Men at Increased Risk of Coronary Heart Disease Are Not Different From Age- and Weight-Matched Healthy Controls in Their Postprandial Triglyceride, Nonesterified Fatty Acid, or Incretin Responses to Sucrose

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Short-term studies suggest that extreme sucrose consumption has a detrimental effect on triglycerides (TG) in hypertriglyceridemic people. There is currently no consensus on the short-term inclusion of a moderate intake of sucrose in middle-aged men at increased risk of coronary heart disease (CHD). It is also unknown whether gut hormones that are released in response to carbohydrate ingestion modulate any of the effects of sucrose. The aim of this study was to further elucidate whether men at increased risk of CHD have an exaggerated response to sucrose compared with age- and weight-matched controls over an acute postprandial period. Twenty middle-aged men were recruited and separated into control (total cholesterol < 5.5mmol/L) and increased risk of CHD (> 5.5mmol/L) groups. We measured postprandial TG, nonesterified fatty acids (NEFA), insulin, glucose, glucagon-like peptide-1 (GLP-1), and gastric inhibitory polypeptide (GIP) concentrations in response to a meal containing 75 g glucose or 75 g sucrose with a moderate fat load. The increased risk group had significantly higher Framingham risk assessment (12% *v* 4%), TG (2.4 ± 1.5 *v* 1.1 ± 0.4 mmol/L), low-density lipoprotein-cholesterol (LDL-C) (4.4 ± 0.5 *v* 2.7 ± 0.4 mmol/L), and lower high-density lipoprotein-cholesterol (HDL-C) (1.2 ± 0.2 *v* 1.5 ± 0.2 mmol/L) (*P* < .05 for all). There was no significant difference in the incremental area under the curve (IAUC, 0 to 360 minutes) for TG, NEFA, glucose, GLP-1, or GIP in response to glucose or sucrose within or between the groups. Absolute total area under the curve (not IAUC) for TG was significantly higher in the increased risk group for both glucose and sucrose, respectively (*P* = .01). A total of 75 g of sucrose given as part of a single meal appears to make little difference in the postprandial TG and NEFA response in men with or without risk of CHD compared with glucose. Although long-term data is needed, this begs the question whether a moderate intake of sucrose has been overemphasized as a detrimental dietary message in middle-aged men.

SOME EVIDENCE SUGGESTS that diets containing atypically large intakes of sucrose increase fasting triglycerides (TG) and exaggerate postprandial lipemia.[1,2] Reduction of refined carbohydrate, particularly sucrose, is traditionally a cornerstone of the dietetic management of hypertriglyceridemia. This is thought to be due to the fructose moiety of sucrose causing increased fatty acid synthesis in the liver, increasing very–low-density lipoprotein (VLDL) synthesis, and possibly decreasing VLDL catabolism.[1] It is also postulated that certain groups of subjects, such as the elderly, sedentary subjects, those with established coronary artery disease,[3,4] males,[5] type 2 diabetes,[6] or hyperinsulinemic subjects[5,7] may be more sensitive than others to very high intakes of sucrose and fructose.

The incretin glucagon-like peptide-1 [7-36] amide (GLP-1) is the most potent known endogenous gut hormone stimulant of insulin secretion in man.[8] In addition to its insulin-stimulating effects, GLP-1 also suppresses glucagon secretion, delays gastric emptying, and is postulated to increase peripheral insulin sensitivity.[9-11]. It is thus being investigated as a new treatment for type 2 diabetes.[12] There is recent evidence that blocking endogenous GLP-1 with exendin 9-39, the specific antagonist, causes deterioration in glycemic control.[13]

It has been suggested that nonesterified fatty acids (NEFA) regulate postprandial GLP-1 secretion, for example, obese subjects with high fasting NEFA have low fasting GLP-1 concentrations.[14,15] This is interesting, because over 30 years ago, Randle[16] suggested that elevated NEFA concentrations competitively inhibit glucose oxidation and lead to impaired glucose tolerance. Ranganath et al[17] went on to demonstrate that manipulation of NEFA concentrations did influence GLP-1 concentrations, which could therefore be responsible for the insulin resistance seen in circumstances of high NEFAs.

Gastric inhibitory polypeptide (GIP) is another incretin gut hormone released in response to carbohydrate that stimulates insulin secretion.[8] Although controversial, Gama et al[18] has suggested that GIP may have a role in the pathogenesis of the hypertriglyceridemia observed in hyperinsulinemic hypertriglyceridemic subjects.

