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Effect of Caffeinated Energy Drink Consumption on Cardio-Reproductive Profile among Adolescent Saudi Men

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ABSTRACT

The objective of this study was to evaluate the effect of caffeinated energy drinks on penile mid shaft circumference and length, penile pulse amplitude, both systolic and diastolic blood pressures, and heart rate in response to erotic stimulation in young Saudi men living in Western region of Saudi Arabia (Makkah). In this free-living population study data was collected from100 men each (mild, moderate and heavy caffeinated energy drinkers) ages between 20 and 35 years with a mean age of 26.42 ± 10.69 years along with 100 age matched healthy nondrinkers who served as controls. Heavy caffeinated energy drinker group showed a significant increase ($p<0.0005$) in mid shaft penile circumference and length and penile pulse amplitude where as both systolic and diastolic blood pressures and heart rate also exhibited a significant increase ($P<0.025$, $P<0.0005$ and $P<0.005$ respectively. However this difference was found to be non-significant in mild drinker group when compared with nondrinker controls. We hypothesized that heavy caffeine intake seems to be associated with an improved fertility which in turn may produce a beneficial effect on men who have erectile dysfunctions. Our finding further indicated that long term intake of caffeinated drinks significantly increased the blood pressure as well as heart rate in healthy men which may act as a potential risk of hypertensive tendencies especially in adolescents Saudi population. We conclude that heavy use of caffeinated energy drinks causes significant alteration in the penile vasculature and cardiodynamics in a dose-dependent manner.

Keywords: Caffeinated energy drinks, penile vasculature, systolic and diastolic blood pressure, heart rate variability, young Saudi men

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INTRODUCTION

Energy drinks are most commonly used to increase energy, mental alertness as well as physical performance. Mostly Men between the ages of 18 and 35 years consume these energy drinks on regular basis. A part from caffeine, energy drinks also contain other ingredients such as sugars, taurine, ginseng, vitamin complex, glucuronolactone, herbs like yohimbe, carnitine, bitter orange and guarana which is another source of caffeine.

Regular use of these energy drinks has raises significant safety concerns for example according to a survey between 2007 and 2011, every one user out of ten was admitted to hospital and the number of energy drink-related visits to emergency departments of the hospital becomes doubled. On the other hand energy drinks have been found to improve physical performance and alertness and an improved reaction time although in some cases these drinks reduce steadiness of the hands[1]. Large amounts of caffeine in these drinks may cause serious problems related to heart and blood vessel like disturbances in heart rhythm and an increase in heart rate and blood pressure. Regular use of Caffeine is associated with anxiety, sleep disorders with increased risk-taking behavior, digestive system problems, and dehydration. Caffeinated drinks in combination with alcohol causes unconscious intoxication leading to the impairment of their motor coordination and reaction time. In a 16-oz. container of an energy drink about 55 to 65 grams of added sugar is present which can cause the chance of the onset of diabetes mellitus and metabolic syndrome. Caffeine in excessive amounts, such as that found in 4-6 cups of coffee per day (400 mg) or more can lower sperm counts [2].

Mode of action of caffeine is mediated via several mechanisms including antagonism of adenosine receptors, antagonism of benzodiazepine receptors, phosphodiesterase inhibition and the release of calcium from intracellular stores. Caffeine is retained quickly and absolutely in the small digestive tract in under one hour and diffuses quickly in different tissues. Caffeine is dissolvable in water and lipids, effectively crosses the blood-brain barrier, and can be found in all body liquids, including salivation and cerebrospinal liquid.

Excess use of caffeine might be associated with genuine heart and vein issues, for example, heart beat aggravations and expansions in pulse and circulatory strain. Among the Youngers Caffeine may hurt cardiovascular and sensory systems. Caffeine use may likewise be related with uneasiness, rest issues, stomach related issues, and drying out.

Caffeine can raise pulse and cause palpitations and additional pulses. Also involving a lot of it for significant stretches can build hazard of having a respiratory failure [3].

Cardiovascular risk factors like physical inactivity, alcohol consumption and smoking have been suggested to increase the risk of erectile dysfunction [4, 5]. Yet, little is known about other

factors that could have a potential benefit on erectile dysfunction such as caffeine intake [6, 7, 8, 9].

