Caffeine Increases Ambulatory Glucose and Postprandial Responses in Coffee Drinkers With Type 2 Diabetes

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Recent laboratory studies demonstrated that caffeine exaggerates glucose and insulin responses to standardized carbohydrate loads in habitual coffee drinkers who have type 2 diabetes (1–3). Similar postprandial effects in everyday life could disrupt clinical efforts to maintain glucose control in patients with type 2 diabetes. The aim of this study was to examine the effects of a moderate dose of caffeine on glucose levels and postprandial glucose responses in free-living coffee drinkers with type 2 diabetes. We specifically predicted that caffeine administration would increase glucose concentrations during the day and exaggerate the glucose increases that followed meals when habitual coffee drinkers with type 2 diabetes were monitored during everyday life.

RESEARCH DESIGN AND METHODS — The research protocol, approved by the Duke University Health Systems institutional review board, employed a double-blind crossover design to compare the effects of a moderate dose of caffeine (500 mg/day) with that of a placebo control. Subjects completed informed consent before testing and received $150.00 in compensation. The study group included 10 habitual coffee drinkers (five men and five women) who drank brewed coffee daily. All had at least a 6-month history of type 2 diabetes managed by a stable regimen of diet, exercise, and oral agents but no exogenous insulin. Subjects were free of major medical disorders, were nonsmokers, and used no psychotropic medications known to affect glucose metabolism. Age (mean ± SD) was 63 ± 13 years, BMI 31.9 ± 5.6 kg/m^2, and A1C 6.4 ± 0.5%. Daily caffeine intake was 520 ± 419 mg/day, based on conversion of self-reported beverage consumption using standard estimates for caffeine content.

Ambulatory glucose concentration was assessed with the validated MiniMed continuous glucose monitoring system (CGMS; Medtronic MiniMed, Northridge, CA) (4). The CGMS provides 288 continuous, 5-min average measurements of interstitial glucose each day using a subcutaneous microelectrode sensor. The CGMS can operate for up to 72 h to provide detailed information about trends over time that can be used to evaluate responses to meals and other events.

Caffeine and placebo treatments were administered on different study days in identical gelatin capsules containing 125 mg anhydrous caffeine plus dextrose filler or dextrose alone. The total caffeine dose (500 mg) was divided as described below. The order of caffeine and placebo treatments was counterbalanced within the group. Subjects consumed no other caffeine on study days.

The CGMS sensor was inserted subcutaneously into the lower abdomen on the day before the first study day. Subjects received coded packets of capsules for the two subsequent study days. Subjects consumed two capsules containing either caffeine (250 mg total) or placebo at breakfast and two more of the same capsules at lunch. Subjects consumed a standard breakfast, consisting of 16 oz. (473 ml) of Boost Plus, which provided 90 g carbohydrate in a 720-kcal liquid meal. Lunch and dinner were ingested ad libitum, although subjects were instructed to consume a similar diet on both days. Subjects recorded the time of each meal and the foods consumed, along with medications taken. Subjects were instructed to carry out normal activities but to avoid strenuous exercise on the study days. The glucose sensor was removed on the day after the second study day.

The CGMS system recorded glucose values continuously for ~72 h. The two 24-h study days were defined beginning at 6 A.M. on the second and third days of monitoring, and overnight glucose values were associated with the prior study day. Recorded mealtimes were used to anchor the 3-h postprandial glucose response assessments. Continuous glucose values were analyzed using a hierarchical linear model to test the effects of treatment in these repeated measures (PROC Mixed, version 9.1; SAS Institute, Cary, NC). Given the sequential nature of the data, an autoregressive error structure was used.

