

An Experimental Study of Short-term Physiological Effects of a Single Dose of Energy Drink in Healthy Male Medical Students

SOHAIL ATTAUR-RASOOL¹, MUHAMMAD AHSAN MUSTAFA², ZEESHAN IQBAL³, WAJIH-UR-REHMAN⁴, ASMA LUQMAN⁵, ASAD MAHMOOD KHAN⁶

¹Associate Professor, Nishtar Medical University, Multan.

^{2,3}Medical Student, Quaid-e-Azam Medical College, Bahawalpur.

⁴Assistant Professor Medicine, Bahawal-Victoria Hospital, Bahawalpur.

⁵Senior Registrar (Radiotherapy), Civil Hospital, Bahawalpur.

⁶Associate Professor Pharmacology, Faisalabad Medical University, Faisalabad.

Correspondence to Dr. Sohail Attaur-Rasool, BX-87, Street 4, New Sadiq Colony, Dubai Palace Road, Bahawalpur.

Email: sohailatta@hotmail.com, Mobile: 03336393910

ABSTRACT

Background: Energy drinks (EDs) target young adults with claims of improving stamina and alertness, using effects of Caffeine as the main ingredient.

Aim: To investigate acute effects of a single dose of EDs on physiological parameters in healthy males.

Design: Open-label, non-randomized study.

Place & duration of study: Department of Physiology, Quaid-e-Azam Medical College, Bahawalpur, Pakistan from June to 2015 to July 2016.

Methods: Sixty healthy male medical students underwent recording of heart rate (HR), blood pressure (BP), peripheral blood oxygen saturation (SpO₂), respiratory rate (RR), and reaction time (RT) on three occasions i.e. before; after 30 minutes; and after 60 minutes of consumption of a single dose of 500mL of EDs. Control-group subjects underwent the same measurements after drinking 2-glasses of plain water.

Results: We found significant rise in systolic BP ($P < 0.001$), diastolic BP ($P = 0.001$), mean arterial pressure ($P < 0.001$) and found significantly quick RT ($P = 0.001$) after consumption of EDs.

Conclusions: A single dose of energy drink increased BP and shortened reaction time in healthy adolescents.

Keywords: Energy drink, blood pressure, heart rate, mobile game, reaction time, oxygen saturation

INTRODUCTION

Energy drinks (EDs) are beverages that are being marketed with claims to improve energy, stamina, athletic performance and mental concentration. Caffeine is the most common ingredient in EDs, which is often combined with taurine, glucuronolactone, guarana, and B vitamins¹. Humans have been consuming caffeine for centuries, which is recognized as safe in doses less than 400 mg [2]. Although the safety profile of caffeine has been relatively well established, there is little published literature on the effects of multi-ingredient energy drinks often containing higher doses of caffeine. Previous case reports of overuse or concomitant alcohol intake had linked EDs with sudden cardiac death, coronary vasospasm, reversible postural tachycardia syndrome, and serious arrhythmias, including ventricular fibrillation³. When higher doses of caffeine are combined with these other substances, the subsequent effect cannot always be predicted.

Advertisements for the majority of EDs are targeted toward young adults who reported to have consumed 1-4 EDs/month⁴. A study on Pakistani medical students showed that more than a 3rd of these had been consuming excess amounts of caffeine and energy drinks primarily to cope up with stress⁵. A clinical review on adverse health events after ingestion of EDs found that >50% of their included case reports were related to the cardiovascular system, followed by neurological complaints⁶

Received on 13-03-2019

Accepted on 25-07-2019

The purpose of this study was to check the effect of a commonly available ED brand "STING" on physiological parameters of body among medical students of Quaid-E-Azam Medical College Pakistan.

METHODS

The study was an open-label, quasi-experimental, non-randomized trial with a three-stage, within-subject design. Study protocol was approved by the Ethical Review Committee of the Quaid-e-Azam Medical College/B.V. Hospital Bahawalpur. Pakistan. All subjects agreed to take part in the study voluntarily and signed an informed consent statement before participating. Assuming that difference in mean values from matched pairs of study groups is normally distributed with a standard deviation of 10; if the true difference in mean values between time points is at least 5, we required 35 pairs of study groups for rejecting the null hypothesis that this response is zero with 90% power

($1 - \beta$) at $\alpha = 0.05$ since

$$n = \frac{(z_{\alpha} + z_{\beta/2})^2 \sigma^2}{\delta^2} = \frac{(1.64 + 1.28)^2 0.10^2}{0.05^2} = 35$$

The study comprised of a study-group and a control-group. The study-group included 60 healthy male medical students, with a mean age of 21.1 ± 1.1 years. These subjects were non-smokers with regular sleeping habits, moderate caffeine consumption (1 to 3 glasses of caffeine-containing beverages per day) and infrequent energy drink consumption (less than one drink per month). The control-group included thirty-five age and BMI-matched male medical students.

