Original article:

The Comparison Effect Of Energy Drinks And Coffee On Creatinin Level In Rats
Mohamad Riza¹ Andina Putri A²

Abstract
Objective: to compare the effect of administration of energy drinks and coffee on creatinine levels in rats. Methods: an experimental laboratory research using the post test only control group design. The study used 18 male white Sprague Dawley divided into three groups to receive one of the following treatments: 2 cc distilled water, 0.072 g / 2cc energy drinks and 0.9 g / cc of coffee for 14 days. The creatinine level was evaluated. Data were analyzed by One Way ANOVA test. Results: The mean creatinine level in the aquades group, energy drinks, coffee group was 0.708 mg/dl, 2.05 mg/dl 1.861 mg/dl, respectively. Post Hoc test the LSD test showed a significant difference among these groups (p <0.05). Conclusion: There was a significant different effect between 0.072 g / 2cc energy drinks and 0.9 g / cc coffee on creatinine levels in rat.

Keywords: Energy drinks, coffee, creatinine levels

Introduction
Consuming energy drinks, type of drinks containing sugar and stimulant compounds, usually caffeine, can increase energy, concentration, alertness, maintain physical strength, reduce drowsiness and enhance clear thinking¹. Caffeine is the main component of energy drinks responsible for these effects². Caffeine has harmful effects that can damage the body organs, especially kidney³. Besides energy drinks, drinking coffee, naturally caffeinated drink, has also been a daily routine of people all over the world. The taste and aroma of coffee may cause an addiction. There have been conflicting findings on the effect of coffee. There are several coffee studies showing a beneficial effect but excessive consumption may have an adverse effect on the health especially to the kidneys⁴.

Both Energy drinks and coffee contain caffeine consumed to increase concentration and reduce drowsiness ². However, the difference in health effect between energy drinks and coffee consumption on kidneys have not been established. Annual consumption of energy drinks increased by 17% from 960 million gallons². In Indonesia, by 2009 energy drink production were 1.2 trillion liters and became 1.38 trillion liters in the following year⁶.

Consumption of energy drinks has been increasing. The Indonesian Diatrans Kidney Foundation (YGDI) explains the number of patients with kidney failure have increased. According to the consultant of International Coffee Organization (ICO), the average coffee consumption in the world is 2% and increased in 2001-2008. While in 2008-2016 the average coffee consumption increased by around 35.5%.

According to the Indonesian Nephrology Association, there are at least 110,000 patients with terminal kidney failure. Kidney failure in Indonesia and other developing countries is generally caused by glomerulonephritis, an autoimmune disease triggered by infection. Other common causes include diabetes, hypertension, kidney stones, the use of drug and supplements, herbs, and the consumption of nephrotoxic foods and beverages. In the beginning, energy drinks were often consumed by athletes to gain extra energy. Lately, it has been consumed by adolescents and adults in the age range of 18-34 years⁸. A survey in 2002 showed that energy drinks have an effect on the incidence of kidney failure⁷.

1. Department of Pharmacology, Faculty of Medicine Universitas Islam Sultan Agung, Semarang
2. Department of Clinical Pathology, Faculty of Medicine Universitas Islam Sultan Agung, Semarang

Correspondence to: Mohamad Riza, Department of Pharmacology, Faculty of Medicine Universitas Islam Sultan Agung, Semarang, Central Java, Indonesia email: riza_dr@unissula.ac.id
Caffeine causes an increase in blood pressure, heart rate, and effects on the kidneys. This increase will cause afferent pressure (blood pressure before entering the glomerulus) increases leading to glomerular stress leading to glomerular damage and impairment of kidney function. The administration of caffeine at the dose of 2.16 ml have been showed to damage the renal interstitial tubules in rats8.

Energy drinks at a dose of 20 mg increased urea levels in rats due to the high concentration of caffeine in9. This effect is associated with the exposure of chemicals contained in these drinks, causing swelling of the proximal tubular and distal tubular epithelial cells of the kidneys. At the advanced stage, it can cause tubular necrosis characterized by damage to the tubular cell nucleus in the form of karyolysis, pyknosis, and karyorrhexis10. Based on this background, this study aimed at comparing the effect of the administration of energy drinks and coffee on creatinine levels in male white Sprague Dawley rats.

**Materials And methods**

**Animals**

This research used post test randomized control study conducted in Biology Laboratory of Faculty of Medicine, UNISSULA. Male Sprague Dawley rats were obtained from the animal breeding facility of Biology Laboratory. The study used 18 male white Sprague Dawley divided into three groups to receive one of the following treatments: 2 cc distilled water, 0.072 g /2cc energy drinks and 0.9 g/cc of coffee for 14 days. The rats were housed in groups of 6 animals. All rats were healthy (not physically disabled, having no injury, active movement). Eighteen rats were randomly divided into 3 groups of 6 rats each.

