Original Article

Effect of Red Bull on Histology of Renal Mesangium

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Abstract

Objective: To determine the consequences of energy drink (Red bull) on renal mesangium of albino rats.

Materials and Methods: This study was carried out at the Anatomy Department of King Edward Medical University, Lahore, from August 2018 to December 2019. It was an experimental randomized controlled trial. Total 90 adult albino male rats, 8-12 weeks old, weighing 130 to 160 grams were taken. Healthy animals were included. Rats were divided into three groups Group A and B experimental groups received 1.5ml/kg and 2.2ml/kg body weight of red bull energy drink, respectively. Group C received 1ml/kg body weight of distilled water.

Results: The mean initial and final weight of animals was around 150g and 170g, respectively. The mean paired kidney weight and relative tissue weight index for all three groups were found insignificant. Microscopic examination showed mesangial hypercellularity and vascular congestion in renal cortex of groups A and B, none in group C. These were significant among two experimental groups with a p-value less than 0.001.

Conclusion: It was found that the use of energy drinks induces histopathological changes in the renal mesangium.

Keywords: Energy drinks, red bull, renal mesangium.

Introduction

Consumption of energy drinks among youngsters has become fashion and it has been increasing day by day in few years throughout the world including Pakistan. The "energy drinks" are categorized as a type of drink that is supposed to lessen physical and mental fatigue, improve mental alertness and cognitive function. Most sportsmen and students trust energy drinks to increase physical and mental stamina.[1] Energy drinks are marketed towards young people with catchy names that convey the idea of strength, power, speed, and sexuality (e.g. Red bull, Full throttle, Power horse, Cocaine, and Daredevil etc.).[2] Alcohol is not present in these types of carbonated beverages. Customarily these canned drinks contain an increased amount of caffeine (>150 mg/L) and sugar in combination with plant stimulants and herbs known to have stimulant properties.[3] Their main ingredient is caffeine and taurine but they also have a combination of methylxanthines, B-vitamins complex, amino acids (carnitine, creatine).[3]

Caffeine in energy drinks is associated with diuresis and fluid-electrolyte imbalance. Undue caffeine intake can cause various psychological and physical signs and symptoms, including irritability, depression, anxiety, sleep disorders, nervousness, and headaches.[4] High blood pressure and dehydrated state are also associated with these forms of drinks. Long-term imbibing of caffeine can result in gastric problems like ulcers, gastroesophageal reflux disorder, or esophagitis.[5] Caffeinated energy drink ingestion showed damaging effects on serum creatinine and urea, ALT, AST, and ALP in rats[9], renal microvasculature, and accelerated progression to chronic renal disease.[6,7] Effects of taurine on renal and liver functions are inconclusive, with the majority of researchers examining energy drinks' effects attributing to caffeine and high sugar contents.[8]

Despite their beneficial effects, massive consumption of these drinks results in life-threatening conditions. Studies indicated that ingestion of the energy drinks affected serum biochemical parameters and hepatic enzyme levels. Studies are showing deranged renal parameters due to overconsumption of energy drinks. The utilization of energy drinks could prove equally hazardous in the long term use, damaging the ultramicroscopic structure of vital organs such as kidneys. Renal glomeruli are microscopic patterns of numerous blood capillaries present in the cortex of the kidney. These are involved in the filtration of blood. Damage to glomeruli diminishes the function of filtrating blood in kidneys, resulting in loss of proteins in urine and holding waste products in the body. Glomerular hypercellularity is one of the renal glomerular lesions, which is specified by a rise in the total number of cellular nuclei in various parts of the glomeruli. Glomerular hypercellularity is a frequently occurring lesion existing in several renal pathologies.[9]

Studies are yet to be done to illuminate the histopathological consequences of such drinks on kidneys[10], so this study is planned to highlight this aspect of impact.

The use of these drinks keeps on rising, but the knowledge about their potential side effects is still lacking. In this study, we aim to see the effects of the frequently used energy drink Red Bull upon the kidneys of Wister rats to determine its safe use by people and create awareness about the effects of these drinks on kidneys. This will open new avenues for research on many other soft drinks being used and will increase the knowledge of medical professionals and the general public about their effects on kidneys.

Materials and Methods

It was an experimental animal study. Total 90 adult albino male rats, 8-12 weeks old, weighing 130 to 160 grams were taken. Healthy animals were included. Sick animals, less than 8 weeks of age and less than 130g weight were excluded. Animals were kept in the Experimental Research Lab (Animal House) of the Postgraduate medical institute Lahore.

