as carbohydrate (212 ± 16 g), 15% protein (74 ± 9 g), and 40% fat (76 ± 1 g). On the other hand, diet B (total cal 1233 ± 106) was virtually fat free, with <5% of the calories from fat (6 ± 1 g). The carbohydrate and protein contents (in g) of diet B were the same as in diet A. Therefore, diet B was hypocaloric or ~65% of the total calories given in diet A. This marked decrease in fat content was the cause for the decrease in calories in diet B. In addition, diet B was relatively high in carbohydrate, because 75% of its remaining calories were derived from carbohydrate and 25% from protein. Diets A and B were identical in foodstuff composition except for the addition of fat to diet A.

Experimental design. Patients were admitted to the metabolic ward and initially fed diet A. The artificial β-cell (Biostator GCIIS, Life Science, Miles, Elkhart, IN) was started the next morning (day 1), and the patient's diabetes was stabilized over the next 8–12 h. The Biostator settings were as previously reported (15). The desired basal blood glucose (BG) level was set at 80 mg/dl. This is the BG level the Biostator attempts to maintain, and at which the insulin infusion is equal to the estimated basal infusion rate. The level below which dextrose is infused was set at 60 mg/dl. With these settings, the preprandial BG values ranged between 80 and 100 mg/dl (mean ± SE 85 ± 11 mg/dl), and postprandial hyperglycemia was <180 mg/dl. The Biostator was continued without interruption throughout the study. BG level was monitored continuously with the artificial β-cell and also was determined every 4 h on the Beckman Glucose Analyzer II (Fullerton, CA). Data for diet A were collected on day 2, after ~16–20 h of stabilization on the Biostator. On day 3, the diet was changed to the hypocaloric fat-free diet B. The Biostator was continued, and data were collected for the diet B study on day 3. Blood samples for plasma glucose (16), free–fatty acid (17), free-insulin (18), cholesterol, and triglyceride (15) levels were drawn 1 h before each meal from 0700 through 2300 h each day.

Data calculation and statistical analysis. BG concentrations were determined from the Biostator record. The start of each meal was marked on the Biostator printout, and the premeal BG was noted. A mean premeal BG value from the five meals on each diet was determined for each subject, and a mean for the group was determined from that value. Maximal postmeal BG, time to maximal BG, and time to return postmeal BG to 100 mg/dl were determined similarly from the Biostator re-

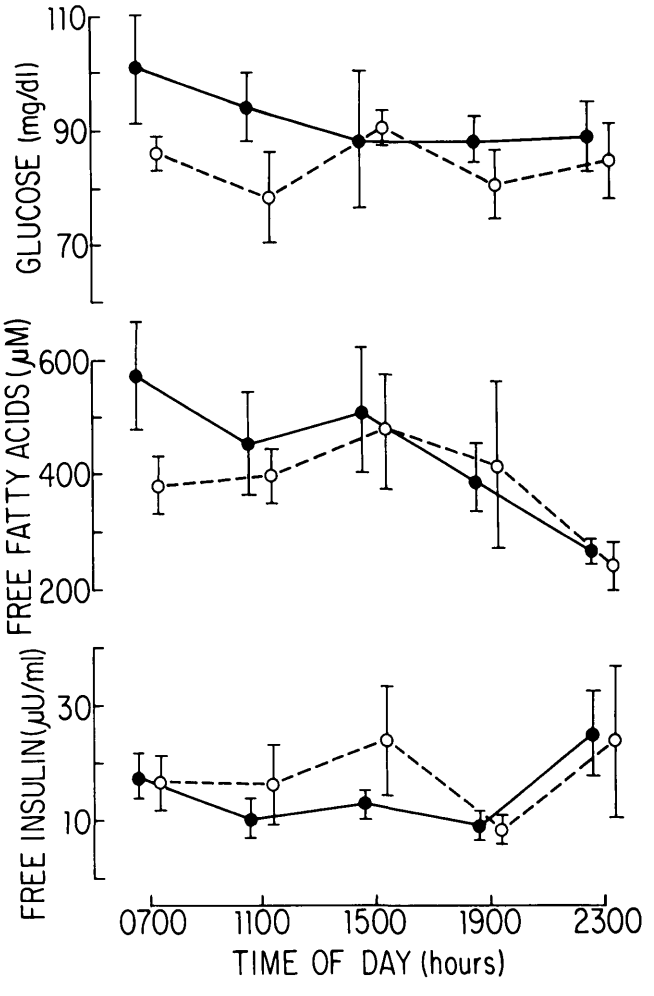

FIG. 1. Mean (±SE) blood glucose, free–fatty acid, and free-insulin levels in 5 type I diabetic patients on diet A (●, isocaloric, 40% fat) and diet B (○, hypocaloric, fat free) and controlled by artificial β-cell.

