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Effects of short-term low- and high-carbohydrate diets on postprandial metabolism in non-diabetic and diabetic subjects

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Abstract *Background and aim:* Low-fat high-carbohydrate diets raise plasma triacylglycerol (TG) concentrations. To test whether the nature of the carbohydrate affects metabolic responses, we conducted a randomized cross-over study using a short-term, intensive dietary modification.
Methods and results: Eight non-diabetic subjects and four subjects with diet-controlled type 2 diabetes participated. They followed three isoenergetic diets, each for 3 days: high-fat (50% energy from fat), high-starch and high-sugar (each 70% energy from carbohydrate). Normal foods were provided. We measured plasma TG and glucose concentrations, fasting and after a standard test meal, on day 4 following each dietary period. Fasting TG concentrations were greatest following the high-sugar diet (mean $\pm$ SEM for all subjects 1900 $\pm$ 420 μmol/l) and lowest following high-fat (1010 $\pm$ 130 μmol/l) ($P = 0.001$); high-starch (mean 1500 $\pm$ 310) and high-fat did not differ significantly ($P = 0.06$). There was a greater effect in the diabetic subjects (diet $\times$ diabetes status interaction, $P = 0.008$). Postprandial TG concentrations were similarly affected by prior diet ($P < 0.001$) with each diet different from the others ($P \leq 0.01$). The elevation of fasting TG on the high-sugar versus high-fat diet was strongly related to the average fasting TG concentration ($P = 0.01$ across both diabetic and non-diabetic subjects). Fasting glucose concentrations were not affected by prior diet but postprandial glucose concentrations were ($P = 0.018$), with significantly higher values after the high-fat than the high-sugar diet ($P = 0.03$).
Conclusions: The short-term TG-raising effect of a very low-fat diet is dependent upon the nature of the carbohydrate, with a greater effect of a sugar-rich than a complex-carbohydrate-rich diet.

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Introduction

There has been considerable controversy about the usefulness and safety of low-fat diets both for the normal, healthy population and for patients with type 2 diabetes. The debate has centred around both their efficacy for weight regulation and their effects on cardiovascular risk factors. Thus, some have argued that the fat content of the diet is not a major determinant of weight regulation [1,2], although others disagree [3], and a meta-analysis of the effects of *ad libitum* low-fat, high-carbohydrate diets shows a beneficial effect on weight loss [4]. In the 6-month European CARMEN dietary intervention study, low-fat diets high in either simple sugars or complex-carbohydrates significantly reduced body weight by an average of 0.9 kg and 1.8 kg, respectively [5]. Very similar observations were made in the 6-month study of Poppitt et al. [6]. Of more concern, especially for people with type 2 diabetes, is the long-standing observation that high-carbohydrate diets tend to raise plasma triacylglycerol (TG) [7] and lower plasma HDL-cholesterol concentrations [8]. Some have argued that this represents a deleterious effect on cardiovascular risk and that it is preferable to replace saturated fat with monounsaturated fat rather than with carbohydrate [1,9,10]; but again, others have argued against this view, not least because if there is weight loss on a low-fat diet it will independently improve the metabolic profile [11].

Often these debates ignore the nature of the carbohydrate. It is well known that ingestion of simple sugars, particularly fructose, will potentiate postprandial lipaemia [12—14]. Diets high in simple sugars similarly tend to raise fasting TG concentrations in non-diabetic subjects and in patients with type 2 diabetes [15,16]. However, a low-fat high-carbohydrate diet based on complex-carbohydrates given *ad libitum* did not adversely affect plasma lipids, perhaps again because of concomitant weight loss [17]. In the 6-month CARMEN study, there were no adverse effects of high-sugar or high-complex carbohydrate diets on plasma lipids, and this might suggest that the TG-raising effect of a high-carbohydrate diet is in any case transient. This is supported by other data [18]. However, the study by Poppitt et al. showed greater plasma TG concentrations after a low-fat, high-simple carbohydrate diet [6].

