Volume : 4 | Issue : 8 | Aug 2015 • ISSN No 2277 - 8179

Research Paper

Medical Science

KEYWORDS : Hypertension, Caffeine, Grape juice, BP.

Acute Effects of Caffeine Ingestion on Blood Pressure in Healthy Normal Volunteers

Dr. Himani D. Kodape Department of Physiology, Seth G. S. Medical College & KEM College, Mumbai.

Dr. Pushpa A. Pazare Department of Physiology, Seth G. S. Medical College & KEM College, Mumbai.

ABSTRACT

Introduction: Caffeine has direct stimulant effects on cardiovascular system at therapeutic doses. The ability of caffeine to increase vascular resistance is fraught with the development of hypertension. Hence, this study was conducted to confirm the acute effects of caffeine consumption on arterial blood pressure in healthy normal volunteers.

Methods: Blood Pressure (BP) was recorded before, immediately and 45-60 minutes after the administration of 250 mgs of caffeine and 100ml of grape juice in 80 healthy normal male volunteers randomized into two equal groups. Mean and Standard Deviation (SD) of Systolic BP (SBP), Diastolic BP (DBP), Pulse Pressure (PP) and Mean Arterial BP (MAP) in the study groups were statistically analyzed using Student's t test with level of significance defined at p value < 0.05.

Results: There was a statistically significant increase in SBP, DBP, MAP but not PP observed immediately after consumption in the caffeine group compared to the grape juice group. However, the increase in BP was transient and there was no statistically significant difference observed between the basal measurements and measurements after 45-60 minute in the caffeine group.

Conclusion: Experimental administration of caffeine in amounts comparable to those consumed in day to day life is followed by an acute and short lasting elevation in BP. Role of daily use of caffeine in the development of hemodynamic intolerance and hypertension needs to be evaluated in long term experimental studies in future.

Introduction:

Global consumption of caffeine has been estimated at 120,000 tons per year, making it the world's most popular psychoactive substance. This amounts to one serving of a caffeinated beverage for every person every day. More than 80% of the world's population ingests caffeine daily, making it the most widely consumed drug in history [1]. Although caffeine is frequently ingested in food (e.g., chocolate) and not infrequently in medication (e.g., some compound analgesics), global consumption is mostly attributable to three beverages: coffee, tea, and caffeinated soft drinks. Considering the ubiquitous and routine use of these beverages, exposure to caffeine is often life-long.

Caffeine is a methyl xanthene (IUPAC name: 1, 3, 7-Trimethylpurine-2, 6-dione) found in varying quantities in the seeds, leaves, and fruit of some plants. It is most commonly consumed by humans in infusions extracted from the seed of the coffee plant (*Coffea arabica*) and the leaves of the tea bush (*Camellia sinensis*), as well as from various foods and drinks containing products derived from the kola nut (*Cola acuminata*) [2]. Caffeine acts as competitive antagonist at adenosine receptors at concentrations well within the therapeutic range. Caffeine predominantly acts as a mild stimulant of central nervous system, temporarily warding off drowsiness and restoring alertness, at doses of usual dietary consumption[3]. Nevertheless caffeine has been to found to exert significant actions on cardiovascular system, renal system and skeletal muscles at doses of dietary consumption[3].

The extensive global prevalence of caffeine use raises serious concerns about the possible impact of the drug on the health of caffeine consumers. The suggestion that dietary caffeine could have a role in disease processes is biologically plausible and have been studied in many epidemiological studies. Caffeine has direct stimulant effects on cardiovascular system at therapeutic doses. The ability of caffeine to increase vascular resistance is fraught with the development of hypertension. The epidemiology of caffeine and cardiovascular disease are closely linked with the epidemiology of caffeine and its effects on BP [4]. However the present epidemiological data on association of caffeine consumption with rise in BP is unequivocal, with many studies showing no association between dietary caffeine and BP[5], while many others reporting a significant positive association for increase in systolic or diastolic pressure or both[6]. The role of confounding factors like smoking, psychological stress and pre-existing co-morbid conditions could not be ruled out in these studies.

Hence, this experimental study was conducted to confirm the acute effects of caffeine consumption on arterial blood pressure in healthy normal volunteers and compared with the control group receiving grape juice.

