Abstract

The project focuses on dietary interventions in type 2 diabetes (T2D). The aim was to investigate how glucose metabolism and other manifestations of insulin resistance should be influenced by a) the composition of macronutrients and b) frequency of meals; and to characterize the possible mechanisms of these dietary interventions in patients with T2D.

A. In a randomized crossover study, 50 patients T2D and 50 age-matched healthy subjects underwent in a random order meal tolerance tests with three isocaloric meals (vegan sandwich; V-meal, hamburger; M-meal, or cheese sandwich; S-meal. Blood samples for analysis were taken at time 0 and after 30, 60, 120 and 180 minutes after meal ingestion. Plasma concentrations of plasma glucose, insulin, C-peptide, lipids, oxidative stress markers and gastrointestinal hormones (GIHs) were investigated.

Both basal and postprandial plasma concentrations of glucose and insulin were significantly higher in patients with T2D (p<0.001); basal and postprandial concentrations of almost all other GIHs (except for ghrelin) and thiobarbituric acid reactive substances (TBARS) were significantly increased (p<0.001), while ascorbic acid, reduced glutathione and superoxide dismutase activity were decreased in patients with T2D compared to healthy controls (p<0.001). The meal rich in saturated fat and protein resulted in higher postprandial increase in GIHs, lipids and persistent postprandial hyperinsulinemia and oxidative stress, particularly expressed in patients with T2D. The plasma glucose levels were significantly higher after the meal rich in carbohydrates only at the peak level (p<0.01). The area under the curve of glucose (AUC) was comparable after the meal rich in saturated fat vs. the meal rich in carbohydrates in both groups.

B. In a randomized, crossover study, we assigned 54 patients with T2D to follow two regimens of a hypocaloric diet (-500 kcal/day), each for 12 weeks: six meals a day (A6), and two meals a day (B2). The diet in both regimens had the same macronutrient and energy content. Insulin sensitivity was measured by hyperinsulinemic isoglycemic clamp, rest energy expenditure (REE) was determined by indirect calorimetry and β-cell function was assessed during a standard meal test and quantified using a mathematical model. Plasma concentrations of GIH were determined using multiplex immunoassay. The fatty acid composition in serum phospholipids was measured by gas-liquid chromatography. The hepatic fat content was measured by proton magnetic resonance spectroscopy.

In patients with T2D less frequent eating (B2 regimen) reduced body weight (p<0.001), hepatic fat content (p<0.05), fasting plasma glucose (p<0.01), C-peptide, glucagon and insulin resistance more than a diet with the same caloric restriction divided into six more frequent meals. Feelings of hunger were only reduced in the regimen B2 (p<0.001). The basal metabolism interference and changes in the composition of fatty acids in serum phospholipids could be one of the potential mechanisms of the favorable effect of reducing the number of meals per day in patients with T2D.

Our data confirmed increased postprandial oxidative stress and increased postprandial concentrations of most gastrointestinal peptides in patients with T2D compared to healthy controls. Our results suggest that the diet composition and the energy content, rather than the carbohydrate count, should be important considerations for dietary management.

Our data suggest that less frequent eating may be more beneficial for a long-term adherence than to apportion a hypocaloric diet into smaller meals during the day for patients with T2D.

Key words: Type 2 diabetes, postprandial state, insulin resistance, oxidative stress markers, frequency of meals, hypocaloric diet, gastrointestinal peptides, hepatic fat content.