## Original article

# Effect of Caffeine on Plasma Glucose and Insulin Response to Mixed Meal Tolerance Test in Type II Diabetes

Moosa A S M[1], Akther S[2]

**Abstract**

*Caffeine containing beverages is widely used and popular world-wide. Studies showed that caffeine acutely decreased insulin sensitivity in young, non-diabetic adults.3-5 This double-blind study was carried out with habitual coffee drinkers who had at least a 6-months history of type II diabetes. The effects of caffeine on fasting glucose & insulin levels and on glucose & insulin response to a mixed-meal tolerance test were studied. The total daily caffeine intake was 375 mg in a divided schedule. Overnight fast and caffeine abstinence baseline fasting blood samples were drawn then after administration of caffeine (250 mg/day) or placebo they consumed a commercial meal that contained 75 gram of carbohydrate for mixed-meal tolerance test. Comparisons of the AUC2h values demonstrated significant caffeine effects for both plasma glucose and plasma insulin ($P < 0.05$) responses to the mixed-meal tolerance test. Caffeine did not affect the fasting levels of plasma glucose or insulin when compared with placebo. It may be concluded that acute administration of caffeine plus carbohydrate impaired post-prandial glucose metabolism and insulin responses. Such effects could have implication for the management of type II diabetic patients.*

**Introduction**

Caffeine containing beverages such as coffee, tea, coca cola, pepsi, chocolate are very popular world-wide. Caffeine is also a widely used drug despite evidence that it has deleterious consequences for health including diabetes[1]. In 1967, a study reported that drinking of instant coffee significantly impaired glucose tolerance in maturity onset diabetes[2]. Recent studies showed that caffeine acutely decreased insulin sensitivity in young, non-diabetic adults[3-5]. This study tested how oral caffeine affects carbohydrate (CHO) metabolism in type II diabetes patients, for whom decreases in insulin sensitivity might result in exaggerated hyperglycemic responses to glucose & other carbohydrates, which would aggravate the glycemic dysregulation found in this disease. The effects of caffeine on fasting glucose & insulin levels and on glucose & insulin response to a mixed-meal tolerance test (MMTT) were studied in this study.

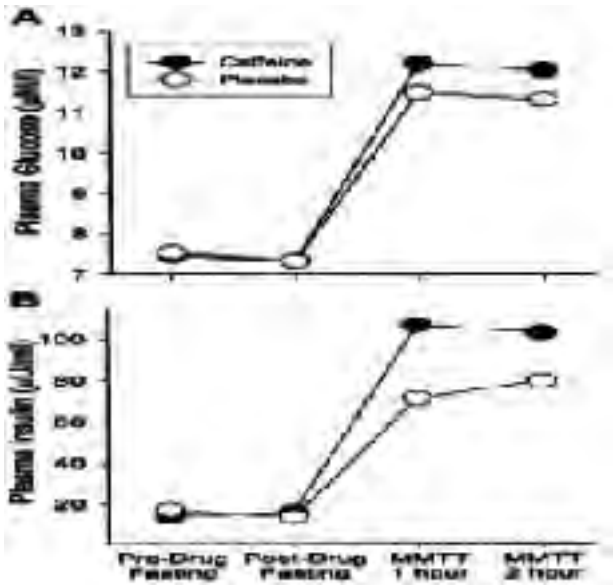
1. Dr. Abu Saleh Md. Moosa, MBBS, DA, MPhil (Pharmacology)
Consultant Anaesthesiologist, Islami Bank Hospital, Rajshahi.
2. Dr. Shahina Akther, DGO, FCPS (Gynae & Obs) Part II
Lecturer Physiology, Rajshahi Medical College, Rajshahi