On the day of experiment, subjects were told not to drink any caffeine containing beverage prior to the test and stop eating after 3:00 pm. They were also prohibited to engage in any exercise or heavy physical work. We ensured that recording of physiological parameters of participants started at 6:00 pm to avoid any diurnal variations. The recorded parameters included heart rate (HR), respiratory rate (RR), blood pressure (BP), oxygen saturation of peripheral blood (SpO₂) and reaction time (RT). Recordings were done in three stages; 1) before consuming energy drink; 2) after 30 minutes; and 3) 60 minutes after consumption of energy drink for study-group and plain water for control-group. The participants in study-group consumed a single dose (500ml) of STING® (Pepsi Co. Pakistan) energy drink. As indicated on the label of the drink available in Pakistan, it contains 100mg of caffeine. The amount of other ingredients contained in the beverage are not provided on the label. The participants in control-group were required to drink two glasses (500ml) of plain water. All recordings were done with subjects comfortably seated on a chair. In the first stage of data recording, parameters were recorded before consumption of ED or plain water. RR was measured by observation of respiratory excursion of chest wall and abdomen per minute. BP and HR were recorded with standard technique using an upper arm digital apparatus (Omron M2 Basic, Omron Healthcare Inc.) on the left arm of the subject. The device provided digital display of values of pulse, systolic (SBP), and diastolic (DBP) blood pressure. Pulse pressure (PP) was calculated as a product of difference between SBP and DBP [PP = (SBP) – (DBP)]. Mean arterial pressure (MAP) was calculate with the formula [MAP = (DBP) + $\frac{1}{3}$ (PP)]. SpO₂ is the percentage of hemoglobin saturated with oxygen and was measured with a digital pulse oximeter (Medisign PO8001, MANA & Co.). Pulse oximeter was applied to proximal phalanx of left index finger during measurements. We used a game running on android smartphone for estimation of RT. The game “World of Warriors: Duel” (ver 1.1.1), Mind Candy Ltd was available on Google Play, Google Inc., and displayed reaction time on smartphone screen. For estimation of RT, gameplay was launched by the researcher on his personal smartphone and microphones from the same phone were placed in subject’s both ears. Subject was instructed to tap on the touch screen of smartphone as quickly as possible after hearing the sound clue “Let’s fight” through the earphones (Figure 1). The time lag between appearance of sound through earphones and touching the screen is displayed as reaction time in seconds (Fig. 2). We repeated the RT gameplay three times and the mean of the values was entered in data sheet. After first stage of recordings, subject in study-group were given a 500ml dose of STING and control-group were given 2 glasses of plain water. In

the next two stages, all parameters of study-group and control-group were assessed after 30 minutes and then after 60 minutes of consumption of STING and plain water respectively.

Data were entered in software SPSS 17.0 and analyzed through the same. Mean \pm SD of all parameters were calculated. Repeated measures ANOVA, with Greenhouse-Geisser correction was conducted to assess whether there were differences between the mean scores. Post hoc tests using the Bonferroni correction were conducted to assess significance level for pair-wise differences between individual time points.

RESULTS

Our study-group population comprised of 60 male medical students with mean age of 21.13 years. The mean height of participants was 173 cm and mean weight was 68.7 kg yielding a calculated mean BMI of 23.0 kg/m². Our control-group included 35 healthy male medical students who were matched to study-group for age and BMI (Table 1).