Tissue processing and staining were done at the Histology Laboratory of Anatomy Department, King Edward Medical University, Lahore.

Photography was performed at the Pathology Laboratory of King Edward Medical University, Lahore.

Table 1: Groups of animals and experimental intervention

Groups N = 30	*Intervention and dosage*	*Duration of administration*	*Route of administration*	*Day of sacrifice*
A	1.5ml/100gm[11]	8 weeks	Oral gavage	60th day of experiment
B	2.2ml/100gm[12]	8 weeks	Oral gavage	60th day of experiment
C	1ml/100g Distilled water	8 weeks	Oral gavage	60th day of experiment

The rats were sacrificed after 24 hours of the last dose. Kidneys were removed after dissection. Gross examination of kidneys was done specimens were placed in labelled jars. Microscopic examination was done after histological processing, Periodic acid-Schiff stain, hematoxylin, and eosin staining. All parameters were noted as follows:

Qualitative parameters	*Quantitative parameters*
Surface of kidneys	Weight of animal in grams
Color change of kidneys	Paired kidney weight in grams
Mesangial hypercellularity	Relative tissue weight index
Vascular congestion	

For microscopic examination, glomeruli were randomly selected and their mesangium was assessed for mesangial hypercellularity that is, an increase in extracellular material in the mesangium and more than 8 cells per mesangial area presented as mesangial hypercellularity.[13] For vascular congestion blood vessels were assessed which was taken as engorgement of vessels with blood.[14]

The data was analyzed by SPSS 20.0 (Statistical Package for Social Sciences). Mean ± SD (Standard deviation) was given for quantitative variables.

Frequencies and percentages were given for qualitative variables. For quantitative variables comparison among groups was made by applying One Way ANOVA. Post hoc analysis was done by Tukey's test. For qualitative variables, the Chi-square test was applied to make a comparison among groups. P-value ≤ 0.05 was taken as statistically noteworthy.

Results

The mean initial weight of animals was around 150 grams with 151.2±5.7g in group A, 152.1±5.7g in group B, and 152.7±5.3 g group C. The difference among the three groups at the initial stage of the experiment was insignificant with a p-value of 0.577.

The mean final weight of animals was around 170 grams with 171.7±6.9g in group A, 171.9±6.3g in group B, and 172.7±5.1g in group C. The difference among the three groups at the final stage of the experiment was insignificant with a p-value of 0.798.

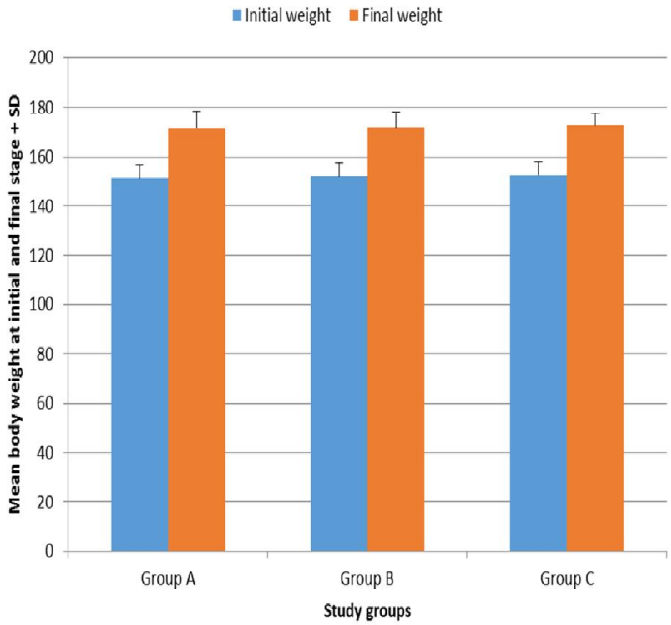

Figure 1: Component bar diagram representing the status of mean bodyweight of animals among three study groups (at the final stage of the experiment)

The mean paired kidney weight for group A was 1.81±0.16 g, 1.82±0.17g for group B, and 1.76±0.17g for group C. Difference among the three groups was found insignificant with a p-value of 0.354. The surface and color of kidneys were found smooth and normal respectively, for all animals in all three groups. So, being constant these parameters were not tested for significance among the three groups.