**MATERIALS AND METHODS**

It was a double-blind, placebo-controlled cross-over study. Study group comprised of 14 habitual coffee drinkers (11 men & 3 women, age 61 ± 9 years) who had at least a 6-months history of type II diabetes. Their daily caffeine intake from all beverages averaged 526 ± 144 mg/day. Mean fasting plasma glucose level was 7.5 ± 1.6 mmol/L. All subjects were using oral hypoglycemic agents except three, they managed with diet and exercise. None required exogenous insulin therapy. They were free of major medical disorders, no such medications that affect glucose metabolism. All of them were non-smokers. Caffeine and placebo treatment were given in identical capsules. Each capsule containing either 125 mg anhydrous caffeine plus dextrose or dextrose only. The total caffeine dose (375 mg/day) was given in a divided schedule. Informed consent and screening data were collected about caffeine consumption before testing. The subjects also completed a 7-day diary of caffeinated beverage consumption, recording the serving size and time of day for beverage. They were studied on two different morning within a two week period, following overnight fast and caffeine abstinence. They took diabetes medications according to their usual treatment regimen. After 30 minute quiet rest, baseline fasting blood samples were drawn from forearm vein. Subjects ingested two capsule (caffeinated or placebo) with water. After 60 minute interval for caffeine absorption, a second set of blood sample was drawn. Subjects then ingested an additional one capsule (caffeinated or placebo) intended to maintained drug levels. Then they consumed a commercial liquid meal (Boost) that contained 75 gram of carbohydrate for MMTT. Subject remained sedentary and relaxed, reading or watching TV throughout the MMTT. Additional blood samples were drawn 1 and 2 hour after the meal. Plasma glucose levels were measured using Beckman Glucose Analyzer ll. Plasma insulin levels were measured by A double-antibody radioimmunoassay (Linco Research, St Charles, MO).

**STATISTICAL ANALYSIS**

To test the effects on responses to the MMTT, the incremental areas under the MMTT 2-h time curves (AUC2h) for glucose and insulin with the trapezoidal rule, using the post drug fasting value and the value 1 and 2 h after meal were calculated. Incremental areas were compared by a repeated-measures ANOVA. Data was




presented as mean ± SE. P < 0.05 was considered statistically significant.

**RESULTS**

Concentration-time curve for plasma glucose and insulin levels are shown in figure below. Effects of caffeine versus placebo on plasma glucose (A) and insulin (B) time curves with fasting and during the 2-h MMTT shown in figure.

Curves illustrate that caffeine increases glucose & insulin during MMTT Caffeine not affect fasting levels of plasma glucose or insulin. ± Caffeine ± Placebo

Comparisons of the AUC2h values demonstrated significant caffeine effects for both plasma glucose (P = 0.04) and plasma insulin (P = 0.01) responses to the MMTT. Average glucose AUC2h after caffeine administration (3.87 ± 0.30 mmol .1-1 . 2h-1 ) was 21% larger than the AUC2h after placebo (3.2 ± 0.36 mmol .1-1 . 2h-1 ). Comparisons of the AUC2h values demonstrated significant caffeine effects for both plasma glucose (P = 0.04) and plasma insulin (P = 0.01) responses to the MMTT. Average glucose AUC2h after caffeine administration (3.87 ± 0.30 mmol .1-1 . 2h-1 ) was 21% larger than the AUC2h after placebo (3.2 ± 0.36 mmol .1-1 . 2h-1 ). Average insulin AUC2h in caffeine condition (66.73 ± 10.49. μU-1 . ml-1. 2h-1) was 48% larger than that in the placebo condition (45.17 ± 5.98μU-1 . ml-1. 2h-1).

Acute administration of caffeine impaired post-prandial glucose metabolism in diabetic patients. In contrast to non-diabetic subjects,[3-5] this study showed exaggerations of both glucose and insulin responses when caffeine was ingested with CHO. Daily consumption of caffeinated beverage with meals could produce higher average glucose levels that increase the risk of diabetes complications. Caffeine abstinence may have beneficial effect that compare favorably with oral agents used to control postprandial glucose. Despite these limitations, the result of this study raise concern about the potential hazards of caffeine for patients with type II diabetes and for individuals who are pre-diabetic.

**REFERENCES**

1. James JE: Caffeine and Health. New York, Academic Press, 1991

2. Jankelson OM, Beaser SB, Howard FM, Mayer J:Effect of coffee on glucose tolerance and circulating insulin in men with maturity-onset diabetes. Lancet 1967;1:527-529

3. Graham TE, Sathasivam P, Rowland M, Marko N, Greer F, Battram D: Caffeine ingestion elevates plasma insulin response in humans during an oral glucose tolerance test. Can J Physiol Pharmacol 2001;79:559-565

4. Greer F, Hudson R, Ross R, Graham T: Caffeine ingestion decreases glucose disposal during a hyperinsulinemic-euglycemic clamp in sedentary humans. Diabetes 2001;50:2349-2354

5. Keijzers GB, De Galan BE, Tack CJ, Smits P: Caffeine can decrease insulin sensitivity in humans. Diabetes Care 2002;25:364-369