RESULTS — Average 24-h interstitial glucose concentration curves for the caffeine and placebo days are shown in Fig. 1. Planned analyses focused on daytime glucose levels (when caffeine was present in pharmacologically active concentrations) and postprandial responses to meals. Testing revealed that caffeine increased average levels of daytime glucose (6 A.M.–10 P.M.) compared with those associated with placebo (8.0 vs. 7.4 mmol/l, $P < 0.0001$). Average glucose concentrations were also elevated ($P < 0.0001$) in the 3 hours following the standardized breakfast (8.7 vs. 8.0 mmol/l), lunch (7.8 vs. 6.8 mmol/l), and dinner (8.6 vs. 6.8 mmol/l) on the days that caffeine was consumed. Testing revealed no difference in the effect of caffeine across the three meals.

CONCLUSIONS — Caffeine had adverse effects on glucose metabolism, producing higher average daytime glucose concentrations and exaggerated post-

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Abbreviations: CGMS, continuous glucose monitoring system.

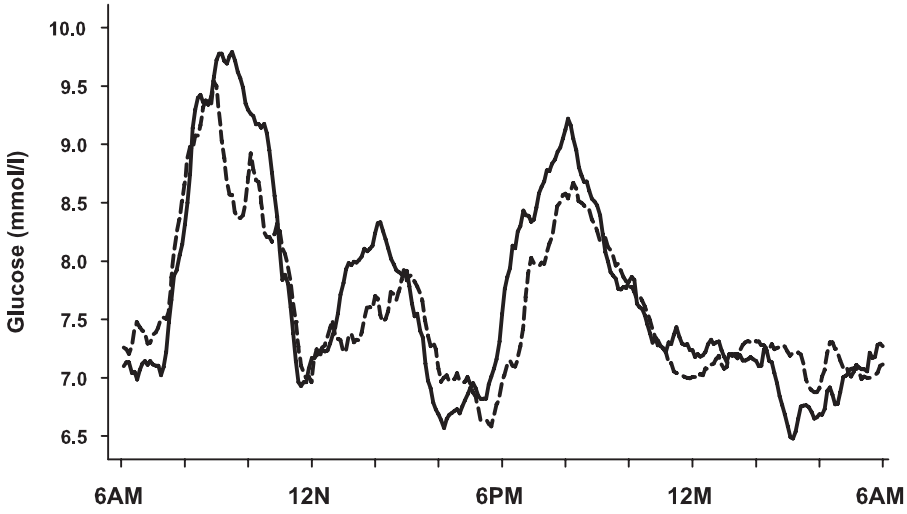

Figure 1—*Interstitial glucose 24-h concentration curves during caffeine intake (500 mg/day) and placebo days* (n = *10). Solid line, caffeine; dashed line, placebo.*

prandial glucose responses in these free-living diabetic patients. These results complement the findings of earlier studies in which caffeine exaggerated glucose and insulin responses to a carbohydrate challenge in the laboratory (1–3).

The mechanisms of action that account for these effects are uncertain at this time. Caffeine could directly inhibit glucose uptake in adipocytes and skeletal muscle through antagonism of adenosine receptors (5,6). Alternatively, caffeine could act indirectly through increased release of epinephrine, which has widespread counter-regulatory effects on glucose metabolism (7).

Although tests of overnight glucose levels were not planned, Fig. 1 suggests that caffeine exposure may have reduced overnight glucose levels compared with placebo (caffeine abstinence). This possibility will be the subject of future studies.

Similar hyperglycemic effects could occur whenever type 2 diabetic patients consume caffeine in daily life. These adverse effects were observed in habitual coffee drinkers, who had sufficient opportunity to develop tolerance to the drug. The caffeine dose administered in this study is roughly equivalent to four 8-oz cups of brewed coffee, a moderate amount consistent with intake reported by these subjects. The presence of hyperglycemic effects in these free-living individuals raises concerns about the potential hazards of caffeinated beverages for patients with type 2 diabetes. Repeated episodes of elevated glucose resulting from daily consumption of caffeinated beverages could impair clinical efforts aimed at glucose control and increase risk of diabetes complications.

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