One group that is vulnerable to coronary heart disease (CHD) is middle-aged men with 1 or more cardiac risk factors. In the clinical setting, most initial screening for CHD focuses on traditional risk factors, such as the nonfasting measurement of plasma cholesterol or body weight. This group forms over 50% of the Western world middle-aged male population. There is conflicting evidence as to the effect a moderate sucrose consumption has on cardiac risk factors in this group.

Here we investigated if men at increased risk of CHD, initially isolated by fasting cholesterol concentrations, had an exaggerated postprandial TG and NEFA response to sucrose compared with glucose and to age- and weight-matched controls. We also tested for possible differences in GLP-1 and GIP responses to account for any shift in postprandial TG and NEFA.

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Submitted April 2, 2001; accepted July 12, 2001.

Supported by the Sugar Bureau, London, UK. C.M.E. is a Diabetes UK R.D. Lawrence Research Fellow.

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0026-0495/02/5102-0035$35.00/0
doi:10.1053/meta.2002.29029

Table 1. Demographic Details of Men at Increased Risk of CHD and Matched Controls

	Cholesterol* (mmol/L)		Age (yr)		BMI (kg/m^2)		Waist (cm)		HDL (mmol/L)		TG (mmol/L)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Control (n = 10)	4.6 (3.4-5.5)	0.5	47.3 (41-58)	6.4	26.6 (22.2-30.4)	3.2	88 (79-102)	8	1.5 (1.03-1.77)	0.2	1.12 (0.47-1.93)	0.4
At risk (n = 10)	6.6 (5.7-7.7)	0.7	51.3 (41-59)	5.1	27.4 (22.6-32.7)	2.8	100 (92-108)	9.2	1.2 (0.73-1.66)	0.2	2.4 (0.89-5.88)	1.5
P value			.14		.60		.01		.03		.02	

NOTE. Range (in parentheses).

*Groups formed on the basis of fasting cholesterol level, which was measured along with TG and HDL in hospital laboratory.

MATERIALS AND METHODS

Subjects

Twenty male volunteers were recruited using posters displayed in local general practice clinics and around the hospital. Imperial College School of Medicine Hammersmith campus Research and Ethics Committee granted ethical approval. All volunteers gave written consent. Exclusion criteria included a history of diabetes, hypertension, or lipid-lowering medication. Initial screening included electrocardiogram (ECG), medical examination, and complete blood count.

The men were separated into a control group (fasting plasma cholesterol $<$ 5.5 mmol/L) (n = 10) and an increased risk CHD group (fasting plasma cholesterol $>$ 5.5 mmol/L) (n = 10). The increased risk group had a 3 times greater absolute CHD risk compared with the control group (12.2% ± 5.5% *v* 4.4% ± 3.5%; *P* = .002) (mean ± SD), calculated by the Framingham CHD risk assessment program.[19]

There was no difference in age (control 47.3 ± 6.4 *v* increased risk 51.3 ± 5.1 years), body mass index (BMI) (26.6 ± 3.2 *v* 27.4 ± 2.8 kg/m^2), blood pressure (control 116/70 ± 13/7 *v* increased risk 124/74 ± 15/9 mm Hg), or ethnic background between the groups (mean ± SD). The increased risk group had a higher waist circumference than the control group (Table 1). The increased risk group demonstrated significantly higher TG (2.4 ± 1.5 *v* 1.1 ± 0.4 mmol/L), low-density lipoprotein-cholesterol (LDL-C) (4.4 ± 0.5 *v* 2.7 ± 0.4 mmol/L), and lower high-density lipoprotein-cholesterol (HDL-C) (1.2 ± 0.2 *v* 1.5 ± 0.2 mmol/L) (*P* $<$ .05 for all by unpaired *t* tests) (Table 1). One subject in the increased risk group reported taking aspirin daily; no other medication was taken by any volunteer. There was no significant difference in family history for diabetes or heart disease between the groups.

The number of smokers, ex-smokers, and nonsmokers were identical in both groups. Alcohol intake did not differ significantly between groups (Table 2). All men were sedentary (as classified by dietary reference values (DRV), Section 2.3.[20] There were no significant macronutrient differences in habitual diet (recorded by 3-day diet diary) between the groups, and both were similar to the United Kingdom (UK) national averages (Table 2).

