

Effects of Coffee Consumption on Fasting Blood Glucose and Insulin Concentrations

Randomized controlled trials in healthy volunteers

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Higher habitual coffee consumption was associated with higher insulin sensitivity (1) and a lower risk for type 2 diabetes (2–6) in diverse populations. In contrast, short-term metabolic studies showed that caffeine intake can acutely lower insulin sensitivity (7–9) and increase glucose concentrations (10–15). Randomized intervention studies are needed to examine whether tolerance to these acute effects develops after longer-term consumption (16). We therefore examined the effects of coffee and caffeine on fasting blood concentrations of glucose and insulin over 2–4 weeks in two crossover studies in healthy volunteers.

RESEARCH DESIGN AND METHODS

The studies were approved by the TNO Nutrition and Food Research Medical Ethics Committee, and all participants gave informed consent. The trials were originally designed to study the effects of coffee and caffeine on plasma concentrations of homocysteine, and the study designs have been reported in detail previously (17,18). Participants were regular coffee consumers (more than five cups/day) and did not have known diabetes.

The first study was a 4-week crossover study that compared the effects of regular paper-filtered coffee consumption with that of coffee abstinence. A total of

40 volunteers used 1 l of coffee (70 g coffee grounds) for 4 weeks and abstained from coffee for 4 weeks in random order. Fourteen participants did not complete the trial because of nausea and restlessness ($n = 7$), possible susceptibility to adverse effects of caffeine intake ($n = 3$), or reasons unrelated to treatment ($n = 4$). Thus, 26 participants were included in the analysis. The second study had a Latin-square design with three treatments given in random order for 2 weeks each: caffeine (a total of 870 mg in six capsules), regular paper-filtered coffee (52 g ground coffee/day in 0.9 l), and placebo (six capsules containing cellulose). Of the 54 volunteers, 6 subjects withdrew because of severe headaches ($n = 2$), study-related illness ($n = 1$), or reasons unrelated to treatment ($n = 3$). For the current analyses, we excluded participants because of missing blood samples ($n = 1$), not completing the whole caffeine intervention ($n = 1$), or who were clear outliers for an insulin concentration ($n = 1$). Thus, 45 subjects were included in the analysis. Caffeine-containing products (other than those provided) were prohibited during the entire trial. Venous blood samples were collected after an overnight fast. Plasma glucose concentrations were measured using the glucose hexokinase method. Serum insulin concentrations were measured using an immunoradio-

metric assay (Medgenix Biosource Diagnostics, Fleuris, Belgium).

In study 1, treatment responses were compared using paired *t* tests. In study 2, we tested for overall treatment effects using ANOVA. All reported *P* values were two sided, and *P* values <0.05 were considered statistically significant.

RESULTS

Study 1

Of the participants that completed the study, 62% were women, mean (\pm SD) age was 37 ± 12 years, and mean BMI was 23 ± 3 kg/m². After 2 weeks, coffee consumption tended to lead to higher fasting glucose concentrations, but no appreciable effect was observed after 4 weeks (Table 1). Fasting insulin concentrations, measured only after 4 weeks, were higher after the coffee period than after the no coffee period (Table 1). Tests for carry-over effects did not indicate that these existed (insulin: $P = 0.79$; glucose: $P = 0.27$).

Study 2

Of the participants that completed the study, 56% were women, mean age was 40 ± 14 years, and mean BMI was 24 ± 3 kg/m². Fasting glucose concentrations were similar after the caffeine, coffee, and placebo period (Table 1). Compared with the placebo period, fasting insulin concentrations tended to be higher after the coffee and caffeine periods (Table 1).

CONCLUSIONS— We found that high coffee consumption for 4 weeks increased fasting insulin concentrations compared with coffee abstinence. Consumption of somewhat weaker coffee and caffeine intake were nonsignificantly associated with higher fasting insulin concentrations. No substantial effects of coffee or caffeine on fasting glucose concentrations were observed.

