EFFECT OF CAFFEINE ON THE RISK OF CORONARY HEART DISEASE – A RE-EVALUATION

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ABSTRACT

The effect of caffeine intake on the risk of coronary heart disease was studied. Twenty-one rats used were randomly divided into three experimental groups, the first group served as the control while the second and third groups were administered caffeine orally at doses of 10mg/kg body weight and 20mg/kg body weight respectively for fourteen days. Caffeine, at 10mg/kg body weight, significantly increased ($P<0.05$) serum LDL- cholesterol concentration and coronary heart disease risk ratio while it significantly reduced ($P<0.05$) serum triacylglycerol concentration when compared with controls. At 20mg/kg body weight, caffeine significantly increased ($P<0.05$) coronary heart disease risk ratio while it significantly reduced ($P<0.05$) serum HDL- cholesterol concentration and serum triacylglycerol concentration when compared with controls. No dose response effect was observed possibly suggestive of a threshold effect. These results suggest that caffeine predisposes consumers of caffeine containing beverages to coronary heart disease.

KEY WORDS

Caffeine, Coronary heart disease, Blood lipids.

INTRODUCTION

Caffeine is a trimethylxanthine whose primary biological effect is the antagonism of the A1 and A2A subtypes of the adenosine receptors (1,2). Caffeine is found in many everyday products like coffee, tea, kola nuts, chocolate, soda beverages, drugs etc. Thus it is widely and immensely consumed. For example, an average American consumes 200mg of caffeine daily (3). In Nigeria and other third world countries, the consumption of caffeine has increased possibly as a result of culture assimilation.

The interest in researches pertaining to caffeine has been increasing in recent years, and this has resulted in a surge of publications dealing with a variety of pharmac-physiological effects of caffeine. Caffeine has been shown to have various pharmacological and cellular responses in a wide spectrum of biological systems (4). These include stimulation of the

central nervous system and cardiac muscle, increased urinary output, and relaxation of smooth muscles (5). It has been reported that caffeine increases endurance in well trained athletes thereby increasing the athlete's ability to increase the intensity or duration of exercise (6). However, caffeine consumption has been reported to increase urinary calcium levels and causes cardiac arrhythmia (irregular heartbeat) in certain people (7,8). It has also been reported to cross the placenta and blood brain barrier thus potentially inducing fetal malformation by affecting the expression of genes vital in development (9).

The fact that caffeine is contained in coffee has led to the overall assessment of the safety of drinking coffee. The publications on the effects of coffee on human health, especially pathogenesis of diseases, indicate that certain controversial issues are still unresolved (10-12). One of such unresolved issues is the correlation between coffee/caffeine intake and coronary heart diseases (13-17). Of recent, some researchers have reported that cafestol and kahweol (belonging to the diterpene family) are the active chemicals in coffee mechanistically responsible for the increase in serum cholesterol level after coffee consumption (18). Gordon *et al* (19) have also reported that increased total cholesterol

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concentration increases the incidence and prevalence of coronary heart disease. It thus implies that these chemicals are responsible for the increased risk of coronary heart disease associated with coffee consumption. In this study we have sought to verify whether caffeine (which is also contained in coffee) on its own increases the risk of coronary heart disease.

MATERIALS AND METHODS

Materials: Twenty-one male rats (*Rattus norvegicus*) weighing between 120 and 160g were obtained from the Department of Physiology, University of Ibadan, Ibadan, Oyo State, Nigeria. Caffeine was obtained from Sigma Chemical Company, U.S.A. The various serum lipid assay kits were obtained from Quimica Clinica Aplicada, S.A. Spain. Other reagents were of analytical grade.

Animal handling: The rats were kept in well-ventilated house conditions (temperature: 28-31°C; photoperiod: 12hr natural light and 12hr dark; humidity: 50-55%) and given normal rat chow (Bendel Feeds and Flour Mills, Ltd., Ewu, Nigeria) and water ad libitum. The twenty one animals used for this study were randomly divided into three experimental groups (A, B and C). Group A served as the control while groups B and C where administered caffeine orally at doses of 10mg/kg and 20mg/kg body weight respectively for fourteen days.

Sample collection and preparation: The rats were sacrificed at the end of the experimental period and the venous blood was collected into clean sample bottles. This was allowed to clot and then centrifuged at 3000rpm for five minutes after which the serum was separated and stored frozen until needed for analysis.

