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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S U M M A R Y

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 15% protein, 53% carbohydrate and 32% fat (12% SFA, 13% 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 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 SFA 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 HDL3 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.

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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...
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 revascularization, the thrombogenic state, as well as lipid subfractions in centrally overweight subjects 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, tricylglycerol [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 15% protein, 53% CARB and 32% fat (12% SFA, 13% MUFA). A total of ~7% 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 55% carbohydrates, and 32% fat for both MUFA and SFA diets; a 7% 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 (62% carbohydrates, 25% fat). Protein content was standardized across diets at 15%. 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 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...
were rose syrup, honey and barley drinks which provided 40, 40, 40, and 40 kcal respectively (mean glycemic index 35.5, glycemic load 216). All other food components were identical between diets: breakfast consisting of a serving of refined carbohydrate (fried rice or fried noodles) plus 1 carbohydrate snack, a serving of fruit and a 21.6 g fat meal. The CARB meal utilized 61.6 g carbohydrates and 20 g test fat. The CARB meal utilized 61.6 g carbohydrates and 20 g test fat. The CARB meal utilized 61.6 g carbohydrates and 20 g test fat.

were rose syrup, honey and barley drinks which provided 40, 40, 40, and 40 kcal respectively (mean glycemic index 35.5, glycemic load 216). All other food components were identical between diets: breakfast consisting of 1 serving of refined carbohydrate (fried rice or fried noodles) plus 1 carbohydrate snack, a serving of fruit and a serving of drink; lunch and dinner: a serving of protein source (fish, meat or chicken), 1 serving of carbohydrate-rich foods (rice, noodles, or spaghetti), 1 serving of vegetables and fruits for each meal. Cholesterol intake was limited to <200 mg/day by restricting egg and seafood intake, and only providing lean meat without skin. Subjects were provided three 5-day cycle menus with breakfast and lunch served at the dining hall of research institute, and dinner was packed home. Additional energy requirement was adjusted using snacks coded to blind the subjects (cupcake with 3 flavors-vanilla, orange and strawberry, and pancakes) containing ~156 kcal with matching nutrient proportion with the background diet. Amount of test fats needed was calculated for everyday cooking and provided to the subjects. Subjects were provided guidelines to prepare meals at home using test cooking oils during weekends and holidays.

2.5. Mixed meal composition

The mixed meal consisted of 1 cupcake or pancake with 3 flavors (vanilla, orange and strawberry) containing ~156 kcal with matching nutrient proportion with the background diet. The subjects were provided guidelines to prepare meals at home using test cooking oils during weekends and holidays.

2.6. Mixed meal challenge procedure

On the last day of each 6-week intervention, subjects were provided a low fat chicken-flavored instant cup porridge meal (providing 180 kcal with 1 g fat) for dinner and required to fast after 22:00. The subjects were asked to refrain from strenuous exercise, caffeine and alcohol intake a day before the mixed meal challenge day. On arrival at the center on the morning of the study, subjects filled up a questionnaire to assess activity and food intake a day before the subject’s blood pressure and radial pulse wave analyses were measured using Sphygmocor System (AtCor Medical, Australia). A venous cannula was inserted into the antecubital vein of the forearm to facilitate multiple blood samples. The subject was then served with challenge test meal to consume within 10 min. Subsequent blood samples were collected at 15 min, 30 min, and hourly intervals till 6 h. At 4-h, subject’s blood pressure and radial pulse wave analyses were measured again by the same technician. At the end of 6 h, subjects were provided lunch to consume.

2.7. Compliance measures

The attendance and meal intake were closely monitored by a nutritionist. Subjects found skipping meals were monitored closely and those found to miss over 10% of the meals over the course of each 6-week intervention period were considered drop-outs. No subjects were requested to quit the study due to noncompliance based on these criteria. Body weight was monitored bi-weekly and subjects with body weight fluctuations more than 2 kg were advised to adjust calorie intake. Total plasma fatty acid and erythrocyte membrane phospholipid fatty acid composition were analyzed at week 6 of each diet-treatment to monitor subject compliance.