Methods:

The study was conducted in 80 healthy male medical students aged between 18-22 years, studying in 1st year MBBS of a Tertiary Health Centre of Municipal Corporation of Greater Mumbai. Approval of the study protocol was obtained from the Institutional Ethics Committee prior to initiation of the study. The study procedure was duly explained and written informed consent was obtained from the study participants.

The study participants were then randomly allocated into test group and control group having 40 male healthy volunteers in each group. Chronic smokers were excluded from the study. The participants were abstained from ingestion of caffeinated beverages, chocolates and smoking 12 hours prior to the study. BP was recorded under standard conditions using mercury sphygmomanometer of appropriate cuff size (covering 80-100 % of the arm circumference & a good quality stethoscope) by auscultatory method. Each student was asked to sit quietly for 3 minutes before BP was recorded. Average of two readings used for analysis. The same sphygmomanometers was used for all students. Following the recording of basal BP at 9 a.m., 250 mg caffeine tablet was administered to participants in the test group and 100 ml of grape juice was administered to the participants in the control group respectively. The caffeine tablets were procured from XXXXXXX for the purpose of the study. Immediately after the administration, BP was recorded in sitting position on right arm and BP recording was repeated after 45-60 minutes. Pulse Pressure (PP) and Mean Arterial Blood Pressure (MAP) were calculated from the values of Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP).

Statistical analysis:

Mean and standard deviation (SD) of SBP, DBP, PP and MAP were calculated and statistically analyzed using Student's unpaired t test between the test and control groups, and Student's paired t test within the same group, with level of significance defined at p value < 0.05.

Volume : 4 | Issue : 8 | Aug 2015 • ISSN No 2277 - 8179

Results:

The mean values of basal SBP, SBP immediately after ingestion of 100 ml of grape juice and SBP 45-60 minutes after the ingestion were 116.8 ± 10.2 mmHg, 116.05 ± 9.03 mmHg and 115.8 ± 8.71 mmHg respectively. While the mean values of basal DBP, DBP immediately after ingestion of grape juice and DBP 45-60 minutes after ingestion 73.95 ± 7.5 mmHg , 73.70 ± 6.94 mmHg and 73.9 ± 7.1 mmHg respectively. The mean values of PP were 40.45 ± 7.5 mmHg, 40.95 ± 7.6 mmHg, 41.6 ± 7.5 and the mean values of MAP are 89.84 ± 8.7 mmHg, 88.75 ± 8 mmHg and 88.3 ± 7.5 mmHg, basally, immediately after ingestion of grape juice and 45-60 minutes after ingestion of grape juice respectively. There was no increase in SBP, DBP and PP but, there is slight decrease in MAP which was not statistically significant.

The mean values of basal SBP, SBP immediately after ingestion of 250 mgs of caffeine tablet and SBP 45-60 minutes after the ingestion were 121.6 ± 7.8 mmHg, 134.1 ± 8.2 mmHg and 134.5 ± 7.7 mmHg respectively. While the mean values of basal DBP, DBP immediately after ingestion of grape juice and DBP 45-60 minutes after ingestion were 75.45 ± 7.3 mmHg, 87.25 ± 4.8 mmHg and 86.85 ± 4.7 mmHg respectively. The mean values of PP were 46.15 ± 5.7 mmHg, 46.85 ± 6.6 mmHg and 47.7 ± 6.4 mmHg and the mean values of MAP are 90.83 ± 7 mmHg, 102 ± 5.3 mmHg and 102 ± 5.7 mmHg, basally, immediately after ingestion of grape juice and 45-60 minutes after ingestion of caffeine respectively. There was a statistically significant increase in SBP of 12.5 mmHg, and DBP of 11.8 mmHg and MAP of 11.17 mmHg after consumption of caffeine from the basal levels. However there was only a slight increase in PP of up to 1.55 mmHg which was statistically not significant. There were no statistically significant changes in SBP, DBP, PP and MAP recordings between the readings immediately after caffeine ingestion and after 45-60 min of taking caffeine. These findings confirm that the rise in BP produced was transient and returned to approximately basal levels 45-60 minutes after the ingestion.