In order to study the effects of different components of the diet in detail, it is useful to conduct an intensive dietary manipulation for a relatively short period, when its effects may be most pronounced. A model of intense 3-day dietary manipulation with isoenergetic high-fat and high-carbohydrate diets has been used to investigate marked effects on both fasting and postprandial TG concentrations [19,20]. We have modified this model to investigate the effects of different types of dietary carbohydrate in non-diabetic subjects and patients with type 2 diabetes. Our aim was to clarify whether the apparently adverse metabolic effects of high-carbohydrate diets, at least in the short-term, are dependent upon the nature of the carbohydrate that replaces the fat.

Methods

Study population and protocol

Eight healthy, non-diabetic subjects (four male) were recruited by advertisement. Their ages ranged from 22 to 53 years (median 47) and their BMI from 19.9 to 26.6 kg/m^2 (median 22.9). Four patients with type 2 diabetes (two male), well-controlled by diet only, were recruited from the Diabetes Clinic. Their ages ranged from 40 to 61 years (median 56) and their BMI from 23.8 to 32.9 kg/m^2 (median 30.4). The studies were approved by the Central Oxford Research Ethics Committee and all subjects gave written, informed consent.

Dietary assessment and prescription

At an initial screening visit, the study coordinator (KSC) assessed the subject's diet and attitudes towards food. Each subject was asked to keep a 7-day diet and activity diary, recording everything they ate, drank, all exercise and any feelings they had about their usual diet. They were provided with digital kitchen scales. The diet and activity diaries were used to calculate each subject's daily dietary energy requirements. Dietary energy requirements were also calculated by calculating resting metabolic rate as described in Ref. [21] and multiplying by a factor to allow for individually reported daily physical activity level. Reported and calculated energy requirements were within 200 kJ/day. The higher number (between reported and calculated energy intake) was used in formulating the diets.

Each subject completed three 3-day diets: one high in starch, one high in sugar, and one high in fat (therefore low-carbohydrate). Spreadsheets were designed in which the subject's daily energy intake could be input, and the diet constituents calculated automatically, although some individual variation was possible. These personal changes were to allow each volunteer to state dislikes and to encourage them to eat what was prescribed. Each experimental diet was discussed with each subject so that they could state if they felt able to comply with it. All food products (including the larger meal as a ready-meal) were provided, along with clear written and verbal instructions. Where possible food portions were pre-weighed and packaged individually for all meals and snacks. Subjects were asked to consume their last food on the third day of each diet prior to 8 pm, and then to drink only water overnight. The study coordinator was always available for consultation by telephone.

The composition of the diets is given in Table 1. Breakfast, lunch and snacks were made up from separate ingredients, but the evening meal was provided as a ready-made meal. For breakfast, lunch and snacks the main sources of carbohydrate for the three diets (high-starch; high-sugar; high-fat) were, in order of importance: high-starch: bran flakes, brown bread, bananas, 'digestive biscuits' with chocolate; high-sugar: Jaffa cakes (McVitie's, United Biscuits UK, Hayes, Middlesex, UK), frosties (Kellogg Co. UK, Warrington, Cheshire, UK), raisins, brown bread, boiled sweets; and high-fat: brown bread. The main sources of fat were as follows (in the same order): chocolate digestive biscuits, butter;

Table 1 Composition of the 3-day diets and of the test meal given on day 4

Three-day diets	Percentage energy			Carbohydrate composition (as % total dietary energy)	
	Fat	Protein	Carbohydrate	Sugars	Complex-carbohydrate
High-fat	50	15	35	10	25
High-starch	15	15	70	30	40
High-sugar	15	15	70	40	30

Test meal composition for the postprandial study day	Amount (g)	Energy (kJ)	Fat content (g)
Decaffeinated tea	Optional	–	–
Cornflakes	40	672	1.4
Milk (skimmed)	100	420	3.4
Banana	100	677	0.5
Milkshake (chocolate flavour)			
Skimmed milk	150	630	5.1
Nesquik	15	105	0.7
Milk powder	15	102	1.1
Macadamia nut oil	40	1376	38.4
Total	N/A	3982	50.6

Further details of the foods eaten are given in the text.

butter, Jaffa cakes; and margarine, hard (Cheddar) cheese. The evening meals were all purchased from Sainsbury's Supermarkets Ltd, London, UK. Each weighed 450 g and they provided from 1790 to 2750 kJ (low-fat) and from 2560 to 3850 kJ (high-fat). Fibre contents of the diets (g/day) were as follows (mean $\pm$ SD): low-fat high-starch, 18.7 $\pm$ 1.8; low-fat high-sugar, 18.2 $\pm$ 1.7; and high-fat, 14.5 $\pm$ 1.6.