It was previously hypothesized that coffee and/or caffeine initiates a series of pharmacological effects that lead to the relaxation of the cavernous smooth muscle and that subsequently could improve erectile dysfunction [10]. Intake of caffeinated high energy drinks have been reported to have an inverse association by improving erectile function. In addition to being a major source of polyphenols, caffeine has the potential to increase testosterone levels [11, 12, 13]. It initiates the relaxation of the cavernous smooth muscle as well as it improves blood supply through penile arteries [14]. A survey report published by National Health and Nutrition and Examination (2001-2004), demonstrated that in United States non institutionalized male population, 2–3 cups of coffee per day was associated with a lower risk of erectile dysfunction, however, men with other complications such as obesity, hypertension and diabetes, were found to be at strong risk for erectile dysfunction [15].

Cardiovascular adverse effects have been widely reported in the literature using energy drinks.

A survey of 20 young healthy humans using high energy drink Red Bull showed that ingestion of a 355 mL can of Red Bull causes a cumulative cardiovascular load, by increasing systolic blood pressure to about 10 mmHg, diastolic blood pressure by about 7 mmHg, and heart rate by 20 beats/minutes, as well as decreasing cerebral blood flow velocity by 7 cm/s [16].

In a more recent study on fifteen recreational runners to complete five exercise trials, subjects ingested one of three energy drinks or a placebo one hour prior to testing, showed that after the fifteen minutes, systolic blood pressure was significantly higher in the three energy drink trials (163.87, 166.47, and 165.00) compared to the placebo trials (156) [17]. Similar results have been reported by Elitok et al.[18], who found that in 50 young, healthy subjects 2 hours after consumption of 355 mL of Red Bull, their systolic blood pressure increased from 112 to 121 mmHg, where as their diastolic blood pressure increased from 73 to 76 mmHg.

In a randomized cross sectional study of twenty-five young non-obese healthy subjects, Grasser et al.[19], showed that as a result of Red Bull consumption both systolic and diastolic blood pressure increased significantly as compared to water intake. Most common cardiovascular adverse effect associated with these drinks were found to be a 35 % increase in the onset of arrhythmias, increased hypertension, acute cardiac myopathies, coronary vasospasm, aortic aneurysm dissection, cardiac arrest and QT prolongation and and ST-elevation in the pattern of electrocardiograph. Other cardiac symptoms include reversible postural tachycardia syndrome, acute coronary thrombosis and myocardial infarction.

There is a paucity of research on the interplay between caffeinated high energy drinks intake, erectile dysfunctions and cardiovascular abnormalities. Moreover the active ingredients in energy drinks have not been thoroughly studied to confirm the cardiovascular safety, increased potency or the proclaimed energy-boosting benefits. There is an overwhelming lack of evidence to substantiate claims that components of energy drinks, contribute to the enhancement of physical or cognitive performance.

No sound information available about the effect of caffeinated energy drinks consumption on cardio-reproductive profile among adolescents in Saudi Arabia. Present study has been designed to evaluate the mechanisms involved in penile hemodynamics through which caffeinated energy drinks as an independent factor influence erectile status. The evaluation of the differential effect of these drinks on the arterial and venous components of penile vasculature and the mediating role of heart rate variability among a sample of younger aged male heavy drinkers from Saudi Arabia can be used to localize the pathophysiology of vasculogenic erectile dysfunctions in these individuals thus adding to a better understanding of this problem.

Therefore, the aims of this study are to investigate the association of caffeinated beverages with cardio-reproductive profile among adolescent Saudi men.

MATERIALS AND METHOD

Study Design

Present study was conducted in the Makkah Region of Saudi Arabia. Umm Al Qura University, Makkah Saudi Arabia, Ethical and Protocol review committee reviewed and approved the study

(Approval No. HAPO-02-K-012-2022-05-1076)**.** Prior to the study all the subjects were provided with a written informed consent.

A total of 300 men in communities within the Makkah region, were spoken. Subjects with the history of chronic urinary tract infection, testicular injury, varicocele, metabolic disorders like diabetes, hypertension and coronary heart diseases were excluded from the study.

