

Short Communication

The beneficial effect of a diet with low glycaemic index on 24 h glucose profiles in healthy young people as assessed by continuous glucose monitoring

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Elevated postprandial glycaemia has been linked to CVD in a number of different epidemiological studies involving predominantly non-diabetic volunteers. The MiniMed continuous glucose monitor, which measures blood glucose every 5 min, over a 24 h period, was used to investigate changes in blood glucose readings before and after instigating a diet with low glycaemic index (GI) for 1 week in free-living healthy individuals. Nine healthy people (age 27 (SEM 1.3) years, BMI 23.7 (SEM 0.7) kg/m², one male, eight females) completed the study. A reduction in GI (59.7 (SEM 2) v. 52.1 (SEM 2), $P < 0.01$) occurred in all nine subjects while energy and other macronutrients remained constant. A significant reduction was also observed in fasting glucose at 06.00 hours (5.4 (SEM 0.2) v. 4.4 (SEM 0.3) mmol/l, $P < 0.001$), mean glucose (5.6 (SEM 0.2) v. 5.1 (SEM 0.2) mmol/l, $P = 0.004$), area under the 24 h glucose curve (8102 (SEM 243) v. 750 (SEM 235) mmol/l per min, $P = 0.004$) and area under the overnight, 8 h glucose curve (2677 (SEM 92) v. 2223 (SEM 121) mmol/l per min, $P = 0.01$). The present study provides important data on how a simple adjustment to the diet can improve glucose profiles that, if sustained in the long term, would be predicted from epidemiological studies to have a favourable influence on CVD.

Diet: Low glycaemic index: Healthy subjects: Continuous glucose monitoring

Glycaemic fluctuations in healthy people are tightly controlled by a number of physiological homeostatic mechanisms. Dietary factors also influence glycaemic excursions in healthy adults, especially during the postprandial period (Frost *et al.* 2003). When blood glucose values rise to levels associated with impaired glucose tolerance or diabetes, the risk of macrovascular disease is greatly increased (Jarrett *et al.* 1982). A number of recent epidemiological studies have shown that the relationship between glycaemia and CVD is a continuum that begins within the normal glucose tolerance range and increases with increasing glycaemia (Coutinho *et al.* 1999). In both glucose-tolerant and glucose-intolerant subjects, studies have suggested that the relationship between CVD risk and blood glucose is greater with the 1 h postprandial glucose value, and/or the 2 h post-glucose challenge value, than with the fasting glucose concentration (DECODE Study Group, 1999).

Further support for the hypothesis that postprandial glycaemia is linked to CVD is given by epidemiological studies showing that habitual diets with a low glycaemic index (GI) are associated with less CVD and diabetes in

glucose-tolerant subjects than are high-GI diets (Salmeron *et al.* 1997a,b).

Most studies report data collected in the laboratory, which may not reflect the free-living situation. The Mini-Med Continuous Glucose Monitoring System (CGMS™) provides a means to measure subcutaneous interstitial fluid glucose over a 3 d period, using an electrochemical detector, in subjects under free-living conditions (Mastroiuto, 1999). The CGMS records values in a pager-sized monitor every 5 min, providing 288 glucose readings every 24 h.

We have previously shown, for type 2 diabetic subjects treated with insulin, a 30% reduction in the 24 h postprandial glycaemic curve after following a low-GI diet for a week (Brynes *et al.* 2003a). It is possible that these insulin-resistant subjects with their higher postprandial glucose levels may be more responsive to the effects of a low-GI diet than healthy euglycaemic subjects. In the present study we examined whether modest dietary changes in free-living healthy young adults aimed at lowering the dietary GI can have a significant effect on daily glucose profiles.