Study Design

Volunteers consumed 2 test meals in random order, separated by at least a week (mean 18 ± 14 days) (mean ± SD). In an attempt to control for fasting lipid concentrations, identical meals were provided on the evenings before the test meals, plus written information on the abstinence of exercise and alcohol for 24 hours before the tests. After an overnight fast, blood samples were taken from an indwelling antecubetal fossa venous cannula at -15, 0, 5, 15, 30, 45, 60, 90, 120, 150 minutes, 3, 4, 5, and 6 hours following the start of the meal.

Nutrient Composition of Test Meals

The test meals contained 38 g cornflakes, 200 mL decaffeinated coffee, 100 g double cream (which was diluted with 100 mL water to make a milk-like consistency) and either 75 g of glucose or 75 g of sucrose. They were otherwise matched for nutrient content (3,696 kJ/880 kcal, 48 g fat, of which 30 g was saturated, 115 g carbohydrate and 5 g protein). We chose 75 g of sucrose as a moderate intake because average daily consumption of sucrose in the UK was reported by the Ministry of Agriculture, Fisheries, and Food (MAFF) to be 102 g/person/d in 1987.[21]

Laboratory Analysis

An initial blood sample was sent to the hospital laboratory for measurement of total cholesterol, HDL-C, and TG (Table 1). All other blood samples were collected into lithium heparin tubes for the measurement of TG, NEFA, and glucose or lithium heparin tubes containing 4,000 kIU aprotinin (Trasylol; Bayer, Newbury, UK) for the measurement of insulin, GIP, and GLP-1. Samples were centrifuged immediately at 3,000 rpm for 10 minutes. The plasma was then aliquoted into plain plastic 2.5-mL tubes. These were immediately frozen and stored at –20°C until analysis. Plasma glucose concentrations were measured using a glucose-oxidase–based autoanalyzer (Technicon; Axon Bayer Diagnostic, Newbury, UK). GLP-1, GIP, and insulin concentrations were measured inhouse using specific radioimmunoassays.[8,22] The interassay and intra-assay coefficients of variation for these assays were less than 10%. The assays were capable of detecting 2 pmol/L with 95% confidence. All samples were included in 1 assay and analyzed in duplicate on the first freeze-thaw. TG concentrations were determined using the method of Humphreys wet al[23] with correction for free glycerol, adapted to an IL Monarch Clinical Chemistry Analyser (Instrumentation Laboratories, Warrington, UK). The plasma NEFA concentration was measured using a commercial kit (Wako

Table 2. Habitual Dietary Intake Recorded by 3-Day Diet Diary in Men at Increased Risk of CHD (n = 10) and Matched Controls (n = 10)

	Energy (MJ)		Protein (%E)		Fat (%E)		Carbohydrate (%E)		Alcohol (%E)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Control	9.6	1.8	15.9	3.4	39.1	4.6	43	8.7	2.1	3.3
At risk	11.3	3.6	15.9	3.3	38.1	6.7	42.8	6.6	3.2	3.7
P value	.2		.9		.7		.9		.5	

Abbreviation: (%E) percentage of total energy intake.

Table 3. Biochemical Response to a Mixed Meal Containing Either 75 g Sucrose or 75 g Glucose in Men at Increased Risk of CHD and Controls

	Sucrose				Glucose			
	Controls		At Risk		Controls		At Risk	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Fasting								
TG (mmol/L)	1.1	0.1	1.92	0.3	0.98	0.1	2.6	0.6*
NEFA (μmol/L)	409	55	606	48	478	94	566	64
Insulin (pmol/L)	88	10	118	21	86	12	123	15
Glucose (mmol/L)	4.3	0.1	5.4	0.4	4.6	0.2	5.5	0.6
GLP-1 (pmol/L)	26.2	4.6	25	1.6	25.9	3.4	24.2	1.8
GIP (pmol/L)	97	17	72	12	70	11†	89	13
IAUC 0 to 360 min								
TG (mmol/L/min)	178.1	43	161.9	24	126.5	45	111	37
NEFA (mmol/L/min)	−60	15	−116	16	−85	25	−109	20
Insulin (nmol/L/min)	37.3	4.9	64	12‡	39	4.6	61.5	6‡
Glucose (mmol/L/min)	237	50	132	81	227	117	343	74
GLP-1 (nmol/L/min)	5.1	0.5	3.9	0.9	4.1	0.7	4.8	0.9
GIP (nmol/L/min)	62	6	66.9	13	63.8	9	70.7	21

*P = .03 TG increased risk glucose *v* increased risk sucrose.
†P = .01 GIP control glucose *v* control sucrose.
‡P < .05 control *v* increased risk.