The mean relative tissue weight index of group A was 1.051 and for the group B was 1.060. The mean index for control group C was 1.021 and the difference among groups was not significant with a p-value of 0.177.

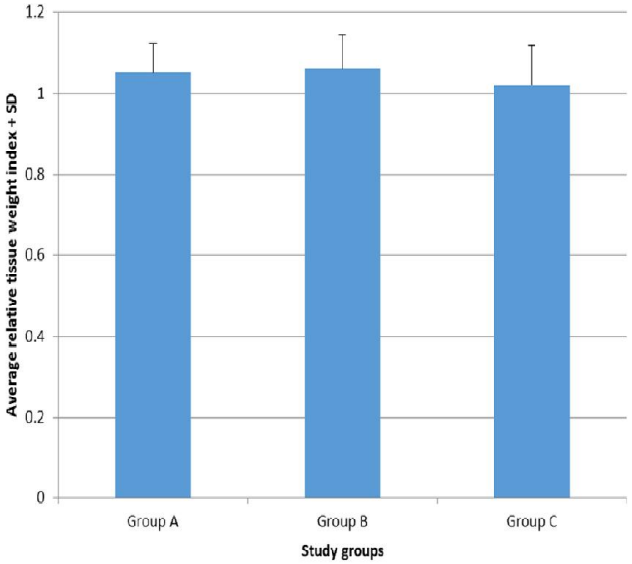

Figure 2: Component bar diagram presenting the status of average relative tissue weight index for animals at the final stage of the experiment in three study groups

There were 17 (56.7%) cases with mesangial hypercellularity in group A while 24 (80.0%) in group B and none in group C. Mesangial hypercellularity was found significantly different among three groups with a p-value <0.001. A difference between group A and B was obvious from group C with p-values <0.001. The difference between group A and B was also found significant with a p-value of 0.050.

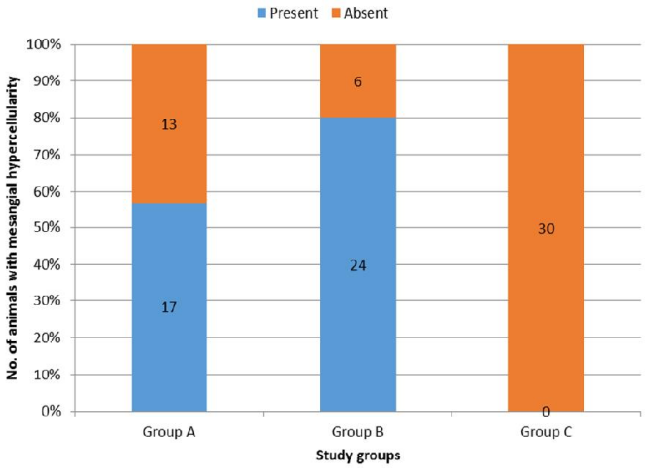

Figure 3: Component bar diagram representing the status of mesangial hypercellularity of animals at the final stage of the experiment in three study groups

On histological examination of kidneys, 19 (63.3%) animals of group A showed vascular congestion while 24 (80%) animals of group B showed vascular congestion. The difference of group A and B from group C was extremely significant with a p-value <0.001.

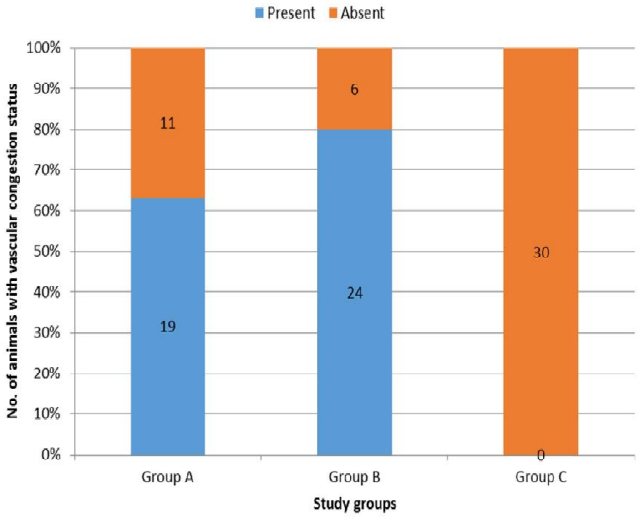

Figure 4: Component bar diagram representing the status of vascular congestion of animals at the final stage of the experiment in three study groups

