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Randomized Control Trials

Effects of exchanging carbohydrate or monounsaturated fat with saturated fat on inflammatory and thrombogenic responses in subjects with abdominal obesity: A randomized controlled trial

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SUMMARY

Background & aims: Modification of the amount and type of dietary fat has diverse effects on cardiovascular risk.
Methods: We recruited 54 abdominally obese subjects to participate in a prospective cross-over design, single-blind trial comparing isocaloric 2000 kcal MUFA or carbohydrate-enriched diet with SFA-enriched diet (control). The control diet consisted of 15E% protein, 53E% carbohydrate and 32E% fat (12E% SFA, 13E% MUFA). A total of ~7E% of MUFA or refined carbohydrate was exchanged with SFA in the MUFA-rich and carbohydrate-rich diets respectively for 6-weeks. Blood samples were collected at fasting upon trial commencement and at week-5 and 6 of each dietary-intervention phase to measure levels of cytokines (IL-6, IL-1β), C-reactive protein (CRP), thrombogenic markers (E-selectin, PAI-1, D-dimer) and lipid subfractions. Radial pulse wave analysis and a 6-h postprandial mixed meal challenge were carried out at week-6 of each dietary intervention. Blood samples were collected at fasting, 15 and 30 min and hourly intervals thereafter till 6 h after a mixed meal challenge (muffin and milkshake) with SFA or MUFA (872.5 kcal, 50 g fat, 88 g carbohydrates) or CARB (881.3 kcal, 20 g fat, 158 g carbohydrates)- enrichment corresponding to the background diets.
Results: No significant differences in fasting inflammatory and thrombogenic factors were noted between diets ($P > 0.05$). CARB meal was found to increase plasma IL-6 whereas MUFA meal elevated plasma D-dimer postprandially compared with SAFA meal ($P < 0.05$). Comparing the 3 meals, there were similar postprandial elevations in IL-6 and D-dimer and postprandial reductions in PAI-1, augmentation index and pressure (time effect: $P < 0.05$). CARB diet was found to reduce HDL_3 by 7.8% and increase small dense HDL (sdHDL) by 8.6% compared with SFA diet ($P < 0.05$). SFA diet increased large HDL subfractions compared with both CARB and MUFA diets by 4.9% and 6.6% ($P < 0.05$), respectively.
Conclusions: Overall, the evidence presented in this study suggests that the replacement of SFA with MUFA or refined carbohydrates may not improve inflammatory and thrombogenic markers in abdominally overweight individuals. Indeed increased refined carbohydrates consumption adversely impacts fasting HDL subfractions.
This trial was registered under ClinicalTrials.gov. Identifier no. NCT01665482.

1. Introduction

Obesity is a major health concern, central obesity is of more clinical relevance and related to a cluster of metabolic disorders. Central obesity predisposes to a higher risk of developing cardiovascular diseases, which is related to early onset of pro-inflammatory and pro-thrombogenic states. Studies have reported higher levels of interleukin-6 (IL-6) and plasminogen inhibitor activator-1 (PAI-1) in abdominally obese individuals [1–3]. The accumulation of adipocytes in the abdominal region triggers the release of an array of fat soluble cytokines [4]. The consumption of high fat diets is thought to increase body weight and abdominal fat

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Abbreviations

IL-6	interleukin-6
PAI-I	plasminogen inhibitor activator-1
SFA	saturated fatty acid
CRP	C-reactive protein
MUFA	monounsaturated fatty acid
IL-1β	Interleukin-1β
MPOB	Malaysian Palm Oil Board
sdHDL	small dense HDL
iAUC	incremental area under the curve

deposition, with saturated fatty acid (SFA) considered the chief culprit [5]. In vivo animal data suggest that SFA in particular palmitic acid increase cytokines e.g. IL-6 and interleukin-1. SFA and *trans* fatty acids have been reported to increase C-reactive protein (CRP) [6] but limited data is available to support this. The recommendation to reduce the intake of SFA by replacing with monounsaturated fatty acid (MUFA) or complex carbohydrates has been proposed by the World Health Organisation [7] and other regulatory parties [8,9] based on the impact of SFA on the lipid profile. Data on other clinically relevant metabolic risk biomarkers however is scarce, in particular in populations at high risk of developing cardiovascular disease. The replacement of SFA with carbohydrates has received much debate as increased refined carbohydrates rather than complex carbohydrates intake has been reported to be linked with impaired insulin sensitivity and inflammatory states [10–13].