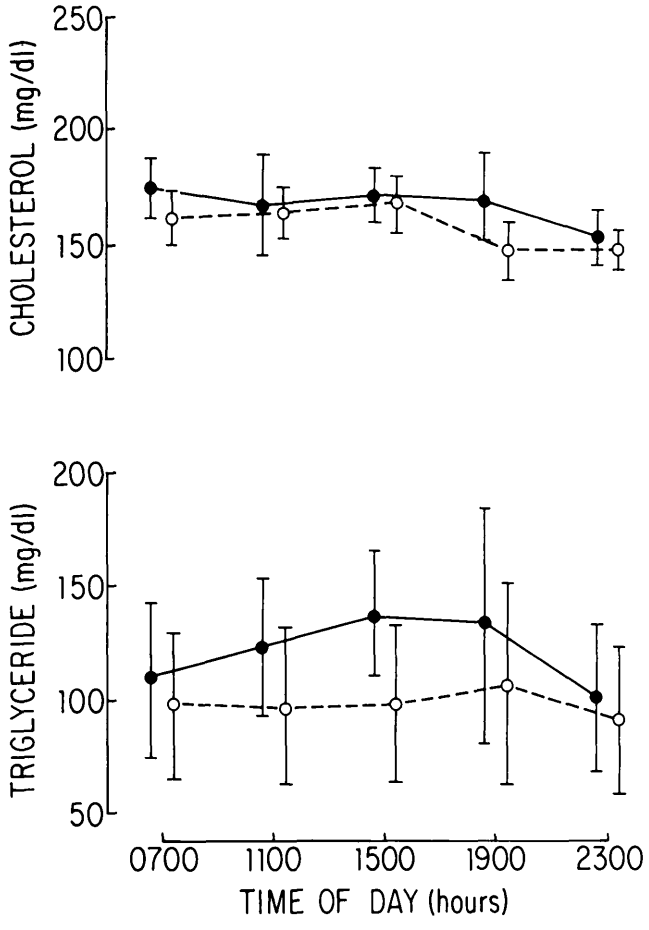

FIG. 2. Plasma lipid concentrations in patients on diet A (●, isocaloric, 40% fat) and diet B (○, hypocaloric, fat free).

cord. Insulin requirements were also determined from the Biostator record. Total units per day were calculated from the amount of insulin infused during the 24 h, starting at 0800 h on each diet. Units per meal were calculated as the amount of insulin given by the Biostator from the start of each meal until BG returned to 100 mg/dl. Basal insulin infusion was calculated as the amount of insulin delivered per hour by the Biostator to maintain a constant BG level from 0200 to 0800 h. From the mean value for each subject on each diet, the mean for the group on each diet was calculated. Paired Student's *t* test was used for comparison between the two diets. All values are reported as means ± SE.

RESULTS

Figure 1 shows BG, plasma free–fatty acid, and free-insulin levels 1 h before each meal on the two study diets. There was no difference in the mean preprandial BG levels during the two study periods. Similarly, there was little change in the mean free–fatty acid (348 ± 79 vs. 321 ± 76 μM) and free-insulin (18.4 ± 4.0 vs. 16.0 ± 4.2 μU/ml) levels on diet A versus diet B, respectively.

TABLE 2
Effect of diets A and B on blood glucose concentrations

	Diet A	Diet B
Premeal BG (mg/dl)	90 ± 4	87 ± 2
Maximal postmeal BG (mg/dl)	152 ± 6	155 ± 6
Time to maximal BG (min)	58 ± 6	56 ± 3
Time to return postmeal BG to 100 mg/dl (min)	129 ± 6	105 ± 12

Values are means ± SE. Diet A was isocaloric, 40% fat; diet B was hypocaloric, fat free. BG, blood glucose.

Figure 2 shows the effect of the two diets on plasma lipid levels. Plasma cholesterol levels were unchanged and similar throughout the day on the two study diets (157 ± 16 vs. 146 ± 17 mg/dl). Plasma triglyceride levels were also similar. However, there was a slight increase in plasma triglyceride levels on diet A (110 ± 29 vs. 92 ± 28 mg/dl), which was most marked later in the day. On diet B, plasma triglyceride levels were virtually unchanged during the day.

Table 2 shows the effect of the two diets on BG concentrations. Mean preprandial BG levels were not different on the two diets. In addition, the maximal postprandial BG level, the time to reach the maximal BG, and the time to return BG to <100 mg/dl were similar for the two diets.

Table 3 shows the insulin requirements as determined by the Biostator on diets A and B. Total insulin requirements expressed as units per day were identical for diet A (70.8 ± 6 U/day) and diet B (74.5 ± 5.5 U/day). The amount of insulin (U/meal) to return BG levels to <100 mg/dl were also virtually identical during the two study periods. During diet A the patients required an average of 10.4 ± 1 U/meal, whereas during diet B the average was 10.3 ± 0.8 U/meal. The basal insulin infusion rate, determined as the units per hour delivered by the Biostator from 0200 to 0800 h, was similar during the two study periods. During diet A, basal insulin infusion was 1.76 ± .10 U/h, and during diet B it was 1.62 ± .13 U/h.

