

Utilizing the Second-Meal Effect in Type 2 Diabetes: Practical Use of a Soya-Yogurt Snack

MEI JUN CHEN, BSC
ANA JOVANOVIC, MD
ROY TAYLOR, MD

OBJECTIVE — To evaluate the effect of a prebreakfast high-protein snack upon postbreakfast hyperglycemia.

RESEARCH DESIGN AND METHODS — We studied 10 men and women with diet- and/or metformin-controlled type 2 diabetes. Metabolic changes after breakfast were compared between 2 days: breakfast taken only and soya-yogurt snack taken prior to breakfast.

RESULTS — There was a significant lower rise in plasma glucose on the snack day. The incremental area under the glucose curve was 450 ± 55 mmol · min/l on the snack day compared with 699 ± 99 mmol · min/l on the control day ($P = 0.013$). The concentration of plasma free fatty acids immediately before breakfast correlated with the increment in plasma glucose ($r = 0.50$, $P = 0.013$).

CONCLUSIONS — Consuming a high-protein prebreakfast snack results in almost 40% reduction of postprandial glucose increment. The second-meal effect can be applied simply and practically to improve postbreakfast hyperglycemia in people with type 2 diabetes.

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Previous studies (1,2) have shown a considerable reduction in hyperglycemia after the second meal of the day, provided that breakfast had been taken. The preservation of this effect in type 2 diabetes was not confirmed until recently (3). Postprandial hyperglycemia acts as an independent risk factor for cardiovascular disease (4–6), a major cause of death in subjects with type 2 diabetes (7).

We hypothesized that postbreakfast hyperglycemia in subjects with type 2 diabetes could be improved nonpharmacologically by using a high-protein, low-carbohydrate prebreakfast snack.

RESEARCH DESIGN AND METHODS

Ten subjects (four female, six male) with type 2 diabetes

treated by diet and/or metformin were recruited (aged 61 ± 2.3 years, waist-to-hip ratio 0.96 ± 0.01 , BMI 28.8 ± 1.0 kg/m², body fat $33.4 \pm 2.6\%$, and A1C $6.7 \pm 0.1\%$). The Newcastle and North Tyneside Research Ethics Committee No. 2 approved the study. All participants gave written informed consent.

Design and protocol

Every subject was studied on 2 separate days in random order with 2–4 week intervals. On both days, breakfast (51 g carbohydrate; 4.8 g fat; 5.8 g protein) was given at 10:00 A.M. On the snack day only, a snack (30 g soya beans; 75 g yogurt) was given 2 h before the breakfast. The details of metabolic testing, hormone, and metabolites assays were as previously described (3,8).

Statistical analysis

Data are expressed as means \pm SEM. Paired Student *t* test was performed by SPSS (version 17.0; SPSS, Chicago). Incremental area under the curve (IAUC) was computed by the trapezoidal rule.

RESULTS

Plasma glucose

At baseline, 2 h before breakfast, fasting plasma glucose was similar on the 2 study days (6.6 ± 0.3 and 6.6 ± 0.4 mmol/l). The snack induced a small peak in plasma glucose at -60 min (7.3 ± 0.4 mmol/l). The concentrations of plasma glucose immediately before breakfast ($t = 0$ min) did not differ significantly between the 2 days (6.6 ± 0.3 vs. 6.4 ± 0.3 mmol/l, $P = 0.45$) (Fig. 1A).

Following breakfast, the rise in plasma glucose was lower on the snack day. IAUC was 450 ± 55 mmol · min/l compared with 699 ± 99 mmol · min/l for snack and control day, respectively ($P = 0.013$) (Fig. 1B). The 2-h postprandial plasma glucose concentration was significantly lower on the snack day compared with the control day (9.8 ± 0.3 vs. 10.8 ± 0.4 mmol/l, $P = 0.001$). Plasma glucose levels were identical in the two groups 5 h after breakfast.

