Is a Failure to Recognize an Increase in Food Intake a Key to Understanding Insulin-Induced Weight Gain?

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The present study aimed to assess the contribution of energy intake to positive energy balance and weight gain with insulin therapy. Changes in energy intake (self-report and weighed food intake), dietary behavior (auto-questionnaires), resting energy expenditure (REE) (indirect calorimetry), physical activity (accelerometry), and glucosuria were monitored over the first 6 months of insulin therapy in 46 diabetic adults. No change in REE, activity, or glucosuria could explain weight gain in the type 1 (4.1 ± 0.6 kg, $P < 0.0001$) or type 2 (1.8 ± 0.8 kg, $P = 0.02$) diabetic groups. An increase in energy intake provides the most likely explanation for weight gain with insulin. However, it is not being recognized because of significant underestimation of self-reported food intake, which appears to be associated with increased dietary restraint.

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Weight gain can result from an increased energy intake, decreased energy output or requirement, or reasons yet unidentified. Meanwhile, weight gain during insulin therapy (1–3) is classically explained by decreases in resting energy expenditure (REE) and glucosuria (4,5). While the former may be applicable to patients with very poor metabolic control, in which REE is initially elevated (6), it appears less relevant to those with milder metabolic disturbances (7). This latter group represents most newly insulin-treated patients given current recommendations to lower GHb (8). Although glucosuria can contribute to weight change (4), it diminishes after a few days of insulin therapy, and therefore is unlikely to invoke long-term gains. Only two studies in newly insulin-treated type 2 diabetic adults (9,10) have considered the role of energy intake. In one study (9), energy intake was restricted for weight maintenance. In the other (10), the authors found no change in ad libitum energy intake despite significant weight gain. However, reported energy intake at 12 months was extremely low (1.1 × REE), suggesting food intake underreporting (11). Underreporting is widely acknowledged in nondiabetic people (12) but only alluded to in the type 2 diabetic population (13–15), despite being greater in the latter group (16). The issue has not been explored in the context of insulin-induced weight gain. We prospectively assessed contributors to positive energy balance, with emphasis on energy intake, when starting insulin therapy.

RESEARCH DESIGN AND METHODS

— Type 1 ($n = 23$) and type 2 ($n = 23$) diabetic adults beginning insulin therapy participated in this study, approved by the local ethics committee. Patients' energy balance was assessed over 6 months.

Hospital assessments

Weight was measured when starting insulin (baseline) and after 3 and 6 months to within 0.01 kg. REE was measured by indirect calorimetry (7), fat and fat-free mass were assessed using a three-compartment method (7), and measurements of glucosuria were conducted by glucose oxidaze (Clinitek; Bayer Diagnostics) and of GHb by HPLC (Varient HemoglobinA_{1c}; Bio-Rad). At baseline, the quantities of food and beverages consumed were directly measured. The Dutch Eating Behavior (17) and Three-Factor Eating (18) Questionnaires assessed dietary behavior.

Home assessments

Home assessments were conducted 2 weeks before each hospital assessment (type 2 diabetic patients only prebaseline). Physical activity was measured over 7 days by triaxial-accelerometry (RT3; Stayhealthy) (19). Patients had ≥600 min of daily data and ≥4 days at each assessment. Food intake was self-reported using a 4-day (2 week, 2 weekend) food diary. All measured and self-reported data were analyzed for energy and macronutrient content using computerized software (Bilnut 4.0, Nutrisoft 95). The significance of 6-month changes was determined by repeated-measures ANOVA. Twenty patients per group was powerful enough ($\alpha = 0.05$, $\beta = 90\%$) to detect a 10% difference in energy intake change between groups. Calculations were performed using Statview (Abacus Concepts, Berkeley, CA).

RESULTS

— At baseline, compared with type 1 diabetic patients (16 men/7 women), type 2 diabetic patients (11 men/12 women) were older (mean ± SEM 59.7 ± 1.6 vs. 32.3 ± 2.6 years, $P < 0.001$), had a higher BMI (32.4 ± 1.6 vs. 21.3 ± 0.8 kg/m^2, $P < 0.001$), and had lower GHb (9.3 ± 0.2 vs. 12.4 ± 0.6%). Weight gain was 4.7 ± 0.6 kg ($P < 0.0001$) in the type 1 and 1.8 ± 0.8 kg ($P = 0.02$) in the type 2 diabetic groups, whereas the respective reductions in GHb were −5.8 ± 0.4% ($P < 0.0001$) and −1.5 ± 0.2% ($P = 0.0003$). Only the type 1 diabetic group reported weight loss (mean 2.97 kg) over the 6 months before starting insulin. REE, which was higher in the type 2 diabetic group at baseline

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Abbreviations: REE, resting energy expenditure.