Fig 2. Shows the comparison in the BP parameters between control group and subject group immediately after taking Grape juice and Caffeine respectively. The mean SBP value in the caffeine group was 134.1 ± 8.2 mmHg compared to 116.05 ± 9 mmHg in the grape juice which is statistically significant (p value < 0.05). Similarly mean DBP value in the caffeine group was 87.25 ± 4.7mmHg compared to 75.1 ± 8.6 mmHg in the grape juice which is statistically significant (p value < 0.05). The mean value of PP in caffeine group was 46.85 ± 6.6 mmHg compared to 40.95 ± 7.6 mmHg in the control group and mean value of MAP was 103 ± 5.3 mmHg in the caffeine group and 88.75 ± 8 mmHg in the control group respectively. Both the values are statistically significant (p value < 0.05). There was an increase of 18.05 mmHg in SBP, 12.15 mmHg in DBP, 5.9 mmHg in PP and 14.25 mmHg MAP after consumption of Caffeine over Grape juice.

Fig 3. Shows the comparison in the BP parameters between control group and subject group 45-60 minutes after taking Grape juice and Caffeine respectively. The mean SBP value in the caffeine group was 134.5 ± 7.7mmHg compared to 115.8 ± 8.7 mmHg in the grape juice which is statistically significant (p value < 0.05). Similarly mean DBP value in the caffeine group was 86.85 ± 4.8 mmHg compared to 74.15 ± 8.1 mmHg in the grape juice which is statistically significant (p value < 0.05). The mean value of PP in caffeine group was 47.7 ± 6.4 mmHg compared to 41.65 ± 7.5 mmHg in the control group and mean value of MAP was 102.7 ± 5 mmHg in the caffeine group and 88.03 ±7.5 mmHg in the control group respectively. Both the values are statistically significant (p value < 0.05). There was an increase of 18.7 mmHg in SBP, 12.7 mmHg in DBP, 6.05 mmHg PP and 14.67 mmHg increase in MAP in even after 45-60 min of taking Caffeine over grape juice group.

Discussion:

There was an increase in BP levels after taking Caffeine in the range of 10-20 mmHg compared to the control group observed in our study. In previous studies acute BP elevations in SBP in the range of 5 to 15 mm Hg and in DBP in the range of 5 to 10 mm Hg are observed after experimental administration of caffeine in amounts comparable to those consumed in everyday life[7].

The pressor effects of caffeine may last for several hours and are evident in both men and women of all ages. Moreover, caffeine induced rise in BP has been frequently found to be synergistic with the effects of other pressor agents such as cigarette smoking and psychological stress. The epidemiology of caffeine and cardiovascular disease are closely linked with the epidemiology of caffeine and its effects on BP[8]. Five epidemiological studies have reported no association between dietary caffeine and BP[5,6,7,8,9], while six epidemiological studies have reported a significant positive association for systolic or diastolic pressure or both[6,10,11,12,13,14,15,16]. However, the role of confounding factors like smoking, psychological stress and pre-existing co-morbid conditions could not be ruled out in these studies.

In addition to interest in the general effects of caffeine on BP, there is also interest in the factors, if any, that encourage individual susceptibility to the BP-elevating effects of the drug. One such line of investigation suggests that increased sensitivity may be experienced by people with existing high BP, including people with borderline hypertension[17] and hypertension[18]. Similarly, there is evidence that caffeine may synergistically increase BP at times of psychological stress, resulting in profound rise in BP in individuals who are anxious or experiencing physical or psychological stress[19].

Several mechanisms have been postulated to account for the rise in BP observed following the consumption of caffeine. These mechanisms include

- Adenosine receptors, both A1 and A2 are primarily responsible for vasodilator effect. Inhibition of adenosine receptors by caffeine causes vasoconstriction and increased peripheral vascular resistance thus increased the blood pressure[9].
- Caffeine also act as a antagonist of endogenous adenosine and inhibits phosphodiesterases and promotes release of calcium ions from sarcoplasmic reticulum. Caffeine thereby stimulates calcium induced positive inotropic effect on cardiac muscle, which increases blood pressure[20].
- Caffeine causes the activation of general stress reactivity systems[20].

There have been very limited studies that studied the chronic hemodynamic effects of dietary caffeine consumption. Modest sustained fall in BP were reported following removal of caffeine beverages and replacement with decaffeinated alternatives in some clinical trials[21,22]. Subsequent studies have also confirmed the decrease in BP wherein ambulatory monitoring was used to measure BP level for extended periods. Confirmation of modest persistent elevations in systolic and diastolic pressures has also been provided by a recent analysis of experimental studies of the effects of coffee drinking on BP[23,24]. These findings are consistent with the consensus that antagonism of endogenous adenosine is the main mechanism of action responsible for caffeine induced elevations in BP.