For the experimental purposes 100 men each (mild, moderate and heavy energy drink) ages of 20 and 35 years with a mean age of 26.42 ± 10.69 years along with 100 ages matched non energy drinkers healthy participant were included in the study. We identified four beverages, coffee, total soda (regular and low-calorie), tea and energy and sport drink ***Red Bull™*** which were dichotomized (“Yes” / “No”) for their intake on any given day. Finally Red Bull™ was used as high energy drink in this study. Red Bull is a brand of energy drinks sold by Austrian company *Red Bull GmbH*. It is one of the most popular energy drinks globally. Since its

launch in 1987, more than 82 billion cans of Red Bull have been sold worldwide, including 7.9 billion in 2020. Each 250 ml (8.3 oz) can of Red Bull contain the following:

1000 mg of taurine

600mg of glucuronolactone

80 mg of caffeine

18 mg of niacin (niacinamide)

6 mg of calcium d-pantothenate (panto- thenic acid)

2 mg of vitamin B6 (pyridoxide HCI), vitamin B2 (riboflavin)

Energy drinkers were defined as subjects who were continuously consume energy drinks for at least 5 years. Taking the energy drink (Red Bull) less than five (<5) cans (250 ml) per day were classified as mild energy drinkers between 5 and 10 cans of energy drink per day as moderate and more than ten (>10) cans per day as heavy energy drinkers.

Experimental Procedure

All recordings were done on a Grass polygraph; while asking the subject to sit relaxed on an easy chair at approximately 70^0 F. whilst left alone in the room subject was asked to fit the penile transducers. Plathesmograph and blood pressure cuff were fitted by the experimenter. Subject was asked for the masturbation through the fantasy by exciting a sexual image as possible and to maintain it until asked to stop and baseline values for all parameters were recorded. Penile vasculature and cardiovascular responses were assessed using simultaneous monitoring of penile mid shaft circumference and length, penile pulse amplitude, systemic arterial systolic and diastolic blood pressures and heart rate during laboratory based erotic stimulation in all the subject groups according to the method described previously [20].

The degree of erection to erotic stimulation distinguished between energy drinkers & non non-energy drinkers etiologies.

For each individual systolic and diastolic blood pressure and heart rate were measured three times with 10–15 min intervals in the sitting position and at the resting state.

In most of the cases calibrated mercury sphygmomanometers were used while the use of electronic devices was kept to the minimum. The mean of each blood pressure and heart rate value was calculated by dividing the total values on the number of measurements and the difference between the maximum and minimum heart rate was calculated.

Statistical analysis

Comparisons between mild, moderate and heavy drinkers were performed by Student *t* tests using SPSS program 17.0 (SPSS Institute, Inc.; Chicago, IL, USA) software. Logarithmic transformation of penile amplitude scores was use in all cases to normalize the data.

All results were tabulated as mean ± standard deviation.

In all the instances probability ($p<0.05$) was regarded as statistically significant.

RESULTS AND DISCUSSION

Data for the measurement of penile mid shaft circumference and penile length in response to film and fantasy in energy drinker (100 each) in comparison with 100 age matched non-energy drinkers are presented in figures- 1 and 2 respectively.

A consistent increase in the level of penile circumference and length in the energy drinker groups was observed, being significant in moderate drinkers ($p<0.005$), and highly significant in heavy drinker group ($p<0.0005$). However this difference was found to be non-significant in mild drinker group when compared with nondrinker controls.

The estimated values of penile pulse amplitude of the drinker groups and their age matched nondrinker controls are presented in figure-3.

Exactly in a similar manner a consistently increased level of penile pulse amplitude was noted in almost all the drinker groups.

The values of the penile pulse amplitude were found to be significant ($p<0.005$) and highly significant ($p<0.0005$) in moderate and heavy drinkers respectively than their respective controls. However this difference was found to be non-significant in mild drinker group when compared with nondrinker controls.

