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Sugars and fat have different effects on postprandial glucose responses in normal and type 1 diabetic subjects

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Abstract *Background and aims:* We aimed to determine the effects on glycemic responses and potential risk of hypoglycaemia in type 1 diabetic subjects of replacing half the starch in a meal with sugars, and of adding fat to the low-sugar and high-sugar meals.

Methods and results: We studied overnight fasted subjects with type 1 diabetes ($n = 11$) and age-, BMI- and ethnicity-matched controls ($n = 11$) using a 2×2 factorial design. The low-sugar/low-fat meal was 110 g white-bread. In the high-sugar/low-fat meal half the white-bread starch replaced by sugars (jam and orange juice). The high-fat meals consisted of the low-fat meals plus 20 g fat (margarine). The significance of the main effects of sugars and fat and the sugar $\times$ fat, group $\times$ sugar and group $\times$ fat interactions were determined by ANOVA. In control and diabetic subjects, respectively, high-sugar significantly reduced time to peak rise by 13% ($P = 0.004$) and 32% ($P = 0.004$; group $\times$ sugar: $P = 0.01$) and increased peak rise by 14% and 10% (ns). Adding fat increased time to peak rise by 17-19% in both groups ($P = 0.003$), reduced peak rise by 31% in normal ($P < 0.001$) but increased peak rise in diabetic subjects by 3% (ns) (group $\times$ fat: $P = 0.022$). Blood glucose nadir and occurrence of hypoglycaemia were similar among the 4 meals.

Conclusions: In type 1 diabetes, insulin adjustment to avoid hypoglycemia may be useful for meals in which the proportion of carbohydrate absorbed as glucose is <0.75, however the precise level which increases hypoglycaemic risk requires further research. The results suggest that people with type 1 diabetes should not be advised to add fat to meals to reduce glycemic responses.

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The importance of tight glycemic control to prevent complications in type 1 diabetes is well established [1,2]. To this end it is recommend that type 1 diabetes be managed using intensive insulin therapy combined with self-monitoring of blood glucose (SMBG) or continuous glucose monitoring [3,4]. Intensive insulin therapy ideally involves taking a dose of insulin before every meal which is sufficient to control postprandial glucose without causing hypoglycaemia. The dose of insulin administered is based on premeal blood glucose, anticipated activity and carbohydrate intake [3,4]. Rapid acting insulins (lispro or aspart) have times of onset and peak action more closely mimicking the postprandial glucose excursion [5] and thus improve glycemic control [6,7] and reduce hypoglycaemia [7,8] compared to regular insulin.

The glycemic effects of carbohydrates are classified by the glycemic index (GI). Foods differ in GI because of differences in the rate of starch absorption and differences in the nature of the monosaccharide absorbed [9]. Of the monosaccharides absorbed, only glucose raises blood glucose to any appreciable extent; fructose, galactose and sugar alcohols have little or no effect [9,10]. It is not known whether the dose of premeal insulin should be adjusted for the source of carbohydrate consumed. To address this question we determined the glycemic responses of 4 starchy foods and pineapple juice (containing sugars) with GI values ranging from ~35 to ~90 in subjects with type 1 diabetes treated with insulin lispro [11]. The area under the glucose response curve (AUC) after the starchy foods was proportional to their GI values and GI did not affect the incidence of hypoglycaemia. However, although pineapple juice elicited a similar AUC as spaghetti (as expected from their similar GI values) blood glucose reached a lower nadir and hypoglycaemia was more common after pineapple juice than spaghetti (82 vs 32%) [11]. This suggested that the dose of premeal insulin may not need to be adjusted for GI, but may need to be adjusted for the proportion of carbohydrate absorbed as glucose (Pg). Since all of the carbohydrate in starch is absorbed as glucose, the Pg of starchy foods is 1. However, only about 50% of the carbohydrate in common foods containing sugars such as milk, fruit, fruit juice, sucrose and high-fructose corn syrup is absorbed as glucose; thus, their Pg is about 0.5. Since most normal mixed meals contain a mixture of starch and sugars, their Pg value is >0.5. For clinical utility, it is necessary to determine the level of Pg associated with an increased risk of hypoglycemia. In addition, it is possible that other components in mixed meals, such as fat, might prevent the rapid fall in blood glucose after a meal high in sugars. It is commonly assumed that fat flattens glycemic responses in people with diabetes by delaying gastric emptying [12–16]. However, there is evidence that fat does not affect glycemic responses in subjects with type 1 diabetes [17,18]. Therefore, as a first step toward determining the Pg which increases risk for hypoglycaemia, and the effect of added fat, we determined the effect of substituting 50% of the starch in a mixed meal with sugars with and without added fat on postprandial glucose in subjects with type 1 diabetes.