In summary, total, meal, and basal insulin requirements determined with the Biostator were not signifi-

TABLE 3
Insulin requirements in patients on diets A and B as determined by artificial β-cell

Insulin	Diet A	Diet B
Total units/day	70.8 ± 6.0	74.5 ± 5.5
Units/meal	10.4 ± 1.0	10.3 ± 0.8
Basal insulin infusion (U/h)	1.76 ± 0.10	1.62 ± 0.13

Values are means ± SE. Diet A was isocaloric, 40% fat; diet B was hypocaloric, fat free.

cantly altered by eliminating fat calories from the diet, despite it being a hypocaloric diet. Glucose, free–fatty acid, free-insulin, and lipid levels were similar on the two study diets. Thus, our data suggest that fat-derived calories did not significantly contribute to short-term insulin requirements in our patients with type I diabetes.

DISCUSSION

Although much recent interest has focused on differences in BG response to various simple and complex carbohydrates (12,13,19–21), little is known about the effect of calories derived from fat on BG excursions and insulin requirements. In this study, we investigated the acute effect of removal of calories derived from fat on BG excursions as well as total, basal, and meal insulin requirements by use of the artificial β-cell. We also studied the acute effect of short-term feeding of hypocaloric fat-free diets on plasma free–fatty acid, free-insulin, cholesterol, and triglyceride levels in type I diabetic patients.

Based on previous studies suggesting that high-fat diets decrease glucose tolerance and insulin sensitivity (22–24), we expected to observe a decrease in insulin requirements on the hypocaloric fat-free diet. However, we observed no significant difference in total, meal, or basal insulin requirements on the two diets. Our data suggest that meal insulin requirements were determined primarily by the carbohydrate and possibly the protein content of the diet rather than by the total caloric content. This finding is consistent with a previous report by Nuttall et al. (25) that carbohydrate is the primary determinant of postmeal insulin concentrations in normal subjects. Our data further suggest that fat-derived calories did not require additional insulin for metabolism in already well-insulinized patients.

These findings are in contrast to previous reports that suggested isocaloric alterations in diabetic diets (decreasing fat content and increasing carbohydrate content) result in no change (9,24,26,27) or a decrease (8) in insulin requirements in patients with type I diabetes. Although these previous studies used less precise methods to determine insulin requirements, we doubt this was responsible for the difference in results. Rather, these previous studies examined the effect of longer-term (≥4-wk) alterations in fat and carbohydrate content. Apparently, the effects of a high-carbohydrate, low-fat diet on insulin needs require >24 h to become apparent.

The mechanism responsible for the change in insulin requirements with alterations in dietary fat appears to be a direct effect of dietary fat on insulin sensitivity. Himsworth (28) first showed that a high-fat diet decreased glucose tolerance and that this was due to a change in the susceptibility to insulin. In rats, short-term feeding of a high-fat diet induces insulin resistance (29–31). In patients with type I diabetes, a low-fat, high-starch, high-fiber diet resulted in reduced insulin doses and improved metabolic control associated with increased monocyte insulin-receptor binding (32). Another effect of fat in the diabetic diet is to decrease postprandial hyperglycemia by delaying glucose absorption (25,33).

A significant criticism of our study's experimental design is that diet B (fat free) was always given second, and thus our results may be influenced by a potential time-dependent effect. Such an effect would be of particular concern if changes in insulin action occur with acute restoration of euglycemia. Because of the latter possibility, each patient's diabetes was controlled for 20 h on the Biostator before collecting data. The original purpose of our experimental fat-free diet was for the study of very-low-density lipoprotein triglyceride metabolism (15). With this protocol, patients were maintained on the Biostator and fat-free diet for 72 h, yet there was no significant change in the amount of insulin delivered by the Biostator on successive days of the fat-free diet. In addition, in a similarly designed study with the Biostator to determine insulin requirements on two diets with different carbohydrate contents, there was little change in daily or meal insulin requirements during 4 days on each diet (14). However, because of the possibility of a time-dependent effect in insulin action, the few subjects studied, and the lack of randomization, the findings of this study should be interpreted cautiously until these results are confirmed in a more rigorous manner.

Our findings should have little effect on the long-term dietary recommendations for patients with type I diabetes. Instead, our findings may be significant in terms of calculating insulin needs for short-term dietary changes. For example, type I diabetic patients treated with insulin-infusion pumps often attempt to keep their postprandial BG levels close to the nondiabetic range by precisely determining their meal insulin dose based on their preprandial BG level and expected dietary composition. Changes in meal composition and amount are unavoidable in the real world. Studies such as ours may be useful in terms of calculating insulin needs associated with short-term dietary indiscretions.

In summary, our study showed that when calories derived from fat were eliminated from the diet in five type I diabetic patients, insulin required to maintain euglycemia, as determined by the artificial β-cell, was unchanged compared with an isocaloric 40% fat diet. We conclude that in relatively well-controlled and adequately insulinized type I diabetic patients, short-term elimination of fat-derived calories from an isocaloric diet does not alter insulin requirements, which implies that calories derived from carbohydrate and possibly protein are the major determinants of meal insulin requirements.

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