NEFA C kit; Alpha Laboratories, Eastleigh, Hampshire, UK) adapted for the IL Monarch Clinical Chemistry Analyser.

Statistics

Power analysis was based on a 15% difference in TG levels between the groups being of clinical relevance with a SD of 15% using a power of 85% and a probability level of 5%. The results are presented as mean ± SD (with range below) in Tables 1 and 2, and all other results are presented as mean ± SEM. Incremental area under the curve (IAUC) above baseline was calculated using the trapezoidal rule. A split unit analysis of variance for each variable with factors for group (controls or increased risk) and treatment (sucrose or glucose) was used.[24] The effect of group is assessed relative to the variability between subjects, while the effect of treatment and its interaction with group are assessed relative to the variation within subjects. The assumption of normality was checked using Shapiro and Francia's W test on the residuals. A log transformation was used for fasting TG and NEFA. P less than .05 was taken as significant.

RESULTS

The baseline increased risk group had significantly higher fasting TG (P = .008) and NEFA (P = .04) (Tables 3 and 4 (Fig 1D and E). There was a trend for fasting glucose (P = .07) and insulin (P = .07) to be elevated in the increased risk group (Tables3 and 4) (Fig 1B and A).

Homeostasis model assessment (HOMA, calculated using 2 fasting insulin and glucose values)[25] demonstrates no difference in β-cell function (%B increased risk 162 ± 69 *v* control 162 ± 40) and a 30% reduction in insulin sensitivity in the increased risk group compared with the control group (%S increased risk 50 ± 16 *v* 71 ± 29; P = .05).[26] The IAUC for insulin was higher in the increased risk group after both sucrose and glucose (P = .01). Taken together, this would suggest the increased risk group was more insulin resistant that the control group. There was no difference in fasting or IAUC for GLP-1 or GIP either between or within groups.

There was a tendency for the plasma glucose response to be lower after sucrose than after the glucose meal (IAUC, 0 to 360 minutes, 35% and 29% lower in the at risk group and the control group, respectively). However, this failed to reach significance over 360 minutes (P = .27) or 180 minutes (P = .07).

There were no significant difference in any of the parameters measured between the glucose and sucrose in the postprandial response (Table 3 and 4) (Fig 1). Despite a tendency for the plasma TG response to be higher after sucrose than after the glucose meal (IAUC, 0 to 360 minutes, 40% and 46% greater in the control and increased risk groups, respectively), this was not statistically significant.

The difference in postprandial TG response to sucrose or glucose does not become significant even if subjects are separated into groups depending on fasting TG (high or low) (control group sucrose 140.6 ± 35 *v* glucose 101.3 ± 39

Table 4. Summary of the *P* Values From the Tests of Assumptions by Split Unit Analysis of Variance

	Group	Treatment	Group × Treatment
Fasting			
TG (mmol/L)*	.008	.37	.02
NEFA (μmol/L)*	.04	.99	.38
Insulin (pmol/L)	.07	.89	.81
Glucose (mmol/L)	.07	.26	.75
GLP-1 (pmol/L)	.74	.69	.83
GIP (pmol/L)	.87	.49	.005
IAUC 0-360 mins			
TG (mmol/L/min)	.67	.22	.99
NEFA (mmol/L/min)	.1	.54	.29
Insulin (nmol/L/min)	.01	.94	.72
Glucose (mmol/L/min)	.96	.27	.2
GLP-1 (nmol/L/min)	.77	.95	.07
GIP (nmol/L/min)	.76	.62	.86

*Log transformed for analysis.