Result indicated that among study-group, mean scores differed significantly between time points for SBP ($P < 0.001$), DBP ($P = 0.001$), MAP ($P < 0.001$), and RT ($P < 0.001$). As seen in Table 2, mean SBP before (121.18mmHg) ingestion of energy drink, significantly increased after 30 minutes (127.38 mmHg) and 60 minutes (126.50mmHg) after ingestion of energy drink. Mean DBP before (77.38mmHg) ingestion of energy drink, was also significantly raised after 30 minutes (80.92mmHg) as well as 60 minutes after (80.98mmHg) ingestion of energy drink. The value of mean scores of MAP before (91.98mmHg) showed a rise (96.40mmHg) 30 minutes after consumption of energy drink and was still raised (96.15mmHg) 60 minutes later. There was significant reduction in mean scores of RT from an initial value of 528 milliseconds to 500 milliseconds 30 minutes after ingestion of energy drink and was recorded as 508 milliseconds after 60 minutes. No significant difference was observed in values of HR, PP, SpO₂, and RR based on values recorded between three time points i.e. before, 30 minutes after and 60 minutes after ingestion of energy drink. Amongst participants of study-group, there were significant differences in SBP, DBP, MAP and RT between time points before ingestion of energy drink and 30 minutes after; as well as between before ingestion and 60 minutes after, are shown in Table 3. However, pair-wise significance of differences for SBP, DBP, MAP and RT were not statistically significant for time points between 30 minutes and 60 minutes after ingestion. For control-group, mean scores did not differ significantly between time points for any of the studied physiological parameters as seen in Table 3.

Table 1. Comparison of descriptive statistics of study-group (males, n=60) and control-group (males, n=35)

Parameter	Study-Group (Mean \pm SD)	Control Group (Mean \pm SD)	P-Value
Age (years)	21.13 \pm 1.17	21.23 \pm 1.26	0.69
Height (cm)	173.00 \pm 5.31	172.29 \pm 5.59	0.53
Weight (kg)	68.73 \pm 10.66	66.05 \pm 5.50	0.16
BMI (kg/cm ²)	23.0 \pm 3.45	22.26 \pm 1.70	0.23

Table 2. Comparison of physiological parameters before, 30 minutes after and 60 minutes after ingestion of a single dose (500mL) of energy drink (STING®) in study-group (males, n=60)

Parameter	Before (Mean ± SD)	After 30 min (Mean ± SD)	After 60 min (Mean ± SD)	P-Value
HR (BPM)	80.28 ± 12.37	79.98 ± 11.54	81.17 ± 11.52	0.42
SBP (mmHg)	121.18 ± 14.32	127.38 ± 14.55	126.50 ± 14.12	<0.001*
DBP (mmHg)	77.38 ± 9.61	80.92 ± 9.83	80.98 ± 9.01	0.001*
PP (mmHg)	43.80 ± 10.55	46.46 ± 11.59	45.51 ± 10.64	0.09
MAP (mmHg)	91.98 ± 10.25	96.40 ± 10.25	96.15 ± 9.76	<0.001*
SpO ₂ (%)	97.93 ± 0.89	98.20 ± 1.05	97.91 ± 0.90	0.05
RR (/min)	19.42 ± 5.12	20.30 ± 5.38	20.18 ± 5.81	0.07
RT (msec)	528 ± 40	500 ± 50	508 ± 60	0.001*

HR = heart rate, SBP = systolic blood pressure, DBP = diastolic blood pressure, PP = pulse pressure, MAP = mean arterial pressure, SpO₂ = peripheral oxygen saturation, RR = respiratory rate, RT = reaction time

Table 3. Pair-wise comparisons of significant mean scores to study effects of a single dose (500mL) of energy drink (STING®) in study-group (males, n=60)

Parameters	Significance of Mean Differences (I-J) ^a		
	Before vs. 30 min	Before vs. 60 min	30 min vs. 60 min
HR (BPM)	1.0	1.0	0.41
SBP (mmHg)	<0.001*	<0.001*	1.0
DBP (mmHg)	0.004*	0.007*	1.0
PP (mmHg)	0.11	0.44	1.0
MAP (mmHg)	<0.001*	<0.001*	1.0
SpO ₂ (%)	0.11	1.0	0.11
RR (/min)	0.11	0.30	1.0
RT (msec)	<0.001*	0.03*	0.81

a. Adjustment for multiple comparisons: Bonferroni post hoc test

* The mean difference is significant at P<0.05 level

HR = heart rate, SBP = systolic blood pressure, DBP = diastolic blood pressure, PP = pulse pressure, MAP = mean arterial pressure, SpO₂ = peripheral oxygen saturation, RR = respiratory rate, RT = reaction time

Table 4: Comparison of physiological parameters before, 30 minutes after and 60 minutes after ingestion of a 2-glasses (500mL) of plain water in control-group (males, n=35)