The increased fasting insulin concentration after high coffee consumption in our study probably reflects decreased insulin sensitivity. In short-term metabolic

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1—Fasting glucose and insulin concentrations after paper-filtered regular coffee consumption, caffeine intake, and coffee/caffeine abstinence

| | Control period | Coffee period | Caffeine period | P* |
|---------------------------|----------------|-----------------|-----------------|-------|
| Study 1 (n = 26†) | | | | |
| Plasma glucose (mmol/l) | | | | |
| After 2 weeks | 5.0 ± 0.3 | 5.2 ± 0.6 | — | 0.08 |
| Difference with no coffee | — | 0.2 (0.0–0.4) | — | — |
| After 4 weeks‡ | 5.1 ± 0.3 | 5.1 ± 0.4 | — | 0.94 |
| Difference with no coffee | — | 0.0 (–0.1–0.1) | — | — |
| Plasma insulin (pmol/l) | | | | |
| After 4 weeks | 57.5 ± 18.8 | 71.4 ± 31.2 | — | 0.002 |
| Difference with no coffee | — | 13.9 (5.9–21.9) | — | — |
| Study 2 (n = 45†) | | | | |
| Plasma glucose (mmol/l) | | | | |
| After 2 weeks | 5.0 ± 0.4† | 5.0 ± 0.5 | 5.1 ± 0.4 | 0.42 |
| Difference with placebo | — | 0.0 (–0.1–0.1) | 0.1 (0.0–0.2) | — |
| Plasma insulin (pmol/l) | | | | |
| After 2 weeks | 51.5 ± 16.0 | 56.6 ± 22.4 | 54.2 ± 21.1 | 0.15 |
| Difference with placebo | — | 4.9 (0.0–9.8) | 2.8 (–2.1–7.7) | — |

Data are means ± SD or difference (95% CI). *P values are for paired t test comparison for study 1 and for existence of an overall treatment effect from ANOVA for study 2. †Numbers are lower because of missing blood samples for glucose data after 2 weeks in study 1 (n = 25 for the coffee period, n = 24 for the no coffee period) and for glucose data in study 2 (n = 41 for the coffee period, n = 43 for the caffeine period, and n = 42 for the placebo period). ‡Mean of values obtained after 25 and 28 days.

studies, caffeine intake acutely lowered insulin sensitivity over 100–180 min (7–9). In a study of 5 days of caffeine intake, complete tolerance to the effects of caffeine on fasting glucose concentrations developed (19), but effects on norepinephrine and free fatty acid concentrations partly remained for the high-dose caffeine treatment. Thus, effects of high amounts of caffeine on catecholamines and free fatty acids may have contributed to a decrease in insulin sensitivity in our studies. However, we cannot completely exclude the possibility that the elevated insulin concentrations after coffee consumption were due to higher insulin secretion (20) or to reduced hepatic insulin clearance as a result of increased free fatty acid concentrations (21).

Our findings seem to be at variance with the inverse association between coffee consumption and risk for type 2 diabetes that has been observed in cohort studies (2–6). Several factors may contribute to this discrepancy. First, the results of cohort studies may reflect the effects of decades of regular coffee consumption, whereas the present study compared 2–4 weeks of coffee consumption with 2–4 weeks of coffee abstinence. Second, we cannot exclude the possibility that the rapid transition to high coffee consumption (equivalent to ~13 conventional cups of coffee in study 1) in our studies had detrimental effects on insulin

sensitivity. For example, experienced psychological stress may have lowered insulin sensitivity through increased stress hormone concentrations. Third, habitual coffee consumption may improve aspects of glucose metabolism that are not reflected in the outcome parameters of the present study (for example, postprandial glucose metabolism).

In conclusion, the present results indicate that tolerance to the adverse effects of high coffee consumption on insulin-glucose homeostasis does not develop within a 4-week period. This stresses that it is premature to advocate high coffee consumption as a means to lower risk for type 2 diabetes. Long-term trials of coffee consumption that include detailed measures of insulin sensitivity and glucose metabolism are warranted to elucidate the apparent discrepancy with studies that observed an inverse association between habitual coffee consumption and risk for type 2 diabetes.

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