The development of tolerance to pressor effects of caffeine consumption is supported merely by meagre empirical evidence. Moreover, the belief that dietary use may lead to complete hemodynamic tolerance is inconsistent with a large body of direct and indirect evidence. It is noteworthy that participants in studies of acute hemodynamic reactivity to caffeine are

typically drawn from the population of habitual consumers. A study in 1981 by Robertson *et al* [25] observed partial development of tolerance. This study has been widely misquoted as having demonstrated complete tolerance. Contrary to claims for the development of complete tolerance, participants in studies demonstrating caffeine-induced increases in BP represented the entire spectrum of consumers, ranging from essential non-users to high consumers. With regard to this diversity, the tolerance hypothesis predicts greater reactivity in low compared with high habitual caffeine consumers, and no such systematic difference in reactivity is evident in the findings[26].

Conclusions:

Experimental administration of caffeine in amounts comparable to those consumed in day to day life is followed by an acute and short lasting elevation in BP as confirmed by our findings. Role of daily use of caffeine in the development of hemodynamic intolerance and hypertension needs to be evaluated using other parameters of cardiovascular function *viz*., ECG, heart rate *etc*., and in different population groups with prehypertension and hypertension in long term experimental studies in future.

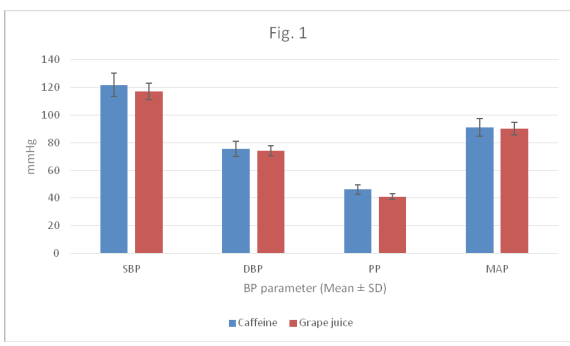

Fig 1. Shows the comparison in the BP parameters between control group and subject group before taking Grape juice and Caffeine respectively.

Unpaired t test level of significance $p < 0.05$

*- p value statistically significant

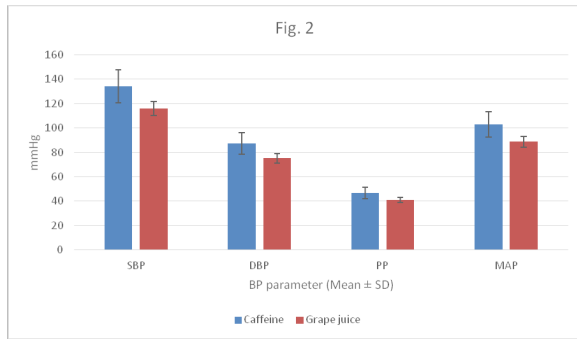

Fig 2. Shows the comparison in the BP parameters between control group and subject group immediately after taking Grape juice and Caffeine respectively.

Unpaired t test level of significance $p < 0.05$

*- p value statistically significant

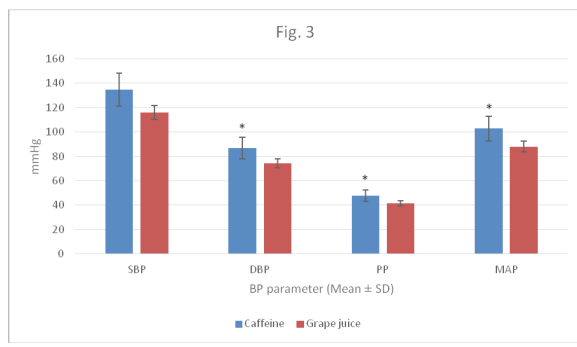

Fig 3. Shows the comparison in the BP parameters between control group and subject group 45-60 minutes after taking Grape juice and Caffeine respectively.

Unpaired t test level of significance $p < 0.05$

*- p value statistically significant

.