Parameter	Before (Mean ± SD)	After 30 min (Mean ± SD)	After 60 min (Mean ± SD)	P-Value
HR (BPM)	81.00 ± 12.28	80.77 ± 12.50	81.17 ± 12.40	0.50
SBP (mmHg)	122.94 ± 14.90	123.26 ± 14.89	123.71 ± 14.45	0.08
DBP (mmHg)	78.71 ± 10.53	78.14 ± 9.90	78.20 ± 9.80	0.12
PP (mmHg)	44.23 ± 9.61	44.82 ± 9.46	45.51 ± 9.66	0.14
MAP (mmHg)	93.45 ± 11.28	93.08 ± 10.88	93.37 ± 10.62	0.24
SpO ₂ (%)	97.91 ± 0.74	98.11 ± 0.79	98.02 ± 0.70	0.29
RR (/min)	19.94 ± 4.98	20.74 ± 4.23	21.03 ± 4.79	0.14
RT (msec)	530 ± 47	531 ± 46	532 ± 48	0.55

P-Value significant at <0.05

HR = heart rate, SBP = systolic blood pressure, DBP = diastolic blood pressure, PP = pulse pressure, MAP = mean arterial pressure, SpO₂ = peripheral oxygen saturation, RR = respiratory rate, RT = reaction time

Fig. 1. Screenshot of smartphone game prompting the player to tap on the screen as soon as possible for estimation of reaction time in study subjects.



Fig. 2. Screenshot of smartphone game showing reaction time (in seconds) after a tap on the screen in response to audiovisual stimulus for estimation of reaction time in study subjects.



DISCUSSION

The purpose of the study reported here was to examine short term physiological effects of EDs. The complete physiological response to EDs is not fully understood; however changes in BP and HR have been associated with intake of EDs⁷. Recent research has proposed that physiological response to consumption of energy EDs is best explained by actions of combination of caffeine and sugar, with negligible role of other ingredients. Caffeine present in EDs binds to Beta-adrenergic receptors present in heart muscle cells, which leads to an increase in the level of cyclic adenosine monophosphate (cAMP) inside the cells, mimicking the effects of Epinephrine. Cyclic AMP activates a large number of protein kinase-A molecules. The overall effect increases the rate of glycolysis and increases the amount of adenosine triphosphate (ATP) available for vascular smooth muscle contraction and relaxation⁸.

Variable acute hemodynamic effects of EDs suggest that magnitude and adverse effects depend largely on the amount of caffeine and sugar of a propriety formula. Placebo-controlled studies conducted on EDs containing high amount of sugars (Rockstar, Monster) have found significant rise in HR [9, 10]. In agreement with our study, HR did not change significantly in studies where EDs with low sugar content (5-h Energy) were consumed^{11,12}. We found significant elevations in SBP, DBP and MAP in agreement with recent research reports of acute cardiovascular effects of EDs [9-12]. Since Caffeine is rapidly absorbed and typically attains a peak concentration at about one hour after consumption, it provides an explanation for the early rise in BP. This effect may be sustained for several hours depending upon the fed state of the individual¹³. An interesting outcome of recent studies has led to the mechanism that caffeine related adverse changes in BP were only found in consumers who are non-habitual users and may take a high dose of caffeine as a recreational drink¹⁴. We have documented a rise in MAP after consumption of a single dose of ED, which was sparingly highlighted in available literature. The raised MAP is an indication that the heart has to work much harder than it should, causing stress on the heart. High MAP can result in advanced heart disease, blood clots, heart attack, and stroke. When high MAP is ongoing, heart muscles enlarge and grow thicker, and jeopardize life expectancy. When MAP goes up quickly in a short period of time, organs can fail⁷. Pulse pressure remained unaffected in our subjects because of simultaneous rise in SBP and DBP. The blood oxygen saturation levels (SpO₂) did not vary a significant amount throughout the recordings. These levels show how fast the subjects' metabolism rate is because if metabolic rate increases the levels of oxygen in blood also increases. Since there was no increase in blood oxygen saturation level in our subjects, we can assume that EDs did not significantly affect metabolic rate. In a study involving ingestion of one can (335mL) of a sugar-sweetened ED resulted in an increase in breathing frequency in contrast with our results. The authors have proposed a possible decreased blood flow capacity and increase in cerebrovascular resistance index as explanation of the effects¹⁵. The marketing slogans of leading brands of EDs

include claims of increased performance, concentration, vigilance and quick reaction speed. We used a novel method of a smartphone game to test RT in our participants. Our study has also reported quicker RT after consumption of a single dose of ED in accordance with available reports¹⁶. In a recent randomized controlled trial of healthy adolescents at CMH Lahore Medical College Lahore, Pakistan; mean RT recorded with PowerLab data acquisition system was significantly reduced after consumption of Red Bull ED¹⁷. The effects of caffeine on the central nervous system (CNS) are linked to the blockade of adenosine receptors, thus preventing decline in neuronal activity and subsequent increase in muscle recruitment¹⁸.