Each 3-day diet was followed by a postprandial study day. All experimental diets and postprandial days were caffeine-free, alcohol-free, and exercise was avoided. (Caffeine-free coffee, caffeine-free tea and caffeine- and sugar-free soft drinks were provided or reimbursed for.) Experimental diets for each subject were separated by at least 4 weeks and the different diets were followed in random order.

Postprandial study day

After 3 days on each diet, the subjects fasted overnight and reported to the laboratory the following morning. An antecubital venous cannula was placed for blood sampling. The hand and lower arm were warmed to achieve partial arterialization. After a 30-minute rest period, two baseline samples were taken 20 min apart. The subject then received a standardized test meal which was identical for all subjects and for all diets. The composition of the test meal is shown in Table 1. Further blood samples were then taken at intervals (as shown on the figures) for 6 h.

Analyses

Blood samples were taken into heparinized syringes (Monovette, Sarstedt, Leicester, UK) and stored on ice before centrifugation at 4 °C to separate plasma, which was stored in aliquots at −20 °C for analysis. Plasma TG, non-esterified fatty acid (NEFA) and glucose concentrations were analyzed by enzymatic methods on an Instrumentation Laboratory (Warrington, UK) Monarch centrifugal analyzer. Plasma insulin concentrations were analyzed by radioimmunoassay (Linco Research Inc, St Charles, Missouri, USA).

Statistical methods

Analysis was performed with SPSS for Windows release 12.0.1 (SPSS Inc, Chicago). Plasma TAG and insulin concentrations were log-transformed before statistical analysis. Effects of dietary period on fasting concentrations were analyzed using repeated-measures analysis, with diet as a within-subject factor. Effects of dietary period on responses to the test meal were analyzed using repeated-measures analysis, with time (after meal) and diet as within-subject factors. Diabetic and non-diabetic subjects were compared by using 'diabetes status' as a between-subject factor for both fasting and postprandial responses. When significant main effects of diet were observed, post-hoc comparisons between diets were made using the Bonferroni correction. Correlations were assessed using Spearman's rank correlation coefficient, r_s.

Results

Plasma TG concentrations

Fasting plasma TG concentrations before the meal test were clearly affected by the dietary preparation, with lowest concentrations following the high-fat diet and highest following the high-sugar (Table 2). Fasting TG concentrations following both high-fat and high-starch diets were significantly lower than following high-sugar, but high-starch and high-fat diets did not differ significantly in their effects ($P = 0.06$). Although there was no overall effect of diabetes status on fasting plasma TG concentrations, there was a significant diet $\times$ diabetes status interaction, indicating a greater effect of diet in the diabetic patients (Table 2).