REFERENCE

1. Geoffrey Burchfield. In Meredith Hopes, ed. "What's your poison: caffeine". Accessed from http://www.abc.net.au/quantum/poison/caffeine/caffeine.htm on 21/09/2014. | 2. http://en.wikipedia.org/wiki/Caffeine Accessed on 20/09/2014. | 3. Arnaud MJ. The pharmacology of caffeine. Prog Drug Res. 1987; 31: 273–313. | 4. Johansson B, Georgiev V, Lindström K, Fredholm BB. A1 and A2A adenosine receptors and A1 mRNA in mouse brain: effect of long-term caffeine treatment. Brain Res. 1997; 762: 153–64. | 5. Bertrand CA, Pomper I, Hillman G, Duffy JC, Michell I. No relation between coffee and blood pressure. N Engl J Med. 1978; 299: 315–6. | 6. Birkett NJ, Logan AG. Caffeine-containing beverages and the prevalence of hypertension. J Hypertens Suppl. 1988; 6: S620–2. | 7. James JE. The influence of user status and anxious disposition on the hypertensive effects of caffeine. Int J Psychophysiol 1990; 10: 171–9. | 8. Jee SH, He J, Whelton PK, Suh I, King J. The effect of chronic coffee drinking on blood pressure: a meta-analysis of controlled clinical trials. Hypertension. 1999; 33:647–52. | 9. Stanton MF, Ahrens RA, Douglas LW. Coffee and cola beverage consumption as heart disease risk factors in man. Experientia. 1978; 34: 1182–3. | 10. Gyntelberg F, Hein HO, Suadicani P, Sorensen H. Coffee consumption and risk of ischaemic heart disease—a settled issue? J Intern Med. 1995; 237:55–61. | 11. Klag MJ, Wang N-Y, Meoni LA, Brancati FL, Cooper LA, Liang K-Y, Young JH, Ford DE. Coffee intake and risk of hypertension: the Johns Hopkins Precursors Study. Arch Intern Med. 2002; 162: 657–62. | 12. Lang T, Bureau JF, Degoulet P, Salah H, Benattar C. Blood pressure, coffee, tea and tobacco consumption: an epidemiologic study in Algiers. Eur Heart J. 1983; 4: 602–7. | 13. Lang T, Degoulet PEA. Relation between coffee drinking and bloodPressure: analysis of 6,321 subjects in the Paris region. Am J Cardiol. 1983; 52: 1238–42. | 14. Rogers P. Association of lifestyle and personality characteristics with blood pressure and hypertension: a cross-sectional study in the elderly. J Clin Epidemiol. 1992; 45:1061–70. | 15. Shirlow MJ, Berry G, Stokes G. Caffeine consumption and blood pressure: an epidemiologic study. Int J Epidemiol 1988; 17:90–7. | 16. Smits P., Boekema P., De Abreu R., Thien T., van'tLaar A. Evidence for an antagonism between caffeine and adenosine in the human cardiovascular system. J. Cardiovasc. Pharmacol. 1987. 10: 136–143. | 17. Lovallo WR, al'Absi M, Pincomb GA, Everson SA. Caffeine and Behavioral stress effects on blood pressure in borderline hypertensive Caucasian men. Health Psychol 1996; 15 11–7. | 18. Smits P, Pieters G, Thien T. The role of epinephrine in the circulatory effects of coffee. Clin Pharmacol Ther. 1986; 40: 431–7. | 19. Lane JD, Williams RB. Cardiovascular effects of caffeine and stress in regular coffee drinkers. Psychophysiology. 1987; 24:157–64. | 20. Robertson D, Frolich JC, Carr RK, et al. Effects of caffeine on plasma renin activity, catecholamines, and blood pressure. N Engl J Med. 1978; 298: 181-6. | 21. James JE. Chronic effects of habitual caffeine consumption on laboratory and ambulatory blood pressure levels. J C ardiovasc Res. 1994; 1: 159–64. | 22. van Dusseldorp M, Smits P, Thien T, Katan MB. Effect of decaffeinated versus regular coffee on blood pressure: a 12-week, double-blind trial. Hypertension. 1989; 14: 563–9. | 23. Biaggioni I, Olafsson B, Robertson RM, Hollister AS, Robertson D. Cardiovascular and respiratory effects of adenosine in conscious man. Circ Res. 1987; 61: 779–86. | 24. Coney AM, Marshall JM. Role of adenosine and its receptors in the vasodilation induced in the cerebral cortex of the rat by systemic hypoxia. J Physiol. 1998; 509:507–18. | 25. Robertson D, Wade D, Workman R, Woosley RL, Oates JA. Tolerance to the humoral and hemodynamic effects of caffeine in man. J Clin Invest. 1981; 67: 1111–7. | 26. James JE. Understanding Caffeine: A Bio behavioral Analysis. Thousand Oaks, CA: Sage Publications; 1997. |