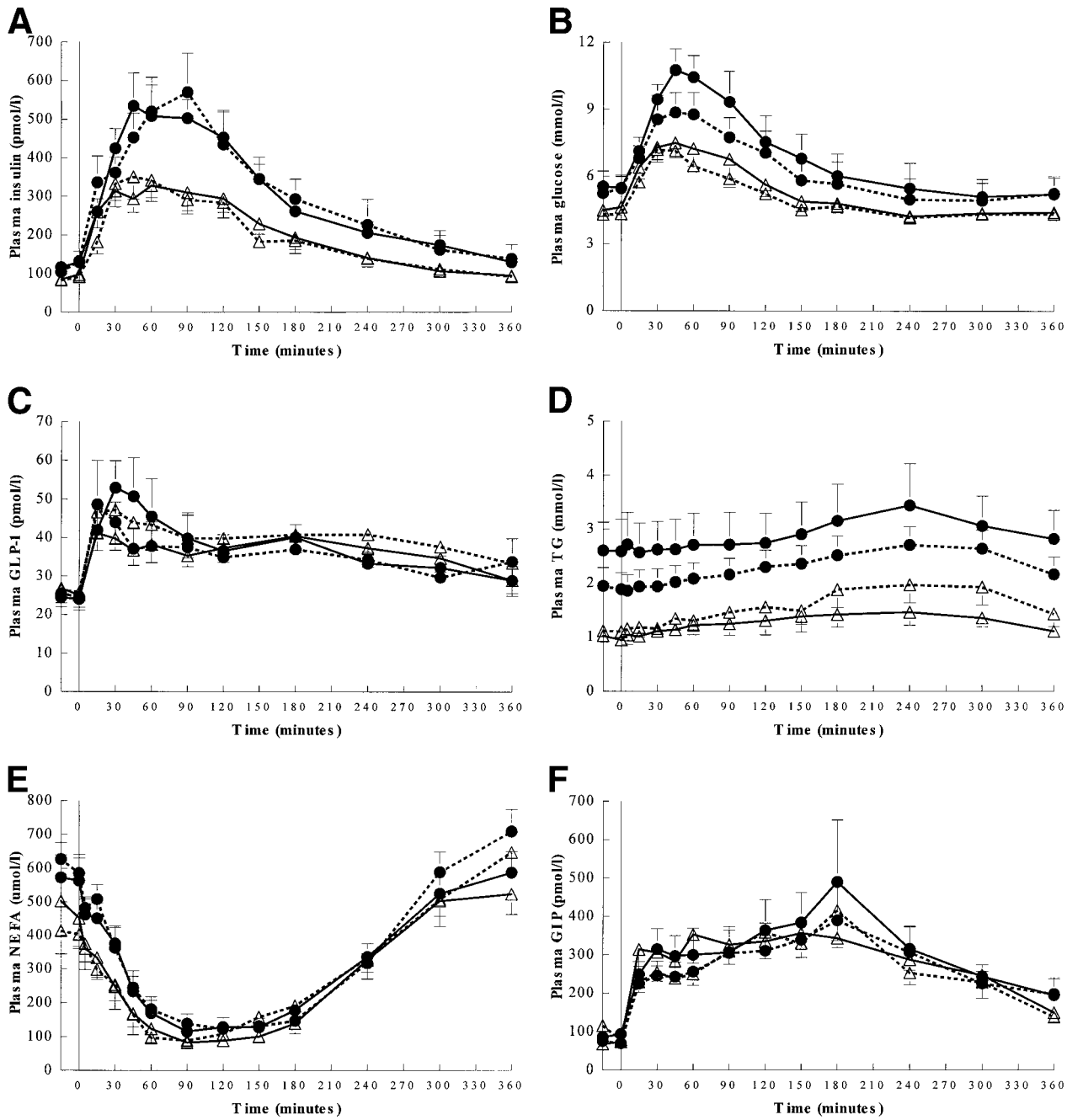

Fig 1. (A) Circulating plasma insulin response to a mixed meal containing either 75 g sucrose (- - - -) or 75 g glucose (—) in men at increased risk of CHD (●) and controls (◁). (B) Circulating plasma glucose response to a mixed meal containing either 75 g sucrose (- - - -) or 75 g glucose (—) in men at increased risk of CHD (●) and controls (◁). (C) Circulating plasma GLP-1 response to a mixed meal containing either 75 g sucrose (- - - -) or 75 g glucose (—) in men at increased risk of CHD (●) and controls (◁). (D) Circulating plasma TG response to a mixed meal containing either 75 g sucrose (- - - -) or 75 g glucose (—) in men at increased risk of CHD (●) and controls (◁). (E) Circulating plasma NEFA response to a mixed meal containing either 75 g sucrose (- - - -) or 75 g glucose (—) in men at increased risk of CHD (●) and controls (◁). (F) Circulating plasma GIP response to a mixed meal containing either 75 g sucrose (- - - -) or 75 g glucose (—) in men at increased risk of CHD (●) and controls (◁).

mmol/L/min, increased risk sucrose 199.3 ± 32 *v* glucose 136.3 ± 42 mmol/L/min; $P = .2$). The increased risk group did not differ in their TG or NEFA response compared with the control group ($P = .99$ and $P = .29$, respectively).

Absolute total area under the curve (not IAUC) for TG was significantly higher in the increased risk group for both glucose and sucrose (AUC at risk 1,063 ± 212 *v* control 462 ± 65 mmol/l and at risk 851 ± 113 *v* control 589 ± 89 mmol/L, respectively; $P = .01$).