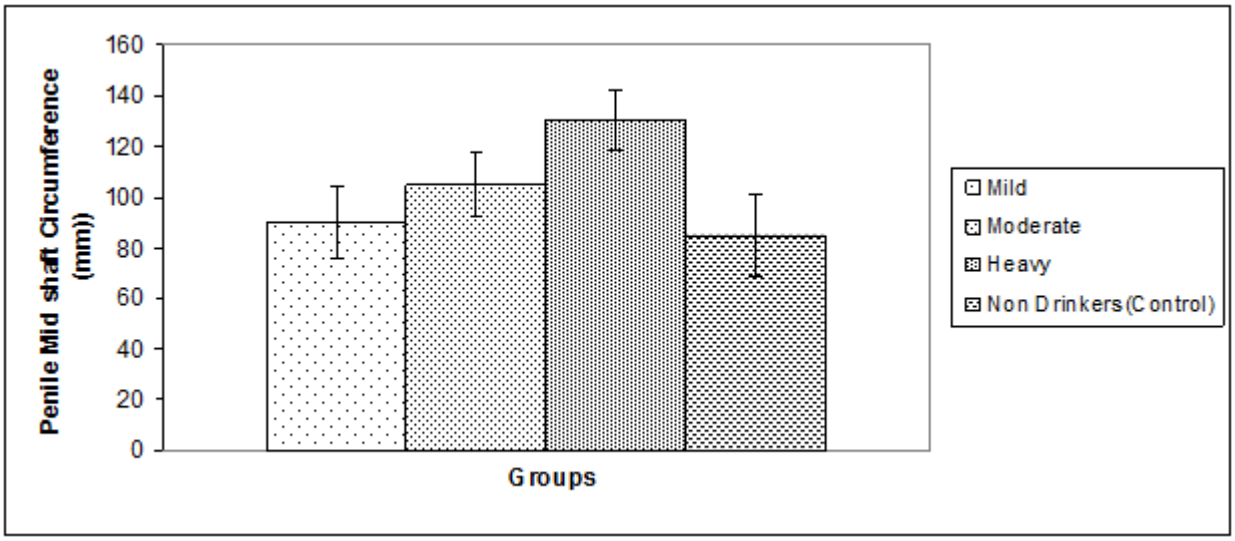

Figure 1: Changes in penile mid shaft circumference (mm) in mild, moderate and heavy drinkers compared with the age matched nondrinker group in Saudi young men.

Values are Mean ± SD, (n = 100). ***Note:*** n = Total number of subjects examined.

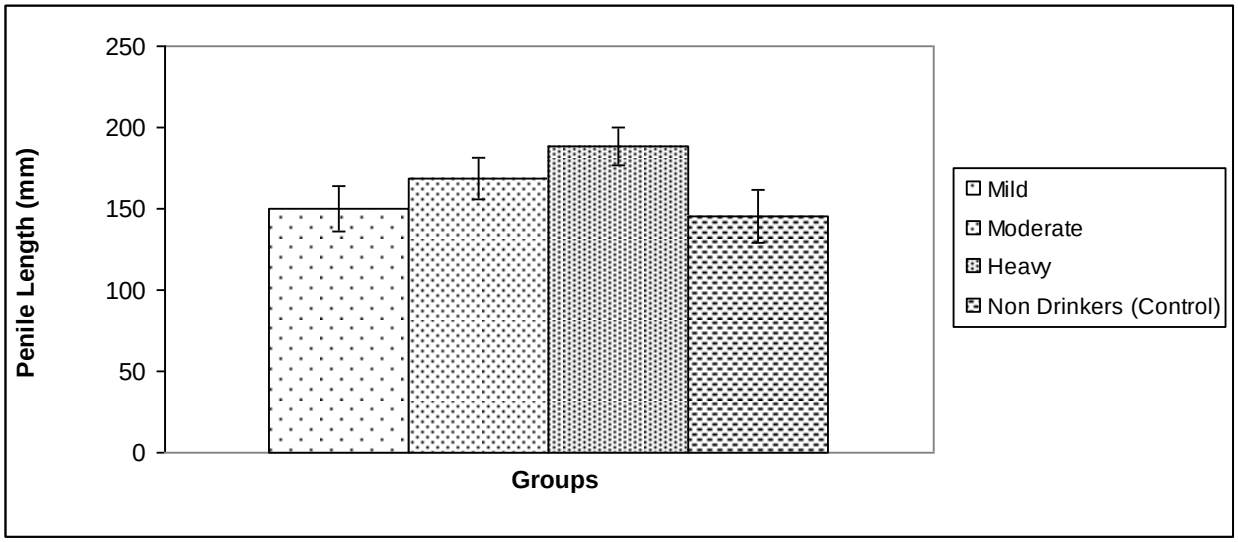

Figure 2: Changes in penile length (mm) in mild, moderate and heavy drinkers compared with the age matched nondrinker group in Saudi young men. Values are Mean ± SD, (n = 100). *Note:* n = Total number of subjects examined

