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Greater impairment of postprandial triacylglycerol than glucose response in metabolic syndrome subjects with fasting hyperglycaemia

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ABSTRACT

Objective. Studies have started to question whether a specific component or combinations of metabolic syndrome (MetS) components may be more important in relation to cardiovascular disease risk. Our aim was to examine the impact of the presence of raised fasting glucose as a MetS component on postprandial lipaemia.

Methods. Men classified with the MetS underwent a sequential test meal investigation, in which blood samples were taken at regular intervals after a test breakfast (t = 0 min) and lunch (t = 330 min). Lipids, glucose and insulin were measured in the fasting and postprandial samples.

Results. MetS subjects with 3 or 4 components were subdivided into those without (n = 34) and with (n = 23) fasting hyperglycaemia (≥5.6 mmol/l), irrespective of the combination of components. Fasting lipids and insulin were similar in the two groups, with glucose significantly higher in the men with glucose as a MetS component ($P < 0.001$). Following the test meals, there were higher maximum concentration (maxC), area under the curve (AUC) and incremental AUC ($P \leq 0.016$) for the postprandial triacylglycerol (TAG) response in men with fasting hyperglycaemia. Greater glucose AUC ($P < 0.001$) and insulin maxC ($P = 0.010$) were also observed in these individuals after the test meals. Multiple regression analysis revealed fasting glucose to be an important predictor of the postprandial TAG and glucose response.

Conclusion. Our data analysis has revealed a greater impairment of postprandial TAG than glucose response in MetS subjects with raised fasting glucose. The worsening of postprandial lipaemic control may contribute to the greater CVD risk reported in individuals with MetS component combinations which include hyperglycaemia.

Abbreviations: AUC, area under the curve; BMI, body mass index; CVD, cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; IAUC, incremental AUC; maxC, maximum concentration; MetS, metabolic syndrome; minC, minimum concentration; LDL-C, low-density lipoprotein cholesterol; NEFA, non-esterified fatty acids; TAG, triacylglycerol; TRL, TAG-rich lipoprotein.

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1. Introduction

Coupled with the increasing prevalence of overweight and obesity, 20%–25% of adults are now classified with the metabolic syndrome (MetS) which is associated with an increased risk of cardiovascular disease (CVD) and type II diabetes. Studies have started to question whether a specific component or combinations of MetS components are associated with a greater relative risk of CVD than presenting with the syndrome *per se* [1–6]. Three- and four-component combinations highly associated with all cause mortality and cardiovascular events include both abdominal obesity and hyperglycaemia, with the addition of either elevated triacylglycerol (TAG) or blood pressure [2,5]. Pigna and co-workers [7] reported elevated TAG and glucose to be independent predictors of the presence of atherosclerotic plaques. These findings indicate that fasting hyperglycaemia may be an important MetS component in relation to CVD risk.

Dysregulation of TAG in the postprandial state has been associated with insulin resistance, and increasingly recognised as an independent CVD risk factor [8]. Using the DISRUPT database, we have shown a linear trend between the possession of increasing numbers of MetS components and the magnitude of the postprandial TAG and glucose responses [9], with an overall worsening of postprandial lipaemic control in men with 3 and 4/5 components. In the present study, we examined the impact of fasting hyperglycaemia as a MetS component on postprandial TAG, non-esterified fatty acids (NEFA), glucose and insulin responses in men classified with the MetS.

2. Methods

The men included in this DISRUPT dataset (n = 57) were from sequential meal postprandial studies conducted using the same test meal protocol at the University of Reading between 1997 and 2007. Briefly, these men were non-smokers, free of CVD and diabetes and were not taking medication known to modify blood lipids or blood pressure [10]. The studies were given a favourable opinion for conduct by the University of Reading Research Ethics Committee and the West Berkshire Health Authority Ethics Committee, and written informed consent was obtained before the studies began.

Subjects were asked to abstain from alcohol and organized exercise regimens on the day prior to the postprandial investigation, and provided with a low-fat evening meal (<10 g fat). After an overnight fast, subjects consumed a standard test breakfast (4.2 MJ energy, 51 g fat, 125 g carbohydrate and 19 g protein) and lunch (2.6 MJ energy, 30 g fat, 79 g carbohydrate and 15 g protein) at 0 and 330 min respectively, with blood samples taken before and at regular intervals until 480 min after the breakfast. No other food or drink except for water and decaffeinated, sugar-free drinks was allowed during the study day.

Fasted high-density lipoprotein cholesterol (HDL-C) was determined in the supernatant following precipitation with dextran-manganese chloride reagent and low-density lipoprotein cholesterol (LDL-C) was estimated using the Friedewald formula. Plasma lipids and glucose were analysed with an automated analyser (Instrumentation Laboratory (UK) Ltd) using kits supplied by Instrumentation Laboratory and Alpha Laboratories (UK). Insulin was measured by ELISA (Dako, UK). The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using fasting glucose and insulin concentrations [11].

Classification of the MetS was defined retrospectively using the National Cholesterol Education Program Adult Treatment Panel III and International Diabetes Federation definitions [12,13]. As previously described, body mass index (BMI) was used as a substitute for waist circumference [9]. The five MetS components therefore included BMI $\geq$ 25.7 kg/m^2, fasting glucose $\geq$ 5.6 mmol/l, TAG $\geq$ 1.7 mmol/l, HDL-C < 1.03 mmol/l and hypertension (systolic blood pressure $\geq$ 130 mmHg or diastolic blood pressure $\geq$ 90 mmHg).

Data were analysed using SAS Software, version 9.1.3 (SAS, N.C., USA). Results are presented in the table as mean values ± SD and in the figure as mean values ± SEM. Summary measures of the postprandial response include area under the curve (AUC), incremental AUC (IAUC) and maximum concentration (maxC). For the NEFA response, minimum concentration (minC) was also calculated. An Independent Samples t-test determined differences in baseline characteristics and postprandial summary measures between those with and without raised glucose as a MetS component. Multiple regression analysis was used to determine the independent associations between the MetS components (BMI, blood pressure, fasting TAG, HDL-C and glucose) and the summary measures of the postprandial TAG, glucose and NEFA responses. Partial R^2 values were calculated to determine the percentages of variation in summary measures explained by the MetS components. $P \leq 0.05$ was taken as significant.

3. Results

Table 1 summarises baseline characteristics and postprandial summary measures in the group as a whole and according to the presence or absence of glucose as a MetS component. Age, BMI, blood pressure and fasting lipids were not different between the groups with and without fasting hyperglycaemia. By definition, glucose concentrations were significantly higher in men with glucose as a MetS component ($P < 0.001$), but insulin and HOMA-IR were not different between the two groups.

Although fasting TAG concentrations were not significantly different, a greater postprandial TAG response was evident in men with fasting hyperglycaemia, which was reflected in the significantly greater maxC (31%), AUC (26%) and IAUC (44%) (Fig. 1A and Table 1). There was a biphasic pattern in the glucose response after the meals, with glucose concentrations falling below baseline levels before ingestion of the second meal (Fig. 1B). Men with glucose as a MetS component had a significantly greater AUC (8%) for the glucose response, but the IAUC was similar in the two groups (Table 1). Differences were not apparent between groups for the NEFA response.