Taking all 20 men together, we found no correlation between

GLP-1 and NEFA in either the fasting ($r^2 = .09$; $P = .7$) or IAUC postprandial ($r^2 = .01$; $P = .5$) state or GIP and TG in either the fasting ($r^2 = .06$; $P = .2$) or IAUC postprandial ($r^2 = .02$; $P = .4$) state.

DISCUSSION

Some evidence suggests that diets containing atypically large intakes of sucrose (in the region of 200 g/day) increase fasting TG and exaggerate postprandial lipemia in hypertriglyceridemic subjects.[1,2,27,28] However, in the general population, not all people at increased risk of CHD present with hypertriglyceridemia. This is demonstrated in our group in which initial screening was by plasma cholesterol. Our increased risk group have higher fasting TG, lower HDL concentrations, and a larger waist circumference despite being matched for BMI. These correspond to an increased risk of CHD profile. They also demonstrate signs of insulin resistance with higher IAUC insulin and fasting glucose and reduced HOMA. None of the parameters, TG, insulin, or glucose are included in the Framingham calculation; however, Wood et al[19] suggests that these factors may be included in the clinical judgement to adjust the calculated risk of CHD upwards. As a group, all of these factors put this group of men at increased risk of CHD compared with the controls.

Despite being matched for smoking habits, which is in itself a major risk factor for CHD, the increased risk group displayed many other factors that are attributable to CHD risk. Absolute total area under the curve (not IAUC) for TG was significantly higher in the increased risk group for both sucrose and glucose ($P = .01$, data not shown) demonstrating that this group does have a larger postprandial TG response compared with the control group. This suggests that some of the increased risks in this group may be due to an abnormal postprandial response, which may be additive to the other risk factors.

In general, only 50% of heart disease incidence can be explained by traditional risk factors. This may be because most risk factor assessments have focused on fasting lipid concentrations as their main criteria rather than postprandial assessments. Increasing recognition of the potential atherogenic and thrombogenic consequences of elevated postprandial TG was recently reviewed by Williams,[29] suggesting that postprandial dyslipidemia is also an important risk factor for heart disease.

Mann et al[30] were among the first to show that the addition of sucrose (60 g) to an oral fat load (25 g sunflower oil) results in 35% amplification of TG at a single test meal. Jeppesen et al,[28] with the addition of 50 g fructose, demonstrated a similar finding; however, this study did not include a control carbohydrate meal. Grant et al[31] found a 29% amplification after sucrose was added to an oral fat load, although this study failed to reach statistical significance. In a recent study reported in abstract form, a blunted lipemic response was seen with the addition of 50 g sucrose to a meal without impairing lipid oxidation; while 100 g of sucrose directed more of the lipid in the meal towards storage, while suppressing net lipid oxidation and prolonging the lipemic response.[32]

We saw a 40% and 46% amplification (control group and increased risk group) that failed to reach statistical significance in this study with the addition of 75 g sucrose to a moderate (0.6 g/kg) fat meal. We used sucrose to investigate the consequent effect of fructose, because this is the predominant sugar in the UK diet. It may be that we failed to give enough sucrose to see a difference in TG and NEFA; however, our aim was to give a realistic amount of sucrose that reflects what would be consumed at a meal, which was in line with the normal UK intake, and easily tolerated. Recent evidence from Daly et al[33] in humans supports our findings suggesting little effect of sucrose on insulin sensitivity or TG.

More importantly in this study, we found no difference in the IAUC TG response between the men at increased risk of CHD and the controls. This is not to say that people with an even greater risk of coronary disease may show differences in TG handling after a high sucrose load.

As expected of insulin secretagogues, both GIP and GLP-1 were stimulated following the test meals to concentrations similar to that seen in previous studies.[8] It is not surprising that the differences in insulin concentrations are not associated with differences in either GIP or GLP-1, as the differences in insulin are more likely to be related to the significant decrease in insulin sensitivity, as measured by HOMA in the increased risk group.