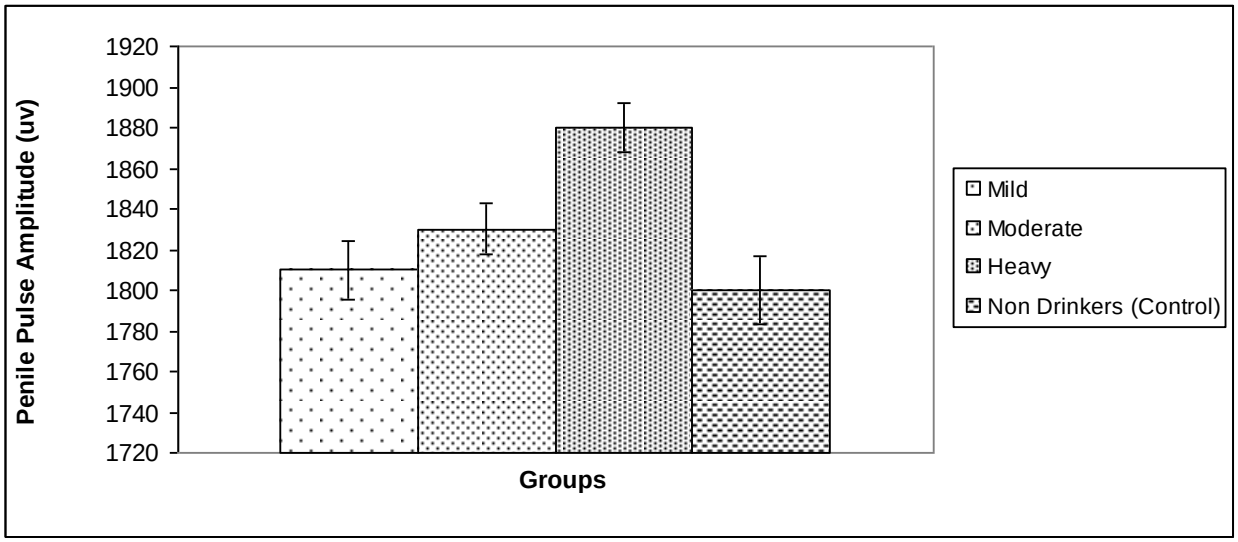

Figure 3: Changes in penile pulse amplitude (UV-Thousands) in mild, moderate and heavy drinkers compared with the age matched nondrinker group in Saudi young men. Values are Mean ± SD, (n = 100). *Note:* n = Total number of subjects examined.

Both moderate and heavy drinker groups showed a significant increase ($p<0.025$) in the values of systolic blood pressure (Figure 4) whereas the values of diastolic blood pressure were found to be significant ($p<0.005$) and highly significant ($p<0.0005$) in moderate and heavy drinkers respectively than mild drinker group and their respective controls (Figure 5).

Both moderate and heavy drinkers showed a significant increase in the values of heart rate ($P< 0.005$) respectively when compared with mild drinkers and the respective control group. However this difference was found to be non-significant in mild drinker group when compared with nondrinker controls (Figure 6).

