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Resting energy expenditure in type 2 diabetic patients and the effect of insulin bolus

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ABSTRACT

Aims: Resting energy expenditure (REE) plays a critical role in the regulation of body weight, with important implications in type 2 diabetes (T2D). However, the relationships between REE and T2D have not been extensively evaluated. We compared REE in persons with diabetes and in persons without diabetes. We also investigated the acute effect of insulin on REE and venous lactate, the latter an indirect measure of neoglucogenetic activity.

Methods: REE was measured using indirect calorimetry in 14 newly diagnosed, untreated T2D adults and in 14 non-diabetic age-, gender- and body mass index-matched persons. The REE and lactate venous concentrations were also measured in a subgroup of 5 T2D patients in the hour following an IV insulin bolus.

Results: The REE normalized for fat-free mass (FFM) was significantly higher in T2D patients than in the group without diabetes (mean ± SD: 27.6 ± 1.9 vs. 25.8 ± 1.9 kcal/kg-FFM·24 h; P = 0.02). REE normalized for FFM was correlated with fasting plasma glucose concentration ($r = 0.51$; $P = 0.005$). Following the insulin venous bolus REE (0′: 2048 ± 242; 10′: 1804 ± 228; 20′: 1684 ± 230; 30′: 1634 ± 212; 45′: 1594 ± 179; 60′: 1625 ± 197 kcal/24 h; $P < 0.001$) and both glucose ($P < 0.001$) and lactate ($P < 0.001$) concentrations progressively declined in the ensuing hour.

Conclusions: Patients with diabetes have a higher energy expenditure, likely a consequence of higher gluconeogenetic activity. This study may contribute to recognizing the nature of body weight reduction that occurs in concomitance with poorly controlled diabetes, and of body weight gain as commonly observed when hypoglycemic treatment is started.

1. Introduction

Type 2 diabetes (T2D) is often associated with obesity, a condition that follows a sufficiently prolonged period in which energy intake exceeds energy expenditure. It cannot be excluded that in diabetes-prone people genetic factors may be responsible for a relative low energy expenditure that facilitates the appearance of obesity [1–3]. Nevertheless, reducing energy intake with diet is the first, and probably

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most important, therapeutic measure in the treatment of diabetes. The relationship between energy balance and diabetes seems even more complex if one considers that spontaneous weight loss often occurs with poorly controlled diabetes [4]. Therefore, studies investigating the energy expenditure of persons with diabetes are of interest in understanding the relationship between body weight changes and diabetes, and also in individualizing medical nutrition therapy [5]. In this respect, resting energy expenditure (REE) is the most important component of total daily energy expenditure, and plays an important role in the regulation of body weight [6]. REE has been investigated in T2D people for some years, though with conflicting results, and it has been found that REE is increased in T2D [7–15] or similar to that of persons without diabetes [16,17].

Neoglucogenetic activity is an energy-consuming metabolic pathway that is increased in T2D because it is responsible for hyperglycemia, especially in the fasting state [18]. We hypothesize that glycemic control and the concomitant use of medications such as metformin [19] or insulin [20], all of which are closely related with the neoglucogenetic activity, may influence REE. Therefore, we investigated REE in persons with newly diagnosed type 2 diabetes before starting hypoglycemic treatment. We also measured the acute effect of a bolus of insulin on REE in a subgroup of patients with elevated fasting plasma glucose concentrations.

2. Subjects

Fourteen persons with newly diagnosed type 2 diabetes (9 males, 5 females) were recruited among the patients seen at the Diabetes and Dietetics Outpatient Department of the Department of Internal Medicine, Cardiovascular and Kidney Diseases of the University of Palermo, Italy. They were compared to 14 non-diabetic, gender-, age-, and body mass index-matched controls. There was no incentive provided to the participants. Inclusion criteria were diabetes diagnosed in the last 3 weeks and not pharmacologically treated, of both genders, and with age in the range of 30–65 years. Exclusion criteria were previously diagnosed cardiovascular or systemic disease, with the exception of hypertension; regular use of medications other than anti-hypertensives; and pregnancy or lactation in the past 6 months. Type 2 diabetes was defined according to the most recent consensus statements [21]. The study was conducted according to the guidelines laid down in the Declaration of Helsinki and the study protocol was approved by the Investigator Revisory Board at the Biomedical Department of Internal and Specialist Medicine (DIBIMIS) of the University of Palermo. Each participant approved and signed an informed consent form.

All participants were investigated between 7:00 and 8:00 in the morning, in a postabsorptive state, after 10–12 h of overnight fasting. In the three days preceding measurements, participants were requested to maintain their habitual diet and to abstain from intense voluntary or leisure physical activity.

Participants with diabetes and fasting plasma glucose (FPG) concentrations $\geq$150 mg/dl were requested to voluntarily undergo measurements before and during the hour (10, 20, 30, 45, 60 min) following an IV bolus of regular insulin (0.15 IU $\times$ kg-body weight; Actrapid®, NovoNordisk, Denmark), and sign a new, specific written informed consent. Two venous catheters were inserted in each arm in an antecubital vein for insulin infusion, and blood sampling and glucose infusion if glycemia reduced below 80 mg/dl, in which case the test was interrupted.

3. Materials and methods

3.1. Measurements

Height and body weight were measured with participants lightly dressed and without shoes (SECA); the body mass index (BMI) was calculated as body weight (kg)/height^2 (m^2). Fat mass (FM, % body weight) and fat-free mass (FFM, kg) were estimated as previously described [6] by means of bioelectrical impedance analysis (BIA; BIA-103, RJL, Detroit, USA/Akern Florence, Italy).

Resting energy expenditure (REE) and respiratory quotient (RQ; VCO_2/VO_2, an indirect measure of the mixture of carbohydrate and lipid oxidation) were obtained by means of the indirect calorimetry method, as described elsewhere [22], using a ventilated hood system (Quark RMR; Cosmed, Roma, Italy). The device was equipped with an infra-red analyzer for carbon dioxide measurement (VCO_2), and a zirconium cell analyzer for oxygen measurement (VO_2). Analyzers were calibrated before each test using gases with known percentages of O_2 and CO_2. Briefly, respiratory gas exchanges were continuously measured for about 1 h, data were obtained from at least 30 min of stable measurements, and the average intra-subject variability was 3.9% for REE. REE was calculated using the equation of Weir [23] and was expressed both in absolute terms (kcal/24 h) and normalized for FFM size (kcal/kg-FFM·24 h).

3.2. Laboratory analysis

Fasting plasma glucose concentrations were measured using a standard clinical chemistry method (Glucosio HK UV; Roche diagnostics, Monza, Italy), and glycated haemoglobin (HbA1c; HbA1c gen.3; Roche diagnostics; Monza, Italy) was also determined. Measurements of blood glucose and lactate concentrations before and during the hour following insulin bolus (six measurements) were obtained from venous samples using an amperometric method (ABL 800 FLEX; Radiometer Copenhagen, Denmark).

3.3. Statistical analysis

All data are expressed as mean $\pm$ SD. The statistical comparisons between the groups were calculated by means of an unpaired student's *t*-test. Repeated-measure ANOVA was carried out to detect significant changes in variables over time following IV insulin bolus. Correlations between variables are expressed as the Pearson's correlation coefficient. A two-tailed *P* of $<$0.05 was considered statistically significant. All analyses were done using Systat (Windows, version 11.0; Systat Software Inc., San Jose, CA, USA).

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