In a retrospective analysis by Ferrannini et al in 1997[33] on the European group for the study of insulin resistance (EGIR) database, insulin-sensitive subjects (BMI = 28.7kg/m^2; n = 174) assessed by the euglycemic insulin clamp had a fasting plasma NEFA concentration of 578 $\pm$ 17 μmol/L (mean $\pm$ SE). Insulin-resistant subjects in comparison (BMI = 31.9kg/m^2; n = 66) had a fasting NEFA concentration of 663 $\pm$ 25 μmol/L. Our results are similar to this, which further reinforces our findings that the differences in fasting NEFA concentrations in this study are clinically significant. However, we found no evidence for the different concentrations of NEFA having an effect on GLP-1 concentrations, leading to differences in insulin resistance. Interestingly, the postprandial suppression of NEFA was not different between the 2 groups. This may be because the men were matched for BMI, unlike other studies, which compared lean with obese volunteers.[14,15]

Unlike Gama, we found no association between our increased risk group and GIP. However, there are marked differences between the subject groups in the 2 studies. Most notably, in Gama's study, the high TG group had a median concentration of 4.7 mmol/L (4.2 to 8.3, 95% confidence interval), and the low TG group had a median concentration of 1.1 (0.8 to 1.5). This contrasts with our study in which the equivalent concentrations were mean 2.6 $\pm$ 0.56 mmol/L in the high group and 1.1 $\pm$ 0.12 mmol/L in the low group. This may suggest that the incretin hormone, GIP, may only be involved in lipoprotein metabolism at concentrations above the mean 2.6 mmol/L we found in this study.

Following the results of these studies, we are currently investigating the chronic and second meal effects of sucrose on postprandial TG, NEFA, and glucose homeostasis.

CONCLUSIONS

A total of 75 g of sucrose, given as part of a single meal, appears to make little difference in the postprandial TG and NEFA response in men with risk of CHD compared with

healthy age- and weight-matched controls. There was no significant difference in the IAUC (0 to 360 minutes) for TG and NEFA in response to glucose or sucrose within or between the groups. This supports other evidence recently reviewed by Frayn and Kingman[1] and Daly et al.[34] We found no evidence to suggest that the gut hormones, GLP 1 and GIP, released in response to carbohydrate ingestion, modulate any of the effects of sucrose. Longer-term data are now needed to clarify the effect of sucrose on TG and to establish whether it is appropriate to focus on a sucrose-reducing message when treating people at risk of CHD.

ACKNOWLEDGMENT

We thank M.L. Clark and Dr K. Frayn of the Oxford Lipid Metabolism Group for the measurement of plasma TG and NEFA and for helpful advice and discussion. Caroline Doré, Medical Statistics Department, Imperial College School of Medicine, gave statistical advice.

REFERENCES

1. Frayn FN, Kingman SN: Dietary sugar and lipid metabolism in humans. Am J Clin Nutr 62:250s-263, 1995

2. Hudgins LC, Seidman CE, Diakun J, et al: Human fatty acid synthesis is reduced after the substitution of dietary starch for sugar. Am J Clin Nutr 67:631-639, 1998

3. Simpson HS, Williamson CM, Olivecrona T, et al: Postprandial lipemia, fenofibrate and coronary artery disease. Atherosclerosis 85: 193-202, 1990

4. Palumbo PJ, Briones ER, Nelson R: Sucrose sensitivity of patients with coronary artery disease. Am J Clin Nutr 30:394-401, 1977

5. Reiser S, Bickard MC, Hallfrisch J: Blood lipids and their distribution in lipoproteins in hyperinsulinaemic subjects fed three different levels of sucrose. J Nutr 111:1045-1057, 1981

6. Abraha A, Humphreys SM, Clark ML, et al: Acute effect of fructose on postprandial lipaemia in diabetic and non-diabetic subjects. Br J Nutr 80:169-175, 1998

7. Hallfrisch J, Reiser S, Prather ES: Blood lipid distribution of hyperinsulinaemic men consuming three levels of fructose. Am J Clin Nutr 37:740-748, 1983

8. Kreymann B, Williams G, Ghatei MA, et al: Glucagon-like peptide-1 7-36: A physiological incretin in man. Lancet 2:1300-1304, 1987

9. Gutniak M, Orskov C, Holst JJ, et al: Antidiabetogenic effect of glucagon-like peptide-1 (7-36) amide in normal subjects and patients with diabetes mellitus N Engl J Med 326:1316-1322, 1992

10. Nathan DM, Schreiber E, Fogel H, et al: Insulinotropic action of glucagonlike peptide-I-(7-37) in diabetic and nondiabetic subjects. Diabetes Care 15:270-276, 1992

11. D'Alessio DA, Kahn SE, Leusner CR, et al: Glucagon-like peptide 1 enhances glucose tolerance both by stimulation of insulin release and by increasing insulin-independent glucose disposal. J Clin Invest 93:2263-2266, 1994