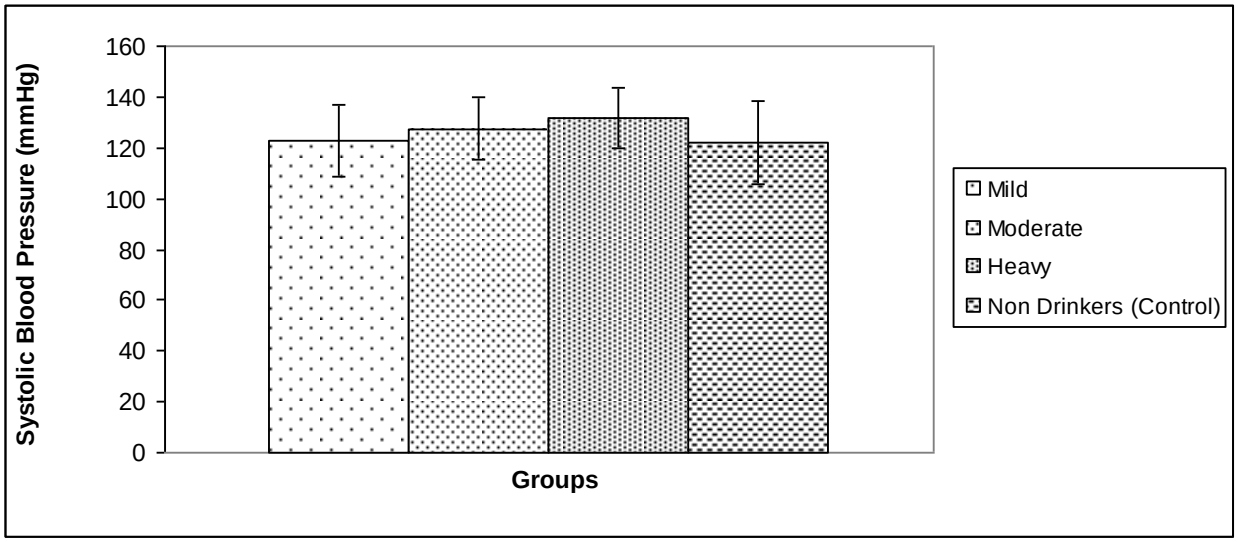

Figure 4: Changes in systolic blood pressure (mmHg) in mild, moderate and heavy drinkers compared with the age matched nondrinker group in Saudi young men. Values are Mean ± SD, (n = 100). *Note:* n = Total number of subjects examined

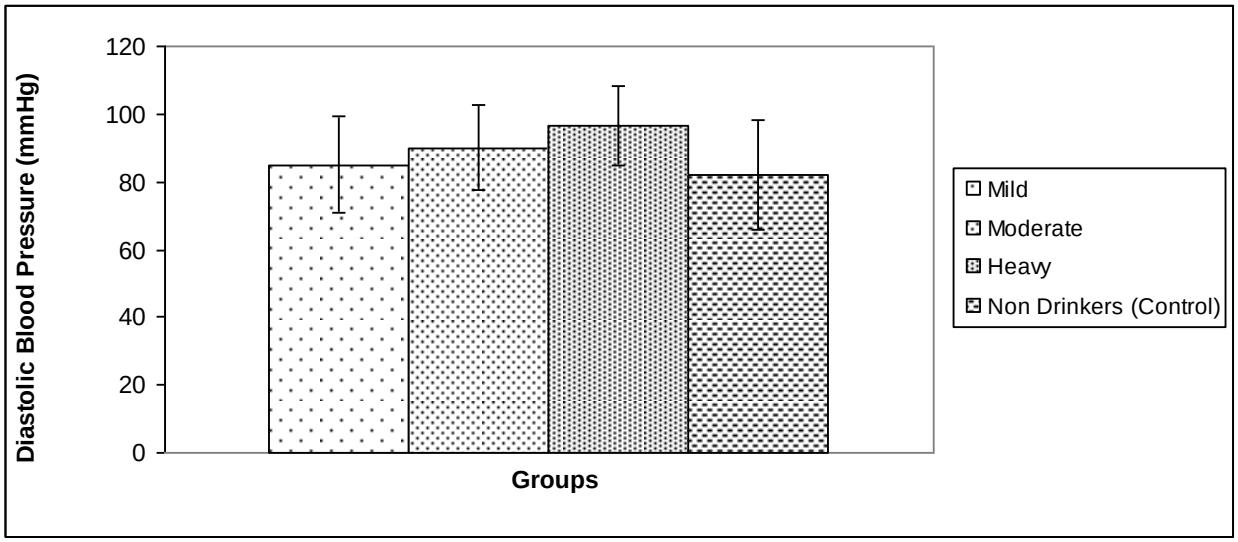

Figure 5: Changes in diastolic blood pressure (mmHg) in mild, moderate and heavy drinkers compared with the age matched nondrinker group in Saudi young men. Values are Mean ± SD, (n = 100). *Note:* n = Total number of subjects examined