Plasma free fatty acid

The fasting plasma free fatty acid (FFA) concentrations on both study days were similar (0.57 ± 0.05 and 0.57 ± 0.04 mmol/l, $P = 0.9$). After ingestion of the snack, plasma FFA concentration declined, falling to 70% of the fasting levels just before breakfast (0.41 ± 0.04 mmol/l). After breakfast, plasma FFA levels in both groups were suppressed (0.16 ± 0.02 vs. 0.14 ± 0.02 mmol/l for snack and control days, respectively) (Fig. 1C). FFA concentration before breakfast was positively correlated with the postprandial IAUC for plasma glucose ($r = 0.50$, $P = 0.013$).

Serum insulin and C-peptide

Fasting mean serum insulin levels were similar on the 2 study days (13.4 ± 2.4 and 13.2 ± 2.7 mU/l). On the snack day,

From the Newcastle Magnetic Resonance Centre, Campus for Ageing and Vitality, Newcastle University, Newcastle upon Tyne, U.K.

Corresponding author: Roy Taylor, roy.taylor@newcastle.ac.uk.

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M.J.C. and A.J. contributed equally to this study.

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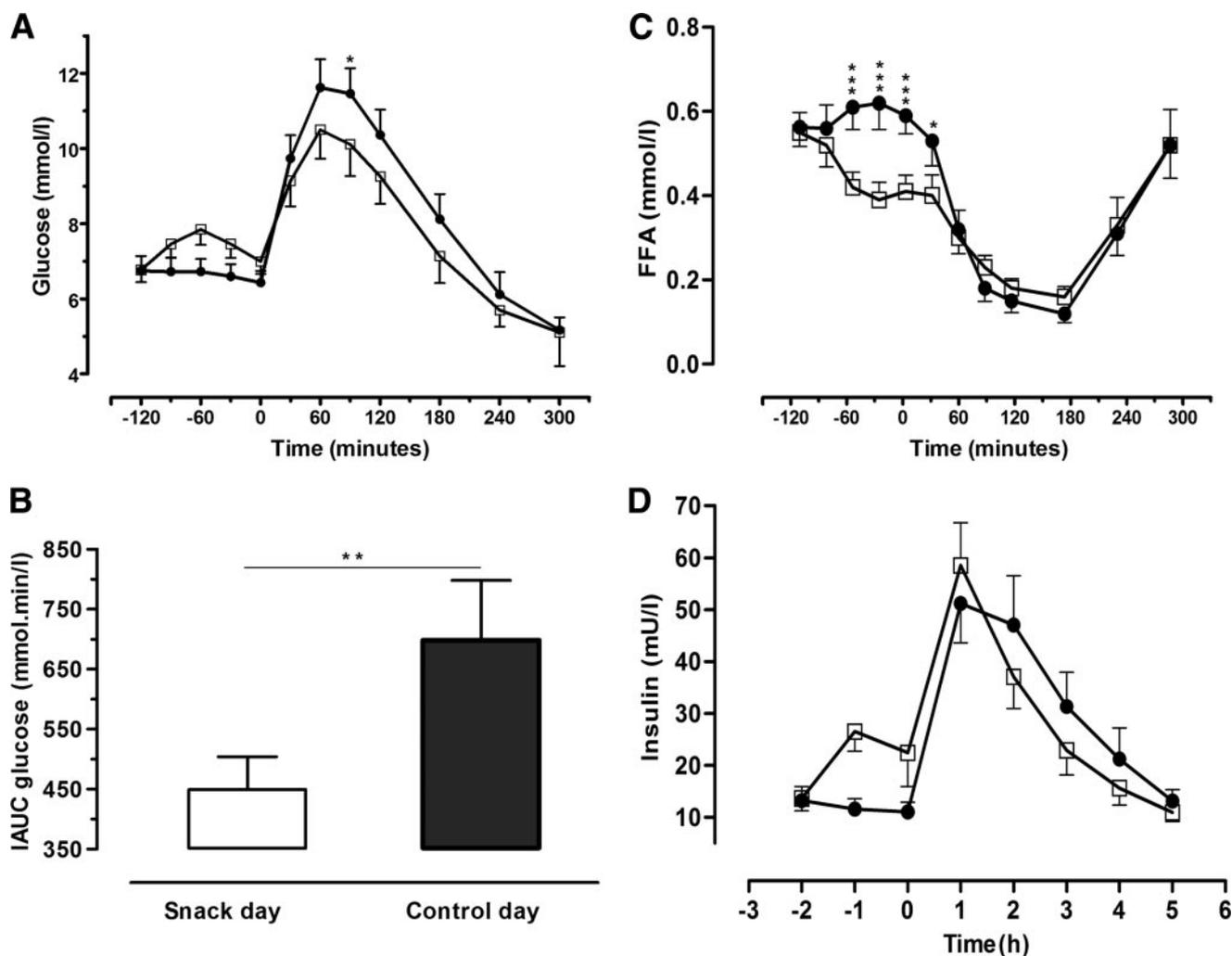