In order to prevent the possible exposure to cardiovascular disease risk in centrally overweight individuals, who comprise 50% of the population in both Western and Asian countries, determining the best dietary macronutrient composition with least negative metabolic and vascular impact is critical. Therefore, we set out to investigate the effect of replacement of SFA with MUFA or refined carbohydrates on subclinical inflammation, the thrombogenic state, as well as lipid subfractions in centrally overweight subjects who are at risk of developing cardiovascular disease.

2. Materials and methods

2.1. Subjects

The study was approved by the Medical Ethics Committee of University Malaya Medical Centre, Kuala Lumpur, Malaysia (reference no.: 871.5) and registered at ClinicalTrial.gov (Identifier: NCT01665482). Of 54 abdominally overweight subjects recruited, 47 completed the study. Abdominally obese males and females (waist circumference >90 cm for male, >80 cm for female), age 20–60 y were included. Subjects with a medical history of cardiovascular disease, diabetes, dyslipidemia; current use of antihypertensive or lipid lowering medication; plasma cholesterol >6.5 mmol/L, triacylglycerol [14] >4.5 mmol/L; alcohol intake exceeding a moderate intake (>28 units per week); pregnancy, smoker and breastfeeding were excluded.

2.2. Study design

This was a prospective cross-over design, single-blind trial comparing isocaloric 2000 kcal/day MUFA or CARB-enriched diet with SFA-enriched diet (control). The control SFA-enriched diet consisted of 15E% protein, 53E% CARB and 32E% fat (12E% SFA, 13E% MUFA). A total of ~7E% of MUFA or CARB was exchanged with SFA in the MUFA-rich and CARB-rich diets respectively for 6-weeks. Subjects were blinded and randomly allocated to 3 consecutive 6-week dietary treatments using an orthogonal allocation process (ABC, BCA, CAB) using Excel software. At any timepoint, each treatment was allocated 18 subjects with equal gender distribution. Blood samples were collected at baseline (prior to the commencement of study intervention), week 5 and 6. A postprandial mixed meal challenge was conducted at week 6 of each dietary treatment where hourly blood samples collection was done after test meal consumption. Radial pulse wave analysis was measured at baseline and week-6 of each intervention (before meal and 4 h after meal during mixed meal challenge). Fasting plasma IL-6 was the primary outcome of the present study. Secondary outcomes were interleukin-1β (IL-1β), CRP, E-selectin, PAI-1, D-dimer, lipid subfractions and radial pulse wave analyses. The study design is reported in Fig. 1.

2.3. Recruitment methodology

The study intervention was carried out between March and July 2012 at the research institute of Malaysian Palm Oil Board (MPOB). Subjects were recruited via advertisement using posters, internal mail circulation and phone call. Subjects were briefed and provided with a study information brochure. The interested subjects were initially interviewed via a questionnaire over the telephone. Those who met the initial inclusion criteria were invited for a health screening session including medical examination and biochemical profile (glucose, full blood count, lipid profile, kidney and liver function tests). The subjects signed informed consent and provided a 3-day dietary record for the assessment of habitual calorie intake.

2.4. Experimental diets

Habitual dietary intake requirement prior to enrolment was estimated from a 3-day weighed food record using Nutritionist-Pro™ (AXXYA Systems LLC., Stafford, TX, USA). As summarized in Table 1, the experimental diets provided 2000 kcal/day with 55E% carbohydrates, and 32E% fat for both MUFA and SFA diets; a 7E% exchange with fat (in the form of SFA) was applied for CARB diet resulting in a higher carbohydrate and lower fat content compared with the other 2 diets (62E% carbohydrates, 25E% fat). Protein content was standardized across diets at 15E%. Test fats were palm olein IV56 (purchased from MOI Food Malaysia Sdn. Bhd., Malaysia) blended with sunflower oil (purchased from Sunlico®, Yee Lee Edible Oils, Malaysia) for SFA diet, high oleic sunflower oil (purchased from Neuvida®, Yee Lee Edible Oils, Malaysia) blended with sunflower oil for MUFA and CARB diets. 45 g test fat was incorporated into cooking for both SFA and MUFA diets; whereas 34 g fat was incorporated into CARB diet. The sugar sources for CARB diet

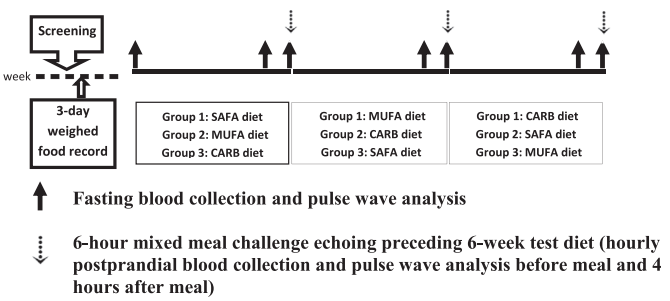

Fig. 1. Study design.

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