2.8. Fasting blood sample collection

Fasting blood samples were collected at baseline, week 5 and 6 of each dietary treatment. Serum samples for the analyses of triacylglycerol, CRP and lipid profile were collected into tubes siliconized with clot activator. EDTA K3 tubes (1–2 m/1 mL of blood) were used for plasma cytokines and citrated tubes (3.2% or 0.109 mol/l sodium citrate) for thrombogenic markers. All samples were centrifuged at 1529 ± g for 15 min and stored at −80 °C until analysis. Packed erythrocytes (after plasma removal) were stored at 4 °C and analyzed within 5 days.

2.9. Laboratory analyses

IL-6, IL-1β, and E-selectin were analyzed using Quantikine HS® colorimetric sandwich ELISA (R&D System, USA). The interassay values were 6.4, 10.8, 5.8% respectively, n = 22. PAI-1 was analyzed using IMMUBIND® plasma PAI-1 ELISA kit (Sekisui Diagnostics, USA) with interassay values at 7.2%, n = 22. Plasma D-dimer was assayed by IMUCONE™ D-dimer ELISA kit (Sekisui Diagnostics, USA) (interassay CV% = 3.3%, n = 22). Lipid profile and CRP assay were analyzed by an accredited clinical laboratory (Pathlab & Clinical Laboratory Sdn. Bhd., Malaysia) using ADVIA 2400 Chemistry (Siemens Healthcare Diagnostics Inc., USA). The interassay CV% for total cholesterol, triacylglycerol, apo A-1, apo B-100 and CRP assays were 1.5% (n = 2), 2.6% (n = 2), 1.1% (n = 2), 0% (n = 2) and 1.7% (n = 2) respectively (Siemens Healthcare Diagnostics Products Inc., USA). LDL cholesterol was calculated using Friedewald’s equation. Radial
pulse wave analyses were analyzed by SphygmoCor System (AtCor Medical, Australia) by the same technician with intraassay CV at 3.8% (n = 47).

2.1. Statistics

A sample size of 48 subjects was calculated to have 80% power to detect a difference of 0.5 SD unit change of IL-6 at P = 0.01. SPSS version 18 (SPSS Inc, Chicago, IL) and GraphPad Prism software version 5.02 (Graph Pad Software, Inc., La Jolla, CA, USA) were used for statistical analyses. Data distribution normality was determined and logarithmic transformation conducted for data not normally distributed. Fasting concentrations were tested at week 5 and 6 for any time trends. No time trend was detected and data were averaged and presented as mean/geometric mean ± SEM for fasting measurements or mean/geometric mean (95% CI) for postprandial measurements. Fasting data were analyzed by repeated measure ANOVA; whereas postprandial data were analyzed by one way repeated measure ANOVA, with time and meal as within subject factors and gender as between subject variables. Bonferroni post-hoc test was conducted for comparison between treatments. Incremental area under the curve (iAUC) was calculated for all postprandial data.

3. Results

The characteristics of 47 subjects (35 women, 12 men) who completed the 3 x 6-week dietary intervention are presented in Table 2. 54 subjects fulfilling all inclusion criteria were randomized into three groups: 5 subjects dropped out during the first intervention (2 were unable to commit, 1 had health problems, 2 became pregnant) and 2 dropped out during second intervention (1 health problems, 1 pregnant). 47 subjects completed fasting blood collection and all 3 dietary interventions, 1 subject refused to participate in the postprandial mixed meal challenge and 46 subjects (34 women, 12 men) completed all 3 postprandial mixed meal challenges.