12. Todd JF, Edwards CB, Ghatei MA, et al: Subcutaneous glucagon-like peptide-I improves postprandial glycaemic control over a 3-week period in patients with early type 2 diabetes. Clin Sci 95:325-329, 1998

13. Edwards CMB, Todd JF, Mahmoudi M, et al: GLP-1 has a physiological role in the control of postprandial glucose in humans. Diabetes 48:86-93, 1999

14. Ranganath LR, Beety JM, Morgan LM, et al: Attenuated GLP-1 secretion in obesity: Cause or consequence? Gut 38:916-919, 1996

15. Ranganath L, Norris F, Morgan L, et al: The effect of circulating non-esterified fatty acids on the entero-insular axis. Eur J Clin Invest 29:27-32, 1999

16. Randle PJ: Regulatory interactions between lipids and carbohydrates: the glucose fatty acid cycle after 35 years. Diabetes Metab Rev 14:263-283, 1998

17. Ranganath L, Norris F, Morgan L, et al: Inhibition of carbohydrate-mediated glucagon-like peptide-1 (7-36) amide secretion by circulating non-esterified fatty acids. Clin Sci 96:335-342, 1999

18. Gama R, Norris F, Morgan L, et al: Elevated post-prandial gastric inhibitory polypeptide concentrations in hypertriglyceridaemic subjects. Clin Sci 93:343-347, 1997

19. Wood D, Durrington P, Poulter N, et al: Joint British recommendations on prevention of coronary heart disease in clinical practice. Heart 80:s1-s26, 1998

20. Department of Health: Dietary Reference Values for Food Energy and Nutrients for the United Kingdom 1991, pp RHSS 41

21. Central Statistical Office: London, HMSO, Annual Abstracts of Statistics, 1989

22. Albano JD, Ekins RP, Maritz G, et al: A sensitive, precise radioimmunoassay of serum insulin relying on charcoal separation of bound and free hormone moieties. Acta Endocrinol Copenh 70:487-509, 1972

23. Humphreys SM, Fisher RM, Frayn KN: Micro-method for measurement of sub-nanomole amounts of triacylglycerol. Ann Clin Biochem 27:597-598, 1990 (abstr)

24. Armitage P, Berry G: Split unit analysis of variance, in Armitage P (ed): Statistical Methods in Medical Research, vol 3. Cambridge, MA, Blackwell Scientific, 1994, Section 8.6

25. Turner RC, Holman RR, Matthews DR, et al: Insulin deficiency and insulin resistance interaction in diabetes: Estimation of their relative contribution by feedback analysis from basal plasma insulin and glucose concentrations. Metabolism 28:1086-1096, 1979

26. Levy J, Matthews DR, Hermans MP: Correct homeostasis model assessment (HOMA) evaluation uses the computer program. Diabetes Care 21:2191-2192, 1998

27. Liu S, Coulston AM, Hollenbeck CB, et al: The effect of sucrose content in high and low carbohydrate diets on plasma glucose, insulin, and lipid responses in hypertriglyceridemic humans. Am J Clin Nutr 59:636-642, 1983

28. Jeppesen J, Chen YI, Zhou MY, et al: Postprandial triglyceride and retinyl ester responses to oral fat: Effects of fructose. Am J Clin Nutr 61:787-791, 1995

29. Williams CM: Postprandial lipid metabolism: Effects of dietary fatty acids. Proc Nutr Soc 56:679-692, 1997

30. Mann JI, Truswell AS, Pimstone BL: The different effects of oral sucrose and glucose on alimentary lipaemia. Clin Sci 41:123-129, 1971

31. Grant KI, Marais MP, Dhansay MA: Sucrose in lipid-rich meal amplifies the post-prandial excursion of serum and lipoprotein triglyceride and cholesterol concentrations by decreasing triglyceride clearance. Am J Clin Nutr 59:853-860, 1994

32. Bennoson J, Sassi K, Jones A, et al: Exogenous lipid oxidation is suppressed with increasing sucrose in a meal. Int J Obes 23:A305, 1999 (abstr)

33. Ferrannini E, Camastra S, Coppack SW, et al: Insulin action and nonesterified fatty acids. Proc Nutr Soc 56:753-761, 1997

34. Daly ME, Vale C, Walker M, et al: Dietary carbohydrates and insulin sensitivity: A review of the evidence and clinical implications. Am J Clin Nutr 66:1072-1085, 1997