Methods

Subjects

Ten healthy adults, nine females, aged 27 (SEM 1.3) years, were recruited from posters displayed within the Hammersmith Hospitals NHS Trust. All subjects were Caucasians, other than one Afro-Caribbean female. No subject was on any medication during the study period or had a history of diabetes or any other medical co-morbidity. Subjects' BMI ranged from 20.3 to 27.2 kg/m², mean 23.7 (SEM 0.7) kg/m², and mean waist circumference was 74.7 (SEM 1.9) cm. All subjects gave written consent, the study having previously been approved by the Imperial College School of Medicine Hammersmith Campus Research & Ethics Committee. During the initial screening process each volunteer had a medical examination to ensure suitability for the study. One subject was withdrawn from the study after the CGMS™ sensor failed to collect a complete set of data.

Power calculation

From data acquired in a previous study (Brynes *et al.* 2003a) we calculated that eight sets of paired data would be required to see a 15% change in the area under the 24 h glucose curve using a power of 85% and a probability level of 5%.

Study design

The study was conducted over 14 d, with each subject having two 24 h glucose monitoring sessions, one at baseline and the second after consuming a low-GI diet. For the three days prior to the initial 24 h glucose monitoring session all subjects completed a record of their dietary intake using a standard 3 d food diary with portion size estimated with the use of a handy household measure. On the fourth day subjects attended the Clinical Investigation Unit at the Nutrition & Dietetic Department, Hammersmith Hospital, where a MiniMed CGMS™ sensor (Medtronic MiniMed, Northridge, CA, USA) was fitted. Although the sensors are capable of recording blood glucose values every 5 min for up to 72 h, only the 24 h values – monitored between 06.00 hours on day 5 and 06.00 hours on day 6 – were used for analysis. Each subject was individually instructed on how to standardise the monitor using four separate capillary finger prick glucose readings using a MediSense Precision glucose meter (Abbott Diagnostic MediSense Products, Maidenhead, UK) every 24 h. On the morning of day 6 the CGMS™ sensor was removed. Thereafter, each subject received advice and written information on low-GI dietary foods with instruction to incorporate one low-GI key food with each meal, while keeping their overall energy and macronutrient intakes constant. In a previous study we successfully used the substitution of a key carbohydrate food at each meal to reduce the overall GI of the diet by up to 20% (Brynes *et al.* 2003b).

All low-GI meal plans were based on the initial 3 d baseline diary obtained from each subject (Table 1). Low-GI bread (high in β -glucans) was provided to aid with

compliance. All subjects were requested to keep activity patterns constant and to refrain from alcohol consumption while wearing the monitors. Subjects were encouraged to discuss any concerns they had on any aspects of the dietary intervention or protocol given.

After consuming a low-GI diet for a minimum of 7 d (range 7–10 d), the CGMS™ monitor was refitted and a second 24 h glucose profile was obtained under similar circumstances as the first.

Statistical analyses

Data are presented as means and standard error of the mean (SEM). Distributions were tested for normality using the parametric Shapiro–Wilk test. Paired-sample *t* tests were used for normally distributed data with the Wilcoxon signed rank test used for non-parametric data that did not normalise on log transformation.

Results

Compliance

Compliance to the prescribed diet was assessed using 3 d food diaries. The GI of the diet was calculated as previously described (Frost *et al.* 1994) using glucose as a standard. Comparison of the diets at baseline and after following the prescribed low-GI diet showed an overall 13% reduction in GI during the 7 d low-GI dietary period (baseline 58.6 (SEM 0.6) *v.* low GI 52.5 (SEM 1.4), $P < 0.01$), with the GI of the diet decreasing for all subjects (Table 1). During the 24 h monitoring periods the GI of the diet remained low (baseline 59.7 (SEM 1.5) *v.* low GI 52.1 (SEM 1.9), $P < 0.01$). There was no significant change in energy or other macronutrients. The percentage of energy from dietary carbohydrate remained unchanged from baseline when following the low-GI diet (54.8 (SEM 2.2) *v.* 50.6 (SEM 3.6)% of total energy, $P = 0.2$) and a significant reduction in glycaemic load was observed (32.7 (SEM 1.4) *v.* 27.7 (SEM 2.1), $P = 0.01$). Fibre increased significantly (13.5 (SEM 2.1) *v.* 22.3 (SEM 2.1) g, $P < 0.01$). The reported number of eating occasions was similar during both 24 h profiles (Table 1).