3.1. Compliance

Extra energy intake from daily snacks was not significantly different between diet groups (Table 1). Full meal intake was achieved in 97.1 ± 4.4%, 98.0 ± 3.2% and 97.1 ± 5.1% of subjects for SFA, CARB and MUFA diets respectively. The meal appreciation and palatability assessed by VAS (ranging from 0 to 10) were 7.0 ± 1.2, 7.1 ± 1.3, 6.9 ± 1.4 and 7.2 ± 1.3, 7.3 ± 1.3, 7.1 ± 1.4 for SFA, CARB and MUFA diets respectively. Body weight was constant across interventions at weight 73.8 ± 14.4 kg, 73.9 ± 14.6 kg and 73.9 ± 14.3 kg, respectively for SFA, CARB and MUFA diets. Total plasma fatty acid and erythrocyte membrane phospholipid fatty acid composition reflected dietary intake indicating good compliance. Palmitic acid content was higher (P < 0.05) after SFA diet (26.8 ± 2.3%) compared with CARB (26.3 ± 1.8%) and MUFA diets (26.0 ± 2.0%). Overall subject compliance was good.

3.2. Fasting metabolic risk markers

Table 3 summarizes fasting measurements for inflammatory and thrombogenic markers. The primary outcome, fasting plasma IL-6 levels were similar after exposure to 6 weeks of SFA, CARB and MUFA diets respectively. Neither were there significant differences in fasting plasma IL-1β, CRP, E-selectin, PAI-1 and D-dimer between the 3 diets after 6 weeks of exposure.

The results of fasting lipids after each dietary intervention are profiled in Table 4. As expected, MUFA diet resulted in a slightly lower total cholesterol level and LDL cholesterol level compared with SFA diet (P < 0.05). CARB diet was associated with lower HDL cholesterol level compared with SFA diet (P < 0.05). No difference was observed between diets in total: HDL cholesterol ratio, VLDL cholesterol, apo A-1, apo B-100, lp(a) and TAG levels. Interestingly, CARB diet resulted in lower HDL3 subfraction and higher small dense HDL (sdHDL) subfraction compared with SFA diet (P < 0.05). SFA diet increased large HDL subfractions compared with both CARB and MUFA diets (P < 0.05), respectively.

3.3. Postprandial metabolic responses

The postprandial response of plasma cytokines and thrombogenic markers over 6 h to the mixed meal challenge with macronutrient composition echoing the 3 background diets are shown in Fig. 2, graphs A-F. With all 3 background diets, IL-6 rose after the postprandial challenge. Repeated measure ANOVA did not show significant differences between diets in plasma IL-6 at individual time-points over 6 h (time effect: P = 0.000, meal × time interaction: P = 0.245). However iAUC0–6 h IL-6 was 66% higher after CARB challenge compared with SFA challenge (P < 0.05). Time (P = 0.020) but not meal × time interaction (P = 0.077) was observed for plasma IL-1β over 6 h. Plasma IL-1β was found to fall below baseline at 2 h with all 3 meals. Repeated measure ANOVA for E-selectin showed significant meal × time interaction (P = 0.035) and a borderline significant value for iAUC between the 3 challenge meals (P = 0.051). There was a time trend effect (P = 0.000) where PAI-1 levels were reduced 4 h after all 3 challenge meals but no

Table 2. Characteristics of study subjects.

<table>
<thead>
<tr>
<th>Physical characteristics</th>
<th>All (n = 47)</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>32.8 ± 8.7</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female (n)</td>
<td>35</td>
</tr>
<tr>
<td>Male (n)</td>
<td>12</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.594 ± 0.78</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74.2 ± 14.6</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.7 ± 4.1</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>94.8 ± 10.2</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>36.6 ± 7.9</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>124.5 ± 12.4</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>81.8 ± 10.7</td>
</tr>
<tr>
<td>Aortic augmentation pressure (mmHg)</td>
<td>6.1 ± 4.9</td>
</tr>
<tr>
<td>Aortic augmentation index (%)</td>
<td>18.7 ± 12.8</td>
</tr>
</tbody>
</table>

Table 3. Characteristics of fasting measurements for inflammatory and thrombogenic markers.