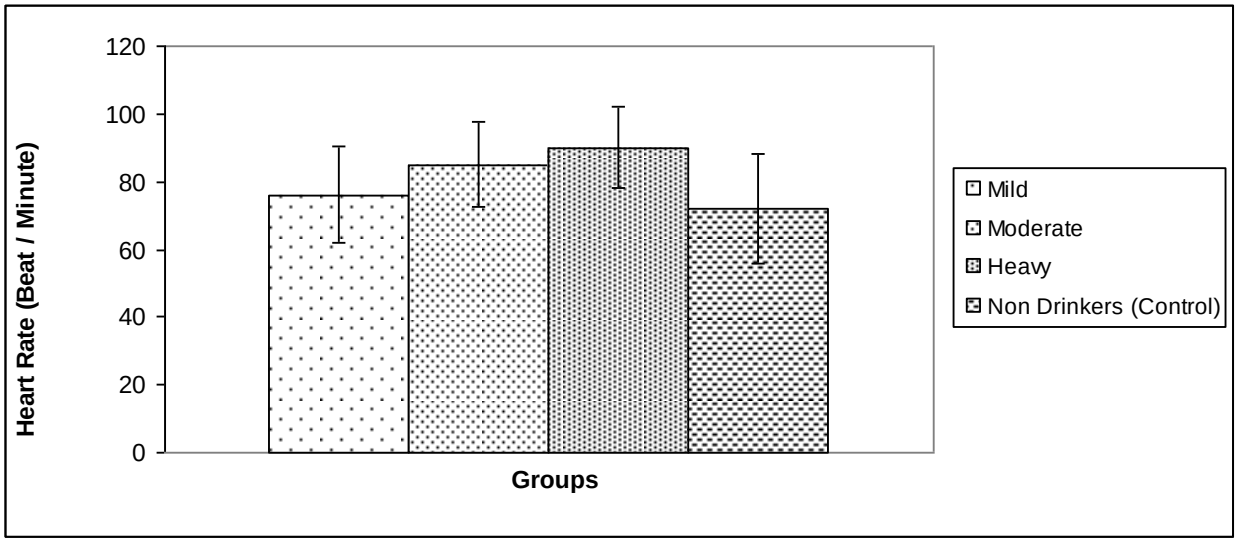

Figure 6: Changes in heart rate (beat / minute) in mild, moderate and heavy drinkers compared with the age matched nondrinker group in Saudi young men. Values are Mean ± SD, (n = 100). ***Note:*** **n = Total number of subjects examined.**

In the recent years, there has been increasing recognition that many cases of erectile dysfunctions are due, at least in part, to physical factors. In addition to parasympathatically mediated arterial vasodilatation, there may also be active reduction of venous drainage [21], and the active closure of intra cavernosal arterio-venous shunts [22].

Our results indicated that during the period of erotic stimulation penile mid shaft circumference, penile length, and penile pulse amplitude exhibited a highly significant increase ($P<0.0005$) in heavy drinkers group, however this difference was found to be less significant in moderate drinkers group ($P<0.005$) and non-significant in mild drinkers group when compared with their respective nondrinker control group. These results are in agreement with two population based previous findings which showed an inverse association between high energy caffeinated drink intake and erectile dysfunctions [23, 24]. An improved erectile response in these individuals may be due to some underlying biological mechanism, since caffeine in these drinks triggers a series of pharmacological actions on penile helicine arteries, and the cavernous smooth muscle that caused the relaxation leading to an increase in penile blood flow [25, 26].

However, our result totally differs from other previous cross sectional findings which showed no correlation between high energy caffeinated drinks consumption and erectile responses [27, 28].

It is of great interest that we found a lower prevalence of erectile dysfunction among men with high energy caffeinated drink intake, especially when this is equivalent to more than 5 cans 2–3 daily (400 mg/day). Similar amount of caffeine intake was found to be associated with beneficial effects on cardio-sexual factors and cardio-vascular health previously [29]. Our

results are further in conformity with a recently published study in which American men age 35 to 54 years had a caffeine intake of 336 mg per day, (close to our amount of caffeine) having a significantly inverse association with erectile dysfunction [30].

Many studies have shown potential health benefits for various health outcomes as a result of Coffee intake [31, 32, 33]. Very limited data is available in the literature regarding the independent association between caffeine intake and erectile responses. Results of our cross section population based studies are in confirmation with the previous findings, in which an inverse association has been documented [34, 35]. However in another population-based 5 years follow-up prospective study of 202 Finish men with erectile dysfunctions, no association between caffeine consumption and erectile responses were observed [36].

We found an increase in the values of systolic and diastolic blood pressures and heart rate in both heavy and moderate drinker groups whereas this difference was found to be non-significant in mild drinker group when compared with their respective control subjects.

