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Adverse effects on insulin secretion of replacing saturated fat with refined carbohydrate but not with monounsaturated fat: A randomized controlled trial in centrally obese subjects

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BACKGROUND: Current dietary guidelines recommend the replacement of saturated fatty acids (SAFAs) with carbohydrates or monounsaturated fatty acids (MUFAs) based on evidence on lipid profile alone, the chronic effects of the mentioned replacements on insulin secretion and insulin sensitivity are however unclear.

OBJECTIVE: To assess the chronic effects of the substitution of refined carbohydrate or MUFA for SAFA on insulin secretion and insulin sensitivity in centrally obese subjects.

METHODS: Using a crossover design, randomized controlled trial in abdominally overweight men and women, we compared the effects of substitution of 7% energy as carbohydrate or MUFA for SAFA for a period of 6 weeks each. Fasting and postprandial blood samples in response to corresponding SAFA, carbohydrate, or MUFA-enriched meal-challenges were collected after 6 weeks on each diet treatment for the assessment of outcomes.

RESULTS: As expected, postprandial nonesterified fatty acid suppression and elevation of C-peptide, insulin and glucose secretion were the greatest with high-carbohydrate (CARB) meal. Interestingly, CARB meal attenuated postprandial insulin secretion corrected for glucose response; however, the insulin sensitivity and disposition index were not affected. SAFA and MUFA had similar effects on all markers except for fasting glucose-dependent insulinotropic peptide concentrations, which increased after MUFA but not SAFA when compared with CARB.

CONCLUSION: In conclusion, a 6-week lower-fat/higher-carbohydrate (increased by 7% refined carbohydrate) diet may have greater adverse effect on insulin secretion corrected for glucose compared

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with isocaloric higher-fat diets. In contrast, exchanging MUFA for SAFA at 7% energy had no appreciable adverse impact on insulin secretion.

Introduction

Central obesity, a component of the metabolic syndrome, is closely linked to insulin resistance and predisposed to the development of type 2 diabetes. The role of defective insulin secretion in the pathogenesis of type 2 diabetes, however, has received less attention. The high-fasting insulin concentration in type 2 diabetes patients in fact resembles insulin deficit rather than hyperinsulinemia under the condition of concurrently elevated glucose concentration.[1] Emerging evidence showed that decline of glucose tolerance may be elicited by the insulin secretory defect rather than by obesity itself.[2] WHO recommends a reduction in saturated fats to <10% energy (en) with the replacement of carbohydrate or monounsaturated fats, for CHD prevention.[3] A recent meta-analysis of observational studies does not support the association of aforementioned replacement of saturated fats with reduction in diabetes risk in healthy individuals.[4] Conflicting findings were reported by three large scale interventional studies[5–7] (to be discussed in Discussion part).

Gastrointestinal peptides such as glucagon-like peptides (GLP-1), glucose-dependent insulinotropic polypeptide (GIP), ghrelin, peptide YY (PYY), and cholecystokinin (CCK) are short-term signals for satiety feedback to the brain and hence play a role in regulating glucose homeostasis.[8,9] For example, lipid-induced CCK release was found to inhibit hepatic glucose production, and high-fat overfeeding was found to impair the gut-brain-liver neuronal mechanism hence leading to hyperglycemia.[10] There is growing clinical evidence that the levels of gastrointestinal peptides are compromised in overweight individuals,[11] impaired glucose tolerance,[12] and type 2 diabetes patients.[13,14] Thomsen et al. reported that the ingestion of monounsaturated fat-enriched (MUFA) meal resulted in a higher GIP[15] and GLP-1[16] concentrations compared with a saturated fat-enriched (SAFA) meal in both overweight with type 2 diabetes and lean, healthy subjects. In this context, the type of dietary fats, in particular triglycerides with different fatty acid chain lengths or degree of saturation may exert a differential impact on incretins, that is, GIP and GLP-1, which play an important role in insulin secretion.

Owing to the limited and conflicting data available on the aforementioned, the present study was designed to investigate the fasting and postprandial effects of the replacement of 7% en SAFA with carbohydrate or MUFA on insulin secretion, insulin sensitivity, glucose homeostasis, and gastrointestinal peptide responses in individuals with central obesity. A 7% en exchange of specific nutrients applied in this study was intended to reflect the practical scenario of the reduction of total SAFA intake. The current dietary guideline recommended by World Health Organization (WHO) is a <10% en intake of total SAFA. In addition, we also performed metabolic challenge test, which reflected a single meal habitual dietary intake at the end of each dietary intervention. Such setting was important as postprandial lipemia and postprandial glycemia after each dietary pattern have been indicated in the etiology of chronic metabolic diseases such as T2DM and CVD.

Materials and methods

Participants

The study protocol was approved by the Medical Ethics Committee of University of Malaya Medical Centre (reference no. 871.5). Participants gave informed written consent and attended a screening clinic. Fifty-four men and women aged 20–60 years with waist circumference ≥80 cm (for women) and ≥90 cm (for men) were recruited. Exclusion criteria were BMI ≤ 18.5 kg/m^2; medical history of CVD, diabetes, dyslipidemia; diagnosed chronic illness; current use of antihypertensive or lipid-lowering medication; plasma total cholesterol >6.5 mmol/L, triacylglycerol >4.5 mmol/L; alcohol intake >28 units/week; and lactating, pregnancy, and smoking. The flow of subject recruitment is shown in the CONSORT diagram (Fig. 1). Subjects' baseline characteristics are shown in Table 1.

Experimental design

This was a randomized, controlled, single-blind, crossover trial under free-living conditions. The study design is outlined in Figure 2. The study intervention was carried out from early March through mid-July 2012 at the Malaysian Palm Oil Board, Malaysia. Subjects were assigned to 3 consecutive 6-week isocaloric diets (~2000 kcal/day): SAFA (control; 55% carbohydrate, 32% fat: 12% saturated fat, 13% monounsaturated fat), carbohydrate-enriched (CARB; 62% carbohydrate, 25% fat: 5% SAFA, 14% MUFA) or MUFA (55% carbohydrate, 32% fat: 5% SAFA, 20% MUFA) in random order using an orthogonal randomization allocation (treatment sequences in SAFA-MUFA-CARB, MUFA-CARB-SAFA, and CARB-SAFA-MUFA). Women