Figure 1—Metabolic changes between the 2 study days in 10 subjects with type 2 diabetes. A: Plasma glucose concentrations. B: Incremental area under the plasma glucose curves during the 5-h postbreakfast period. C and D: Change in FFA and insulin concentrations, respectively. * $P < 0.05$; ** $P < 0.02$; *** $P < 0.01$; □, snack day; ●, control day.

insulin concentration rose promptly after ingestion of the snack to 26.5 ± 4.0 mU/l at -60 min and fell before breakfast (Fig. 1D). Following breakfast, insulin levels increased similarly on both days (58.5 ± 7.9 vs. 51.2 ± 7.6 mU/l) at 60 min. The mean insulin-to-C-peptide ratios from the area under the curves ($t = 0-5$ h) were similar on both days (13.6 ± 3.2 vs. 16.9 ± 1.4 mU/nmol, $P = 0.36$) implying similar hepatic insulin extraction.

Substrate oxidation

Fasting glucose oxidation rates were not significantly different on the 2 study days (0.55 ± 0.18 vs. 0.77 ± 0.25 mg/kg \cdot min, $P = 0.37$). On the snack day, glucose oxidation rate increased to 1.38 ± 0.24 mg/kg \cdot min at 90 min after breakfast compared with 1.09 ± 0.25 mg/kg \cdot min on the control day ($P = 0.11$). Fasting lipid oxidation rates were similar ($0.7 \pm$

0.1 vs. 0.63 ± 0.12 mg/kg \cdot min) and 90 min after breakfast decreased to 0.39 ± 0.09 vs. 0.51 ± 0.09 mg/kg \cdot min, respectively ($P = 0.09$).

CONCLUSIONS— This study demonstrated for the first time that the provision of a practical, high-protein, low-carbohydrate snack prior to breakfast reduced by 40% the postprandial plasma glucose increment in people with type 2 diabetes. These findings confirm a potent expression of the second-meal effect in people with type 2 diabetes similar to that resulting from intravenous arginine infusion (3). The importance of the present observation is that a more practical means of improving glucose tolerance could potentially be of therapeutic benefit in people with type 2 diabetes.

We observed no effect of the prior snack on insulin secretion after breakfast.

The mechanism underlying the second-meal effect has been shown to be due to suppression of plasma FFA, allowing greater storage of glucose as muscle glycogen (2). We previously demonstrated a strong negative correlation between the decrease of preprandial plasma FFA levels and the postmeal glucose increment. In the present study, a significant positive correlation was found between prebreakfast plasma FFA and the rise in postprandial plasma glucose concentration. This observation is analogous to the acute effect of the antilipolytic nicotinic acid analog acipimox (9).

The snack used in the present study was empirically designed. It will be important to optimize both the composition of the snack and the interval before breakfast to maximize the benefit of this approach. In everyday life, the gap between snack and breakfast would have to be ac-

commodated, for instance, by delaying breakfast until mid-morning. Although the snack induced a small increase in plasma glucose, it was minimal and unlikely to contribute to the hyperglycemic burden. The sample size was dictated by prior power calculation (80% power with 10 subjects).

We have demonstrated that a high-protein, low-carbohydrate snack before breakfast attenuates postbreakfast hyperglycemia, and further studies must determine whether long-term use is associated with improvement in A1C.

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No potential conflicts of interest relevant to this article were reported.

M.J.C. conducted the study, researched the data, and drafted the manuscript. A.J. designed the study and revised the manuscript. R.T. conceived the overall research question, researched the data, and revised the manuscript.

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