Determination of serum lipid parameters: The determination of serum total cholesterol concentration was done using the chod-pap method reported by Fredrickson *et al* (20) and Allain

et al (21). The determination of the serum HDL-cholesterol concentration was done using the dextran sulphate-Mg(II) method reported by Benzie (22). The determination of the serum LDL-cholesterol concentration was carried out using the polyvinyl sulphate method reported by Assmann *et al* (23). The determination of the serum triacylglycerol concentration was carried out using the glycerol-phosphate oxidase method described by Fossati and Prencipe (24). The coronary heart disease risk ratio (CHD risk ratio) was obtained by calculating the ratio of serum total cholesterol concentration to serum HDL-cholesterol concentration.

Statistical analysis: Data were analyzed using Least Significant Difference (LSD) test following one – way analysis of variance (ANOVA).using SPSS 10.0 computer software package. Differences at $P < 0.05$ were considered significant.

RESULTS AND DISCUSSION

The effect of caffeine on the serum lipid profile is shown in Table 1. Caffeine significantly increased ($P < 0.05$) coronary heart disease risk ratio at both doses administered when compared with control. However, the increase in serum LDL-cholesterol concentration observed after the administration of caffeine was only significant ($P < 0.05$) at the dose of 10mg/kg body weight while the reduction in HDL-cholesterol concentration observed was only significant ($P < 0.05$) at the dose of 20mg/kg body weight when compared with controls. The increase in serum total cholesterol concentration observed after the administration of caffeine was not statistically significant ($P > 0.05$) when compared with control. Many epidemiological studies have shown a strong inverse relationship between serum HDL-cholesterol concentration and the risk of coronary heart disease (25). Also, increased serum LDL-cholesterol concentration has been associated with increased risk of coronary heart disease (26). Thus, the increased serum LDL-cholesterol concentration and reduced

Table 1 : Effects of Caffeine on some serum lipid parameters in rat

Groups	Total cholesterol Concentration (mmol/L)	HDL-cholesterol Concentration (mmol/L)	LDL-cholesterol Concentration (mmol/L)	Triacylglycerol Concentration (mmol/L)	CHD risk ratio
Control	2.22 ± 0.08 ^a	1.45 ± 0.15 ^a	0.70 ± 0.10 ^a	1.25 ± 0.19 ^a	1.60 ± 0.11 ^a
Caffeine (10mg/kg body weight)	2.25 ± 0.16 ^a	1.12 ± 0.13 ^{a,b}	1.00 ± 0.09 ^b	0.80 ± 0.08 ^b	2.15 ± 0.19 ^b
Caffeine (20mg/kg body weight)	2.34 ± 0.09 ^a	0.99 ± 0.04 ^b	0.93 ± 0.11 ^{a,b}	0.87 ± 0.04 ^b	2.38 ± 0.14 ^b

Values are Mean ± SEM, n = 7. Values with different alphabetical letter superscripts are significantly different at $P < 0.05$.

serum HDL-cholesterol concentration coupled with increased coronary heart disease risk ratio observed in this study suggest that caffeine on its own may predispose those who take caffeine-containing beverages to coronary heart disease.

Caffeine significantly reduced ($P < 0.05$) triacylglycerol concentration at both doses administered when compared with control. The reduction of triacylglycerol concentration by caffeine intake may not imply any significance with respect to coronary heart disease. The National Institute of Health (USA) consensus on triacylglycerols and coronary heart disease held in 1993 failed to establish increased fasting triacylglycerol concentration as an independent risk factor (27). However, the finding in this study is in opposition to the report by Lewis *et al* (28) which stated that there is no association of caffeine and beverage intakes with triacylglycerol concentration. The reduction observed in the triacylglycerol concentration may imply that caffeine stimulates or increases the intake of triacylglycerols from the blood by tissues or it leads to an increased breakdown of triacylglycerols. It may also be that caffeine impairs the incorporation of triacylglycerol into lipoproteins in the liver. Since caffeine intake reduced triacylglycerol concentration, the possibility of triacylglycerol concentration serving as a risk factor should still be further investigated.

Also, there was no significant difference ($P > 0.05$) between the concentrations of the various lipid parameters in rats administered 10mg/kg body weight caffeine and those administered 20mg/kg body weight caffeine. Thus there was no dose response effect. This suggests a possible threshold effect, 20mg/kg body weight being the minimum at which coronary heart disease risk was noticeable. It also suggests the possibility of a dose response effect existing at lower dose range which was not evaluated by this study.

Although cafestol and kahweol in coffee have been implicated in increasing the risk of coronary heart disease by increasing serum cholesterol level after coffee consumption (18,19), the results of this study suggest that caffeine on its own also increases the risk of coronary heart disease.

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