Methods

Males and non-pregnant/non-lactating females with type 1 diabetes (using rapid acting insulin at breakfast and with HbA1c <9.0%) or without diabetes (controls), aged 18–45 y, with waist circumference <102 cm (males) or <88 cm (females) and who usually ate breakfast were recruited by advertisement from St. Michael's Hospital and University of Toronto. Exclusion criteria included: triglycerides >10 mmol/L, serum creatinine >150 μmol/L, surgery or antibiotic use within 3mo, cardiac event within 6mo, history of liver disorder, gastroparesis or hypoglycaemia unawareness. The protocol was approved by the research ethics boards at St. Michael's Hospital and University of Toronto. All subjects gave informed consent to participate.

Subjects attended on 4 mornings after 10 h overnight fasts. They were asked to have the same type of meal at the same time on the evening before and to avoid alcohol and maintain the same exercise on the day before each test. For subjects with diabetes the test was canceled if nocturnal hypoglycaemia had occurred or if blood glucose before leaving home was <4.0 or >11.1 mmol/L. To minimize within subject variation, each subject's fasting glucose across the 4 study days had to vary by ≤5.0 mmol/L; tests outside this range were repeated ($n = 2$).

After a fasting blood sample, subjects with diabetes administered the type and dose of insulin they would normally take for a 50 g carbohydrate meal; the same type and dose of insulin was taken on each test occasion. Subjects then ate a test meal within 10 min and had blood samples taken at 15, 30, 45, 60, 90 and 120 min (for controls) or every 30 min for 4 h (for subjects with diabetes) after starting to eat. Blood samples (2–3 drops), taken by finger-prick, were collected into fluoro-oxalate tubes for glucose analysis by YSI (Model 2300 STAT, Yellow Springs Instruments, Yellow Springs, OH). Subjects with diabetes also tested each blood sample with a glucometer (One Touch Ultra Smart, Lifescan Canada, Burnaby, BC). If hypoglycaemia occurred (defined as glucometer reading <4.0 mmol/L with symptoms or glucometer reading <3.0 mmol/L without symptoms), the test was stopped and the subject was provided with juice and a snack. Missing glucose values after hypoglycaemia were replaced with the last available value; eg. if a test was stopped for hypoglycaemia at 180 min, blood glucose was not measured at 210 and 240 min; the missing values at these times were taken to be the value at 180 min.

Four test meals were given in randomized order. The composition of the meals was as follows: low-sugar/low-fat (LSLF), 110 g white-bread and 107 g water (1050 kJ, 0.8 g fat, 11 g protein, 50 g starch, 0 g sugars, 1 g fiber, glycemic index (GI) 71, Pg 1.0); high-sugar/low-fat (HSLF), 55 g white-bread, 25 g strawberry jam and 107 g orange juice (950 kJ, 0.4 g fat, 6 g protein, 25 g starch, 25 g sugars, 1 g fiber, GI 64, Pg 0.75); low-sugar/high-fat (LSHF), the LSLF meal plus 25 g margarine (1810 kJ, 21 g fat, 11 g protein, 50 g starch, 0 g sugars, 1 g fiber, GI 71, Pg 1.0); and high-sugar/high-fat meal (HSHF), the HSLF meal plus 25 g margarine (1690 kJ, 20 g fat, 6 g protein, 25 g starch, 25 g sugars, 1 g fiber, GI 64, Pg 0.75).