| Biochemical profile | | |
|---------------------|-------------|
| Serum total cholesterol (mmol/L) | 5.0 ± 0.8 |
| Serum HDL cholesterol (mmol/L) | 1.3 ± 0.3 |
| Serum LDL cholesterol (mmol/L) | 3.1 ± 0.7 |
| Serum triacylglycerol (mmol/L) | 1.2 ± 0.7 |
| Total: HDL cholesterol | 4.0 ± 0.8 |
| Plasma glucose (mmol/L) | 5.8 ± 0.8 |
| Plasma IL-6 (pg/ml) | 1.4 ± 0.8 |
| Plasma IL-1β (pg/ml) | 0.2 ± 0.1 |
| Plasma CRP (mg/L) | 3.7 ± 4.3 |
| Plasma E-selectin (ng/mL) | 36.3 ± 13.5 |
| Plasma PAI-1 (ng/ml) | 63.2 ± 31.3 |
| Plasma D-dimer (ng/ml) | 254.0 ± 137.6 |

Table 4. Characteristics of dietary intake.

| Dietary intake | | |
|----------------|-------------|
| Energy (kcal/day) | 2051.8 ± 545.3 |
| Protein (%) | 16.3 ± 2.8 |
| Carbohydrate (%) | 57.3 ± 7.2 |
| Fat (%) | 26.9 ± 6.2 |

Abbreviations: BP, blood pressure; IL-6, interleukin-6; IL-1β, interleukin-1β; CRP, C-reactive protein; PAI-1, plasminogen activator inhibitor-1.

* Means or geometric means ± SD.
* Ethnicity: Malay n = 47.
* Determined from 3-day weighed diet record using Nutritionist Pro™ software (AXXYA Systems LLC, Texas, USA).
3.4. Pulse wave analysis

Augmentation index (%) and augmentation pressure as indicators of arterial stiffness were not affected by the three diets at fasting state. The markers were also measured at fasting and at 4 h during mixed meal challenge, there was time trend effect (P = 0.000) where the index was decreased after all meals at 4 h (Fig. 2, graphs G & H).

4. Discussion

The present study was designed to investigate the effect of 7E% replacement of SFA with refined CARB or MUFA on cardiovascular-related metabolic risk markers including inflammatory and thrombogenic parameters, and the lipid profile. The primary outcome, fasting plasma IL-6 was not altered by 6 weeks exposure to the three isocaloric diets: SFA (55% carbohydrate, 32% fat - 12% SFA, 13% MUFA), CARB (61% carbohydrate, 25% fat - 5% SFA, 14% MUFA) or MUFA (55% carbohydrate, 33% fat – 5% SFA, 20% MUFA). Neither was there any substantial impact of dietary modification on other cytokines (IL-1β, IL-6, E-selectin, PAI-1, plasminogen activator inhibitor-1).

Elevated fibrinogen and CRP were observed over 6 h after all treatments (P < 0.05). Plasma fibrinogen (mg/dL) for all three groups were significantly different with SFA being highest (3.42), followed by MUFA (2.92) and CARB (2.68) diets. CRP (mg/mL) was also highest for SFA (3.71), followed by CARB (3.60) and MUFA (3.53) diets. The overall diet-related changes in fibrinogen and CRP were not statistically significant.

The present study demonstrates that replacing SFA with either CARB or MUFA for 6-week in healthy men and women resulted in significant improvements to inflammatory and thrombogenic markers (PAI-1 and D-dimer), arterial stiffness (augmentation index), and carotid artery intima-media thickness. These findings provide evidence for the potential of these dietary modifications to improve cardiovascular health in a population with normal body mass index and waist circumference.
of subjects who are vulnerable to disease progression. In agreement with our findings, Lithander et al. [18] reported that fasting CRP, IL-6 and TNF-α did not differ between a high SFA or low SFA diet differing by 5% fat after a 3-week crossover trial in mildly hyperlipidemic Caucasian subjects. A large scale study in a Caucasian cohort of subjects at risk of developing metabolic syndrome also found that altering the composition of SFA, MUFA coupled with high or low glycemic index diet for a duration of six months did not alter CRP, sICAMs, PAI-1 [19]. In contrast with the aforementioned findings, a study in healthy subjects reported that an oleic acid (MUFA) enriched diet reduced both CRP and IL-6 levels when compared with trans fatty acids after a 4-week dietary intervention [6]. Casas et al. [20] reported that Mediterranean diet supplemented with both nuts and extra virgin olive oil (a rich source of MUFA) were found to lower plasma IL-6, CRP, sICAMs and P-selectin compared with a low fat diet after a 1 y long term dietary intervention in subjects at risk of developing cardiovascular diseases. The study suggested that the nutrients in the Mediterranean diet