Although several studies have been published in the recent years on this topic, however, there is no firm consensus on the relationship between caffeinated high energy drinks and blood pressure and heart rate and this issue still remains controversial due to multiple confounding factors since the precise effect of caffeinated drink habits on blood pressure and heart rate is unclear. According to a study conducted with fifteen healthy adults, after abstaining from caffeine for 48 hours, participants were asked to take 500 mL of a caffeinated energy drink daily for the next 5 days. Heart rate and systolic blood pressure were found to be increased by 5-7 beats/min and 10 mmHg, respectively, however no significant ECG changes were noted in these subjects thus summarizing that cardiovascular effects were greater after five days of consumption than after the first day of consumption [37]. In an other study energy shot users showed significantly high diastolic blood pressure when compared to both the no drink and placebo drink conditions [38]. Results of both the above mentioned finding are in conformity with our studies. Consumption of energy drinks and the development of cardiovascular ailments such as atrial fibrillation are documented in a number of published studies. For example, in a 16-year-old boy after consuming an unknown amount of Red Bull™ mixed with vodka atrial fibrillation was noted [39].

Caffeine is a methylxanthine which generally causes an increase in sympathetic nerve activity due to inhibition of phosphodiesterase. As a result an elevation in myocardial cyclic AMP occurs which exerts a positive inotropic effect on the myocardium. At the same time, the inhibition of adenosine receptors stops the negative inotropic effect elicited by adenosine, thus blocking the vasodilatory effect of adenosine and its inhibitory effects in platelet aggregation, catecholamine levels, renin release, and lipolysis. Therefore caffeine administration may increase blood pressure as well as an increase in the levels of

catecholamine, renin, and free fatty acid in the plasma [40]. It is thus very well clear from the literature survey that caffeine moderately increases blood pressure and heart rate [41, 42] and a drop in myocardial blood flow [43]. However, the exact amounts and concentrations ideal minimize the health risks are still not very clear. In a more recent meta-analysis of cohort study revealed that coffee consumption reduced the risk of hypertension in a dose–response manner [44]. An acute increase of blood pressure in hypertensive patients has also been reported by Mesas el al. [45].

In the present study, we included only non-hypertensive individuals. Our results suggested an acute increase in both systolic and diastolic blood pressure elevation as well as a significant rise in heart beat / minutes in the moderate to heavy caffeinated drinkers. This increase may be attributed to the activation of caffeine receptors of the sympathetic ganglia leading to increase in norepinephrine release and elevation of blood pressure. The dose-effect correlation of high energy caffeinated drinks on heart rate was positive and significant in our studies. This may be interpreted as an effect of the caffeine which enhances local and systemic catecholamine release, and may also stimulate vasopressin release by acting as an adrenergic agonist. Our results are thus in conformity with most recently published data [46]. In agreement with our results, a prompt increase in heart rate and blood pressure has been observed in these individuals. The mechanism of acute caffeine-induced changes in heart rate variability is probably complex; however, most of the acute effects of caffeine on neuro-cardiovascular regulation have been mainly attributed to caffeine which is the main constituent of these drinks. Caffeine is known to exert both acute and chronic cardiovascular effects, mainly through sympathetic activation as a consequence of enhanced release of catecholamine. Indeed, caffeine is implicated in a wide spectrum of cardiac rhythm disorders, including transient sinus arrest and/or bradycardia, sinus tachycardia, atrial fibrillation, sinoatrial block, atrio-ventricular block, and ventricular tachyarrhythmias, therefore, caffeine may in part be associated with the changes in heart rate variability as observed after intake of these high energy drinks.

FOOT NOTE

This study is a part of ongoing M.Sc. Research project, Department of Physiology, College of Medicine, Umm-Al- Qura University, Makkah, Saudi Arabia

CONCLUSION

On the basis of our findings, we concluded that caffeinated energy drinks have a reduced likelihood to report erectile dysfunction among the younger aged Saudi men using about 175 to 400 mg caffeine per day. Caffeine seems to initiate a series of pharmacologic reactions which lead to the relaxation of the penile cavernous smooth muscle, and improve blood

supply through penile arteries due to inhibition of $Ca2^{+}$ signaling mechanism. Caffeinated energy drinks thus may seem to benefit men who have erectile dysfunctions.

Our finding further indicated that long term intake of caffeinated drinks significantly rises the blood pressure as well as heart beat in healthy men which may act as a potential risk of hypertensive tendencies especially in adolescents Saudi population. We suggest that caffeinated energy drink producers should display warning signs of the side effects / overdose especially for those individual who have underling cardiovascular ailments.

However, further additional large scale randomized, placebo controlled studies to investigate the potential adverse or beneficial effects of these beverages are needed.

In summery current study might serve to guide further studies investigating the pathophysiological basis of penile hemodynamics in caffeinated high energy drink user younger aged males.

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