The limitations of this study include open-label nature of the protocol as well as the fact that we used interval recordings of data in contrast to researchers having facility of continuous data recordings including beat-to-beat cardiovascular data for improved accuracy of results. Physicians should be aware of adverse effects of EDs and should routinely ask for ED consumption in young patients seeking treatment for symptoms related to CVS.

CONCLUSIONS

Ingestion of a single dose of energy drink increases blood pressures and shortens reaction time in healthy adolescents who use energy drinks occasionally.

Financial Support: None

Conflict of Interest: None

REFERENCES

1. Reissig CJ, Strain EC, Griffiths RR. Caffeinated energy drinks - a growing problem. *Drug Alcohol Depend.* 2009; 99:1-10.
2. FDA to investigate added caffeine. US Food and Drug Administration Consumer Health Information; 2013. Available at: <http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM350740.pdf>. Accessed June 27, 2017.
3. Higgins JP, Tuttle TD, Higgins CL. Energy beverages: content and safety, *Mayo Clin Proc.* 2010; 85(11): 1033-41.
4. Malinauskas BM, Aeby VG, Overton RF, Carpenter-Aeby T, Barber-Heidal K. A survey of energy drink consumption patterns among college students. *Nutr J.* 2007; 6:35.
5. Rizvi AH, Awaiz M, Ghanghro Z, Jafferi MA, Aziz S. Pre-examination stress in second year medical students in a government college. *J Ayub Med Coll Abbottabad.* 2010; 22:152-5.
6. Ali F, Rehman H, Babayan Z, Stapleton D, Joshi DD. Energy drinks and their adverse health effects: a systematic review of the current evidence. *Postgrad Med.* 2015; 127:308-22.
7. Bichler A, Swenson A, Harris MA. A combination of caffeine and taurine has no effect on short term memory but induces changes in heart rate and mean arterial blood pressure. *Amino Acids.* 2006; 31: 471-6.
8. Guessous I, Eap CB, Bochud M. Blood pressure in relation to coffee and caffeine consumption. *Curr Hypertens Rep.* 2014; 16:468.
9. Nelson MT, Blitz GR, Dengel DR. Cardiovascular and ride time-to-exhaustion effects of an energy drink. *J Int Soc Sports Nutr.* 2014; 11:2.
10. Svatikova A, Covassin N, Somers KR, Somers KV, Soucek F, Kara T, et al. A randomized controlled trial of cardiovascular responses to energy drink consumption in healthy adults. *JAMA.* 2015; 314:2079-82.

11. Marczinski CA, Stamatos AL, Ossege J, Maloney SF, Bardgett ME, Brown CJ. Subjective state, blood pressure, and behavioral control changes produced by an "energy shot". *J Caffeine Res.* 2014; 4:57-63.
12. Phan JK, Shah SA. Effect of caffeinated versus non-caffeinated energy drinks on central blood pressures. *Pharmacotherapy.* 2014; 34:555-60.
13. Liguori A, Hughes JR, Grass JA. Absorption and subjective effects of caffeine from coffee, cola and capsules. *Pharmacol Biochem Behav.* 1997; 58:721-6.
14. Zimmermann-Viehoff F, Thayer J, Koenig J, Herrmann C, Weber CS, Deter HC. Short-term effects of espresso coffee on heart rate variability and blood pressure in habitual and non-habitual coffee consumers - a randomized crossover study. *Nutr Neurosci.* 2016; 19:169-75.
15. Grasser EK, Yepuri G, Dulloo AG, Montani JP. Cardiovascular and cerebrovascular effects in response to Red Bull consumption combined with mental stress. *Am J Cardiol.* 2015; 115:183-9.
16. Santos VG, Santos VR, Felipe LJ, Almeida JW Jr, Bertuzzi R, Kiss MA, et al. Caffeine reduces reaction time and improves performance in simulated-contest of taekwondo. *Nutrients.* 2014;6:637-49.
17. Tauseef A, Akmal A, Hasan S, Waheed A, Zafar A, Cheema A, et al. Effect of energy drink on reaction time, haemodynamic and electrocardiographic parameters. *Pak J Physiol.* 2017;13:7-10.
18. Lazarus M, Shen HY, Cherasse Y, Qu WM, Huang ZL, Bass CE, et al. Arousal effect of caffeine depends on adenosine A2A receptors in the shell of the nucleus accumbens. *J. Neurosci.* 2011; 31:10067-75.