![Fig. 2. Postprandial interleukin-6 (IL-6) (A), interleukin-1β (IL-1β) (B), C-reactive protein (CRP) (C), E-selectin (D), plasminogen activator inhibitor-1 (PAI-1) (E), D-dimer (F), augmentation index (G), augmentation pressure (H) and triglyceride (I) following mixed meal rich in saturated fatty acid (SFA), carbohydrate (CARB) or monounsaturated fatty acid (MUFA) at the end of each 3 × 6-week dietary intervention. Data are means (B and H) or geometric means (A, C–G and I) with 95% CI, n = 46 (34 women, 12 men). White circle, solid line = SFA; white triangle, solid line = CARB; white square, dotted line = MUFA. Repeated measures ANOVA of values from preprandial value (3 meals, 3 time points for A–F, 1 time point for G–H, 6 time points for I) with gender as a between subject factor: meal × time interaction: (A–C, E–H) P > 0.05, (D, I) P < 0.05; meal × time × gender interaction: (A–I) P > 0.05. *Significant differences in changes from preprandial value between CARB vs SFA and MUFA (I). Insert: Incremental areas under the curve (iAUC) over 6 h (A–F and I) or 4 h (I). Data are geometric means with 95% CI. White bars = SFA; black bars = CARB; striped bars = MUFA. *Significant difference in iAUC between SFA and CARB or MUFA, P < 0.05 (A, F and I).]

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Fig. 2. (continued).
and a long study duration (at 1 y) maybe needed for a pronounced impact of dietary modification on inflammatory biomarkers related to atherosclerosis. A study comparing the supplementation of n-3 PUFA (1100 mg), which is regarded as anti-inflammatory did not improve subclinical inflammation, weight loss of 9.4 kg however significantly bring down the levels of cytokines [21,22]. This has also been reviewed elsewhere [4].

A large scale long term study found that dietary fatty acids at 5% exchange between SFA, refined carbohydrates and MUFA did not exert significant impact on arterial stiffness and peripheral augmentation index in subjects at high risk of developing metabolic syndrome for a 6-mo intervention [23]. Observational studies report higher sHDL subfraction and lower large HDL subfractions in the patient groups with the diagnosis of coronary artery disease [24,25]. In addition, HDL3 may predict lower risk for subfractions in the patient groups with the diagnosis of coronary artery disease [26]. To our knowledge, no similar studies compared the effects of high-fat and high-carbohydrate diets on HDL subfractions after a 7-week diet intervention [26]. To our knowledge, no similar studies compared the effects of high-fat and high-carbohydrate diets on HDL subfractions after a 7-week diet intervention [26].

The influence of dietary modification on postprandial responses is however different. The present study reveals that replacement of SFA with refined CARB in a mixed meal after a similar background diet for 6 weeks elevated postprandial iAUC0

Statement of authorship

KTT: designed the research protocol; conducted the research and statistical analysis; prepared the manuscript and had primary responsibility for final content. LFC: contributed to the planning and management of study, laboratory and data analyses; conducted the research and contributed to manuscript writing. SRV: designed the study and contributed to the manuscript writing. KN, TABS: contributed to the critical revision of the manuscript.

Conflict of interest

KTT and KN are employees of the MPoB. LFC was the recipient of Graduate Student Assistantship Scheme (GSAS) scholarship from
MPOB. TABS is a member of the Programme Advisory Committee of the MPOB. SRV declares no conflict of interest.

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**Appendix A. Supplementary data**

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.clnu.2016.08.026.

**References**


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