Table 2 Fasting plasma values following 3 days on diet

	High-fat		High-starch		High-sugar		Significance[a]
	Mean	SEM	Mean	SEM	Mean	SEM	
Triacylglycerol (μmol/l)[b]							
Overall	1010	130	1500	310	1900	420	Diet: $P = 0.001$[c]
Non-diabetic subjects	950	150	1110	240	1330	240	Diet × status: $P = 0.008$
Diabetic subjects	1130	270	2300	680	3040	1030	Diabetes status: $P = 0.23$
Non-esterified fatty acids (μmol/l)							
Overall	617	78	544	61	545	72	Diet: $P = 0.28$
Non-diabetic subjects	515	83	428	37	431	36	Diet × status: $P = 0.80$
Diabetic subjects	7964	124	748	90	744	148	Diabetes status: $P = 0.012$
Glucose (mmol/l)							
Overall	4.93	0.19	4.82	0.22	4.97	0.16	Diet: $P = 0.45$
Non-diabetic subjects	4.69	0.25	4.52	0.27	4.75	0.17	Diet × status: $P = 0.60$
Diabetic subjects	5.35	0.17	5.34	0.16	5.35	0.23	Diabetes status: $P = 0.047$
Insulin (mU/l)							
Overall	11.3	1.1	15.1	3.1	13.1	1.3	Diet: $P = 0.23$
Non-diabetic subjects	8.9	0.5	13.8	4.6	10.9	1.1	Diet × status: $P = 0.90$
Diabetic subjects	16.1	0.8	17.7	1.2	18.3	0.7	Diabetes status: $P = 0.008$

[a] Significance by repeated-measures analysis of variance, with diet as a within-subjects factor and diabetes status as a between-subject factor.
[b] Plasma TG and insulin concentrations are shown as arithmetic mean ± SEM but were log-transformed for statistical analysis.
[c] Post-hoc tests showed significant differences ($P = 0.001$) between fasting TG concentrations following high-fat and high-sugar and high-starch and high-sugar diets, but no significant difference between high-fat and high-starch ($P = 0.06$).

For the TGs throughout the test (Fig. 1), there was a significant effect of prior diet with each diet different from the others. The high-starch diet was intermediate between high-sugar (the highest TG concentrations) and high-fat. No difference was observed in TG responses between diabetics and non-diabetics ($P = 0.13$) but there was a significant interaction between prior diet and diabetes status (Fig. 1), indicating, as for the fasting values, a greater effect in the diabetic patients. This is at least partly explained by the close relationship between the increase in fasting TG on the high-sugar diet, and the average fasting TG concentration (Fig. 2).

Plasma glucose, insulin and NEFA concentrations

Fasting plasma glucose concentrations (Table 2) were not affected by prior diet. As expected, they were significantly higher in the diabetic patients. Plasma glucose concentrations throughout the postprandial test (Fig. 3) showed a significant effect of diet, with highest concentrations following the high-fat diet. Only the high-fat and high-sugar diets differed significantly in their effects on glucose concentrations. Again as expected, plasma glucose concentrations throughout the postprandial test were higher in diabetic than non-diabetic subjects ($P < 0.001$), and there was a significant interaction between prior date and diabetes status (see Fig. 3).

Fasting plasma insulin concentrations did not differ according to prior diet, but were higher in the diabetic than the non-diabetic subjects. Insulin concentrations rose after the test meal (effect of time, $P < 0.001$), and again there were no significant effects of prior diet. Again, however, the concentrations were higher in the diabetic patients ($P = 0.026$).

Plasma NEFA concentrations were highest in the fasting state and decreased following the test meal, as expected.

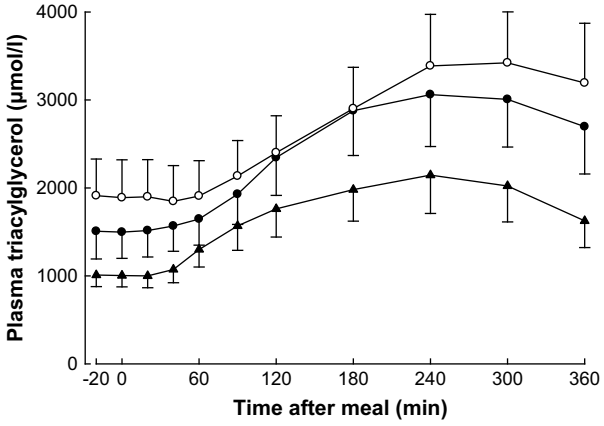

Figure 1 Plasma triacylglycerol (TG) concentrations before and after a meal test, following 3 days of different diets. For clarity, non-diabetic ($n = 8$) and diabetic ($n = 4$) subjects have been combined for the figure. Solid triangles, high-fat diet; solid circles, high-starch diet; and open circles, high-sugar diet. Values are shown as arithmetic mean ± SEM, but statistical analyzes were conducted on log-transformed values. For statistics on fasting data, see Table 2. For values throughout the test, there was a significant effect of prior diet ($P < 0.001$) with a significant diet × diabetes status interaction ($P < 0.02$), but no time × diet interaction. Each diet was different from the others on post-hoc testing ($P \leq 0.01$).