Discussion

Consumption of energy drinks has picked up a lot of admiration all over the world especially from the young generation. These drinks are marketed as natural substitutes that escalate mental and body performance such as alertness and physical endurance. Teenagers are obsessed with these type of beverages.[15]
A detailed research project was conducted to observe the consequences of an energy drink named Red Bull on the kidneys of albino Wister rats. Red Bull was given orally via gavage tube, group A was given 1.5ml/100g and group B was given 2.2ml/100g. Animals stayed healthy and active throughout the duration of the experiment.
Mean initial weights of animals in groups A, B (experimental groups) and C (control) were the same as 151.2±5.7g. Mean final weights of animals in experimental groups were increased and were almost the same as 172±6.9g. Our study showed that the difference in the initial mean weights among the three groups and its difference with the mean final weights at the end of the experiment was statistically insignificant. This result collaborates with the finding shown by Rangin et al in 2017, they demonstrated the effect of energy drink on the brain and liver of Sprague Dawley rats, they reported no change in weight and food intake after energy drink consumption for 14 days.[16]

Other studies conducted by Ayoub N et al in February 2016, Yoojin et al in April 2017, and Schuchwsky E et al in December 2017 suggested no significant weight gain or loss with the use of energy drinks on rats.[17,18,19] No considerable weight change with energy drink due to stimulation of fat oxidation and thermogenic activity because caffeine has the capability to impede the phosphodiesterase-induced breakdown of cAMP (intracellular cyclic adenosine monophosphate) and caffeine's antagonism of adenosine on increased norepinephrine release which is responsible for weight control up to some extent. But contrary to the above results, Fahad in his study, related to energy drink effects on albino Wister rats, reported energy drink given for 21 days significantly reduce body weight. It may be due to caffeine consumption reduced food intake and lessen time-dependent rise in body weight.[20]

Mean paired kidney weight for group A was 1.81±0.16g, 1.82±0.17g for group B and 1.76±0.17g for group C and relative tissue weight index (RTWI) of kidney for group A was 1.051, for group B was 1.060 and for the control group, C was 1.021. It was observed that the difference among groups for the weight of kidney as well as for relative tissue weight index was insignificant. A study conducted by Schuchwsky E et al in December 2017 suggested similar insignificant findings for kidney weight and relative tissue weight index. It is stated that likelihood was because of mingled outcomes of caffeine on stimulation of β-adrenergic lipolysis and on antagonistic action of the antilipolytic outcomes of adenosine to some extent which causes no significant effect on relative tissue weight index and weight of kidney and it is also observed that oxidation of fatty acids increases due to caffeine, causing the energy surge and glucose rise in the blood.[21] Caffeine is an antagonist to adenosine receptors and decreases catecholamines' secretion.[22]

Amongst histological features, mesangial hypercellularity was found as 56.7%(17) in group A while 80.0%(24) in group B and none in group C. Mesangial hypercellularity was found significantly different among the three groups with a p-value <0.001. This finding of mesangial hypercellularity is reconcilable with a project run by Dalia EL et al to show the effect of energy drinks on the renal structure of adult albino rats.[23] It is suggested that at the level of nucleus tractus solitaries, arousal of A2A receptors slows sympathetic nerve activity of kidneys and it is stated that blockade of adenosine receptors by caffeine may at once raise angiotensin II in renal tissue and reduce the effects of adenosine on renal vasculature, thus creating increase transmission of raised arterial blood pressure to capillaries of glomeruli. Hypertension in glomerular capillaries would lead to renal tissue damage by increased stimulation of sympathetic nerves. Chronic stimulation of the renin-angiotensin system would have bad effects on glomerular structure and function.

While on the contrary, the study of Akande et al reported normal structure of glomeruli of a kidney after giving caffeinated energy drink for 3 weeks.[24]

Vascular congestion is present in both experimental groups A and B with more than 80% in group B as compared to group A (63%) while absent in group C (control group). The results are inconsistent with findings shown by Mansy et al in December 2017 and Nadia et al in December 2018, on kidneys of rats and rabbits respectively.[10,12] It may be due to nonspecific edematous endothelial cells of blood vessels due to oxidative injury caused by caffeine or a combination of caffeine with other ingredients.[18] While contradictory to the above findings Akande et al in 2011 showed in their study that there are no histopathological changes in kidneys of rats after treating with an energy drink for 3 weeks period.[24]

Conclusion

It was found that the use of energy drinks induces histopathological changes in the renal mesangium.

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