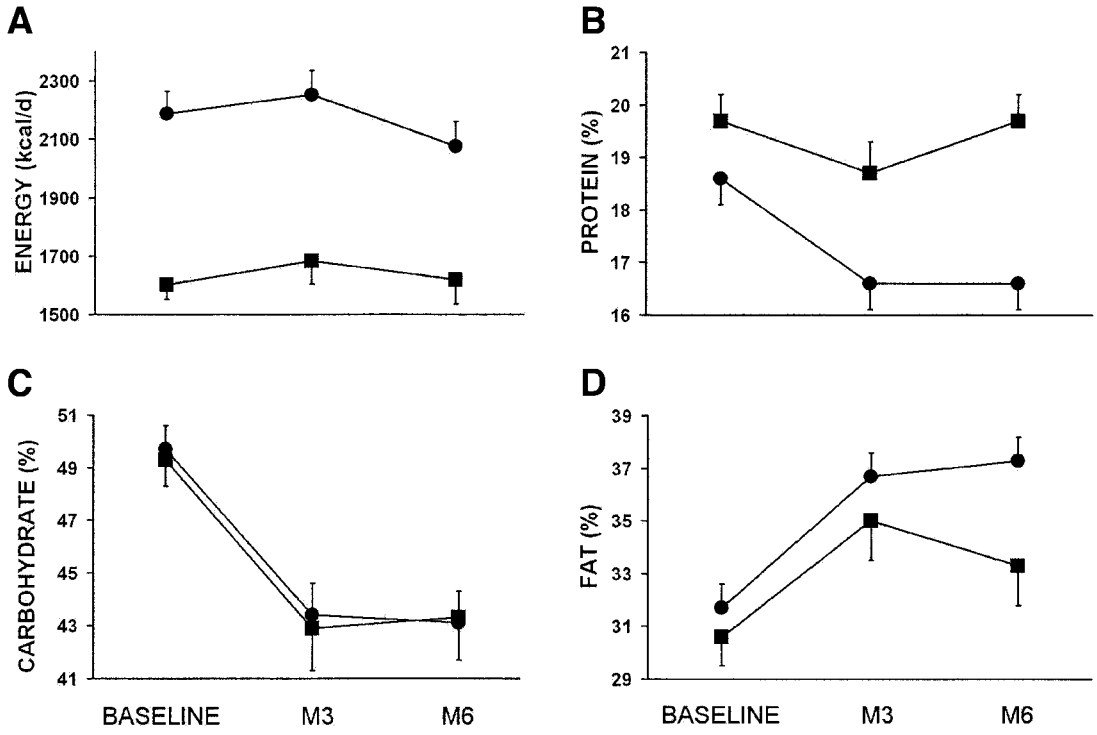

Figure 1—*Mean changes in energy intake in kilocalories per day* (A)*, percentage protein intake per day* (B)*, percentage carbohydrate intake per day* (C)*, and percentage fat intake per day* (D) *in the type 1 diabetic patients* (●) *and type 2 diabetic patients* (■) *between baseline, month 3 (M3), and month 6 (M6). Values are expressed as means ± SEM.*

(1,726 ± 63 vs. 1,559 ± 41 kcal/day, P = 0.03), remained unchanged by month 6 (P = 0.70) and increased by 8% (P = 0.005) in the type 1 diabetic group. No change in weight/fat-free mass–adjusted REE occurred in either group. No change in percentage time spent at low-, moderate-, or high-intensity activity was observed over 6 months. Hence, no component of energy expenditure could explain weight gain. Glucosuria diminished in the type 1 (from 12.6 ± 2.2 to 2.1 ± 1.2 g/day, P = 0.0003) but not in the type 2 (from 2.8 ± 1.1 to 1.3 ± 0.9 g/day, P = 0.25) diabetic group. Figure 1 shows that measured energy intake was significantly lower in the type 2 diabetic group (1,634 ± 67 vs. 2,172 ± 82 kcal/day, $P <$ 0.0001). No significant change in self-reported energy intake was detected over 6 months in either the type 1 (−110 kcal/day, P = 0.19) or type 2 (+18 kcal/day, P = 0.76) diabetic groups. Reported carbohydrate intake decreased in both groups, reciprocated by increased fat and decreased protein intake in the type 1 diabetic group. Six-month weight and energy intake changes were unrelated in both groups. An energy intake–to–REE ratio below a cut off value of 1.395 identifies patients in whom energy intake is underreported (11). Calculated energy intake–to–REE ratio was 0.95 ± 0.04 × REE at baseline and 0.97 ± 0.05 × REE at month 6 in the type 2 diabetic group. Although calculated energy intake–to–REE ratio was 1.43 ± 0.07 × REE at baseline in the type 1 diabetic group, the ratio had significantly (P = 0.02) decreased to 1.23 ± 0.05 × REE by month 6. Dietary restraint, which increased with therapy in both groups, was positively associated with energy intake–to–REE ratio at baseline ($P < 0.01$) and month 6 ($P < 0.05$). Weight gain, but not energy intake change, was significantly correlated with the number of hypoglycemic episodes in the type 1 diabetic group only (r^2 = 0.83).

CONCLUSIONS — Present results show that no change in REE, physical activity, or glucosuria could adequately explain insulin-induced weight gain; therefore, increased energy intake is the only plausible mechanism. Accurate energy intake assessment was severely hampered by the underreporting of food intake, with most energy intakes being insufficient to meet even basal energy requirements. Such underreporting appears to be associated with increased dietary restraint, indicating that routine measures of restraint using self-report questionnaires could predict a patient's potential to underreport. Although it is difficult to evaluate the effect of insulin per se, this comprehensive assessment of energy balance parameters shows that an increase in energy intake, associated with overeating in response to hypoglycemia for example (3), provides the most likely explanation for positive energy balance during insulin therapy. The underreporting of food intake requires more concerted effort to detect its presence and magnitude.

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