Glucose results

There was a significant reduction in fasting glucose at 06.00 hours (5.4 (SEM 0.2) *v.* 4.4 (SEM 0.3) mmol/l, $P < 0.001$), mean glucose derived from the 288 individual readings over the 24 h (5.6 (SEM 0.2) *v.* 5.1 (SEM 0.2) mmol/l, $P = 0.004$), 24 h total area under the curve (AUC) glucose (8102 (SEM 243) *v.* 7350 (SEM 231) mmol/l per min, $P = 0.004$) and overnight (from 22.00 to 06.00 hours) 8 h AUC glucose (2677 (SEM 92) *v.* 2223 (SEM 121) mmol/l per min, $P = 0.01$; Fig. 1). Eight out of the nine subjects moved in the same direction. The one subject who did not reduce 24 h AUC glucose, despite a reduction in GI, already had the lowest AUC at baseline.

Compliance with the low-GI diet was demonstrated by the significant correlation between change in GI and change in 24 h AUC ($r = 0.73$, $P = 0.04$).

Table 1. Macronutrient content of the baseline diet and the diet with low glycaemic index (GI) as determined from 3 d diary and over 24 h when wearing a monitor

(Mean values and standard error of the mean for nine healthy subjects)

	3 d diary				<i>P</i>	24 h				<i>P</i>
	Baseline diet		Low-GI diet			Baseline diet		Low-GI diet		
	Mean	SEM	Mean	SEM		Mean	SEM	Mean	SEM	
GI	58.6	0.6	55.5	1.4	0.001	59.7	1.5	52.1	1.9	0.001
Glycaemic load	30.5	1.5	26.4	1.9	0.01	32.7	1.4	26.4	2.1	0.01
Energy (kJ/d)	9016	1109	7958	477	0.2	9125	1318	9159	632	0.73
Carbohydrates (% energy)	52.1	2.5	50.2	3.3	0.3	54.8	2.2	50.6	3.6	0.2
Fibre (g/d)	12.6	1.7	17.5	1.8	0.002	13.5	2.1	22.3	2.1	0.000
Fat (% energy)	30.7	2.3	29.0	2.6	0.5	28.5	2.2	31.9	3.5	0.4
Protein (% energy)	13.9	0.6	15.1	0.8	0.13	13.8	1.1	15.4	0.8	0.3
Eating episodes (n/d)						5.9		5.7		0.6

Reproducibility of glucose measurements

The reproducibility of glucose measurements was checked by comparing seventy-two paired data points (eight from each of nine patients) between the CGMS readings and the capillary blood finger prick tests obtained from the MediSense Precision glucose meter. These results were highly correlated ($r = 0.68$, $P < 0.0001$) with a mean absolute error of 10.5%.

Discussion

Today, the health of the Western world is threatened by the economic and technological successes of the last century. Mortality from diabetes and obesity-related diseases continues to rise. As these disorders are increasing most quickly among young adults, a rise in premature mortality from diabetic-related macrovascular disease is to be expected unless radical population changes are made to habitual life-style. In the non-diabetic state, the 2 h postprandial blood glucose concentration is a predictor of CVD (DECODE Study Group, 1999).

It has been shown that intensive individual intervention with exercise and dietary modification is efficacious in reducing the development of type 2 diabetes among at-risk individuals. However, to deliver such a programme

on a population basis poses enormous, and probably unrealistic, challenges. What is urgently required is the introduction of a number of simple habitual life-style changes that can be adopted by a large number of the population and which have a significant effect in correcting early metabolic factors that contribute to impaired glucose tolerance and diabetes.