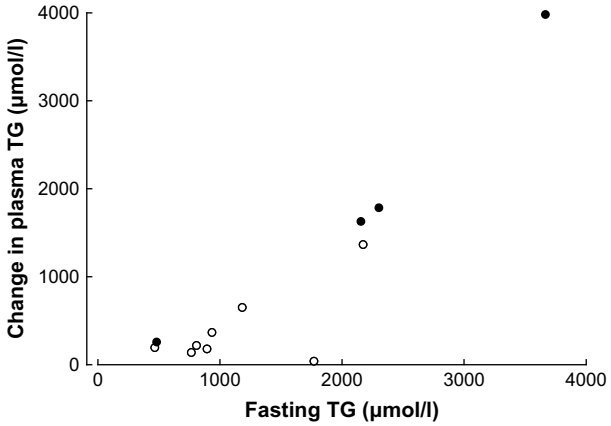

Figure 2 Change in fasting plasma triacylglycerol (TG) concentration (high-sugar diet minus high-fat diet) plotted against overall average fasting TG concentration. Open points, non-diabetic subjects; and solid points, diabetic subjects. For the group as a whole, relating change in TG to average fasting TG, $r_s = 0.706$, $P = 0.010$; for the diabetics only $r_s = 1.000$, $P = 0.01$; and non-diabetics only, not significant.

Unlike plasma TG and glucose concentrations, there was no significant effect of prior diet neither on fasting plasma NEFA concentrations, nor on concentrations after the test meal (Table 2). Plasma NEFA concentrations were higher in diabetic than in non-diabetic subjects ($P = 0.001$).

Discussion

We have shown that using this intensive, 3-day intervention, a low-fat high-carbohydrate diet increases fasting and postprandial TG concentrations as has been shown previously [19]. However, our data show clearly that the effect is more pronounced when the carbohydrate content is rich in simple sugars, and that the effect on fasting TG concentrations was almost abolished when the diet was rich in complex-carbohydrate. There was a greater effect of diet on TG concentrations in the diabetic patients than the non-diabetic controls, emphasizing that the TG-raising effect of high-carbohydrate diets is dependent upon the prior metabolic state of the subject [22]. The marked correlation between TG elevation on the high-sugar diet compared with the high-fat diet, and the baseline fasting TG concentration, seems to imply that the increased effect seen in diabetic patients is a reflection of their generally higher TG concentrations at baseline.

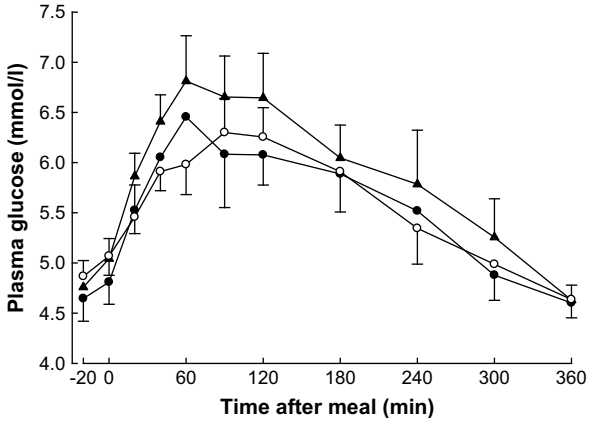

Figure 3 Plasma glucose concentrations in all subjects ($n = 12$) before and after a meal test, following 3 days of different diets. For clarity, non-diabetic ($n = 8$) and diabetic ($n = 4$) subjects have been plotted together. Solid triangles, high-fat diet; solid circles, high-starch diet; and open circles, high-sugar diet. Values are shown as arithmetic mean ± SEM. For statistics on fasting data, see Table 2. For values throughout the test, there was a significant main effect of diet ($P = 0.018$) with a significant diet × diabetes status interaction ($P < 0.05$). Post-hoc tests showed only the high-fat and high-sugar diets to differ ($P = 0.031$).