This present paper shows how the adoption of a simple change to an individual diet, namely the incorporation of one low-GI key food with each meal, can have a profound effect on both fasting blood glucose and overall 24 h glucose profiles. After only 1 week of lowering the GI of the diet, eight out of nine subjects showed a reduction in their overall glycaemic profile.

Plasma glucose values vary depending on whether an individual is fasting or in the postprandial or post-absorptive state. Today's eating patterns result in a high proportion of the day being spent in the postprandial state and diets that specifically reduce postprandial glycaemia may be particularly protective against CVD, as high postprandial glycaemic excursions appear to be metabolically disadvantageous (de Vegt *et al.* 1999). Plausible biochemical mechanisms involve glucose-induced activation of the diacylglycerol-protein kinase C pathways that link hyperglycaemia to oxidative stress, changes in endothelial function and altered coagulation (Shige *et al.* 1999). Because it is during the postprandial period that plasma glucose is at its highest, it seems rational that life-style changes that specifically lower glycaemia at this time may be beneficial.

Several epidemiological studies in predominantly non-diabetic populations have shown an association of post-glucose load values with adverse cardiovascular outcomes. The DECODE study (1999) was a meta-analysis that covered more than 25 000 subjects, predominantly non-diabetic, with a mean follow-up of 7.3 years. The risk of death was assessed according to both fasting plasma glucose and glucose levels 2 h after an oral glucose challenge. Fasting plasma glucose concentration did not modify the risk of death attributable to 2 h post-glucose challenge levels. However, the risk of death increased with elevated 2 h post-glucose challenge levels across all fasting plasma glucose concentrations. In the National Health and Nutrition Examination Survey in the USA, which followed 3092 adults for 16 years, isolated post-load hyperglycaemia

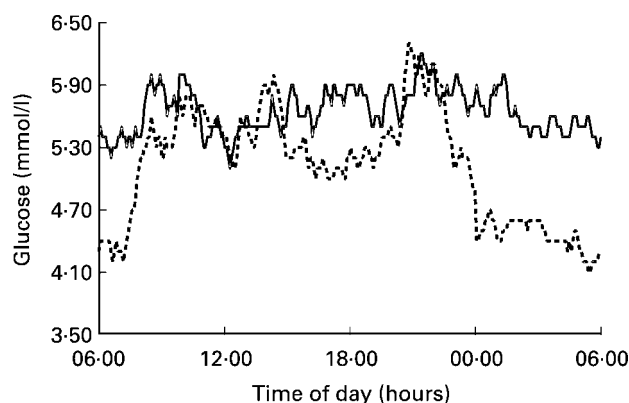


Fig. 1. Mean 24 h area under the curve for glucose at baseline (—) and in response to a diet with low glycaemic index (- - -) for eight subjects.

was again found to be associated with increased all-cause and CVD mortality (Saydah *et al.* 2001).

One of the advantages of using the CGMS™ is that volunteers were in their home environment and able to continue with daily living. This is important, as it is likely to reflect a more representative situation than a laboratory-based study.

Clinical studies involving low-GI diets have consistently shown that such diets favourably influence postprandial metabolism, lowering insulin resistance and lipid and clotting parameters. Together these metabolic effects may explain the long-term benefits of low-GI diets on CVD observed in large cohort follow-up studies.

In the present study, daytime glucose concentrations were reduced by 5% while overnight concentrations were reduced by as much as 16%. This is potentially an important finding, because the literature tends to refer to improvements in postprandial glucose concentrations, rather than fasting concentrations, with changes in GI. The finding that low-GI diets significantly lowered fasting plasma glucose in these healthy young adults suggests that switching to a low-GI diet improved hepatic insulin sensitivity, effectively decreasing hepatic glucose output.

We believe that the present study provides important data on how a simple adjustment to the diet can have a significant effect on glucose metabolism, which, interpreted in the light of recent epidemiological studies, would be predicted to have a favourable influence on CVD if adopted in the long term.

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