Another finding of potential interest was the small but significant elevation of postprandial glucose concentrations after the high-fat diet. This could be seen as a normal part of metabolic adaptation to extreme diets: when the fat content of the diet is increased, fat tolerance improves and vice versa for carbohydrate and glucose tolerance. The impairment of glucose tolerance following low-carbohydrate diets has long been recognized [23]. It extends even to the composition of the previous evening's meal [24]. It is also long established that a low-carbohydrate diet impairs glucose control in patients with type 2 diabetes [25]. There have been previous investigations of the nature of the carbohydrate in high-carbohydrate diets. Peterson et al. compared a high-sucrose diet with a high-complex carbohydrate diet (each with ~53% energy from carbohydrate, 27% energy from fat) fed for 6 weeks in patients with type 1 or type 2 diabetes [26]. At the end of the study, they found no differences in diurnal glucose or triglyceride concentrations during an experimental day. Although that study provides reassurance for dietary management of diabetes with less extreme diets than we employed, it may be that the more extreme dietary composition that we used (70% energy from carbohydrate) and perhaps the short-term nature of our intervention have unmasked the potentially adverse aspects of excess dietary sugars.

The issue of carbohydrate content of the diet and postprandial glucose or TG concentrations is sometimes confounded by studying the effects whilst the diet is maintained. Thus, patients with type 2 diabetes on a high-carbohydrate versus a moderate-carbohydrate diet had greater daytime glucose concentrations [16], but they were consuming more carbohydrate. In a study by Raben et al. [27], high-carbohydrate diets rich in sucrose and in complex-carbohydrate were compared with a high-fat diet. Diurnal concentrations of TGs were elevated during both high-fat and high-sucrose diets, compared with high-starch, whilst diurnal glucose concentrations were lowest on the high-sucrose diet. Similarly, high-fructose diets in patients with type 2 diabetes have been shown to improve glycaemic control assessed by HbA1 concentrations [28], presumably because of the lower glycaemic effect of fructose than glucose. We sought to avoid such effects by using a standard test meal at the end of the dietary intervention period. At least in the short-term, it seems that the potentially adverse effects of low-fat diets on postprandial lipaemia could be balanced by beneficial effects on carbohydrate tolerance.

We have investigated specifically responses to low-fat diets. There are also indications of beneficial effects of carbohydrate-restricted diets, on both weight loss and plasma lipid profiles [29—32]. However, even in the context of a carbohydrate-restricted diet, the addition of soluble fibre improved effects on plasma lipid profiles [32]. Therefore there may be some positive aspect to the inclusion of complex-carbohydrates other than the simple displacement of simple sugars from the diet.

There are some limitations to this study that should be borne in mind before extrapolating the results to formulate dietary advice. One is that we designed the diets to be isoenergetic, so avoiding effects of concomitant changes in energy balance. In an *ad libitum* feeding situation, it is likely that the nature of the carbohydrate would also affect energy intake, as was seen in the CARMEN study [5] and the study by Poppitt et al. [6]. This is likely to accentuate favourable effects of a high-complex carbohydrate diet compared with one high in sugars. Although our study was small, the use of a cross-over design means that group sizes were comparable with larger, parallel-group studies [6]. However, these results now need to be confirmed in larger, longer-term studies in which effects of other risk factors for coronary heart disease can be assessed, including HDL-cholesterol and LDL particle size. It is important to stress that the short-term but intensive design we used was intended to maximise the metabolic effects of the different diets and might not be the representative of changes seen with more typical diets fed for longer periods, as noted earlier in connection with the study by Peterson et al. [26].

We conclude that the apparently adverse effects of dietary carbohydrate on plasma TG concentrations are highly dependent upon the nature of the carbohydrate. More research is needed to understand better why high-sugar diets have their potentially adverse effects on TG fasting and postprandial TG concentrations.

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