The rats were placed in a room maintained at 25°C and with free access to food and water. Body weight was 140-200 gr. The experimental procedures were approved by the Ethical Committee for Use of Human or Animal Subjects of Medical Faculty of UNISSULA.

**Procedure**

The tools used are rats cage equipped with food and drink places, digital scales to weigh coffee and feed rats and heavy rats, feeding tube, syringes, micropipettes, glassware (glass beaker, measuring cup, stirring rod, tube reaction, drop pipette), microhematocrit to take rat blood samples, Scientific centrifuge Rotofix 32 brands, rack and test tube, eppendorf tube, pipette 20-200 µl, Pipette 100-1000 µl, 1 cc Spuit and 10 cc Sterilized cotton, Automatic Spectrophotometer, Orbital Shaker. The ingredients used are sachet packaged energy drinks, BR-12 standard diet, aquades, rat venous blood serum, pellets, creatinine examination reagents.

**Coffee and energy drink dosage preparation**

The dosage of energy drink was determined based on the daily average consumption of 1 sachet/day, so that 1 x 4.4 grams = 4.4 grams/day (Putriastuti R., 2007). Energy drinks were converted from human (70 kg) to rat (200 grams) 4.4 x 0.018 = 0.0792 grams / day (Laurence, 2008). The coffee dose used was the conversion of human doses that have an effect on the kidneys. Consumption of coffee per day is about one spoon or 5 grams /day (Wiji, 2009) Coffee is converted from a dose of human (70 kg) to rats (200 grams) thus 5 x 0.018 = 0.09 grams /rat/ day.

**Administration of the treatment**

Caffeine was administered to experimental animals according to their body weight, such that animal weighing 200 g, 150 g, 170 g received 2 ml, 1.5 ml and 1.7 ml respectively. Caffeine was administered orally.

**Statistical Analysis**

All results were expressed as Mean ± Standard deviation. Significant difference between groups was assessed by SPSS. The data obtained were tested for normality and homogeneity with Saphiro-Wilk Test and Leuvene’s Test then One Way Analysis of Variance (ANOVA) test followed by Post Hoc LSD Test for data with normal and homogeneous distribution, when the data were not normal and not homogeneous the data would be analyzed with Kruskal Wallis and followed by Mann Whitney test. A probability level of less than 5 (p< 0.005) was considered significant.

**Results**

Table 1 shows the highest to lowest creatinine levels were treatment group 2 (K2) with levels of 2.051 ± 0.480 mg / dl, treatment group 3 with levels 1.861 ± 0.3188 mg / dL, treatment group 2 with levels of 2.051 ± 0.480 mg /dL, and positive control with levels of 0.708 ± 0.292 mg / dL. The normality and homogeneity test showed that the data were normally distributed and homogeneous so that the One Way Anova test was carried out and followed by the Post Hoc test, the One Way Anova test resulted in value of p = 0.000 showing that at least two groups had significant differences in mean creatinine levels. The Post Hoc test shows a p value of 0.000 (p <0.05) for all comparisons.
between the two groups meaning that the comparison between groups had a significant difference in creatinine levels showing that energy drinks and coffee had a significant effect on creatinine levels in white wistar rats.

**Tabel 1. Results of Creatinine Levels of Treatment Groups**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Average Creatinin Level (mg / dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>K1</td>
<td>0.708 ±0.292</td>
</tr>
<tr>
<td>K2</td>
<td>2.051 ±0.480</td>
</tr>
<tr>
<td>K3</td>
<td>1.861 ±0.3188</td>
</tr>
</tbody>
</table>

The mean creatinine level in the aquades treated group was 0.708 mg/dl, in the treatment group the energy drink were 2.05 mg/dl and in the coffee group were 1.861 mg/dl. The Post Hoc test the LSD test showed a significant difference between these groups (p <0.05). This is in line with the research conducted by Nirmalasari 2016 concluding that energy drink increase creatinine levels in rats at the dose of 100 mg of energy drinks. This is caused by the high caffeine concentration in energy drinks. Caffeine can induce inflammation and increase glomerulosclerosis causing an increase in protein and a decrease in creatinine clearance. Energy drinks have an effect because they are associated with exposure to chemicals contained in energy drinks causing swelling of the proximal tubular and distal tubular epithelial cells of the kidneys. In advanced stage, it can cause tubular necrosis characterized by damage to the tubular cell nucleus in the form of karyolysis, pyknosis, and karyorrhexis.

**Discussion**

We investigated the effect of administration of energy drinks and coffee on creatinine levels in rats. In the present study, the effects of energy drink and coffee on renal parameters were studied. Elevated creatinine level indicate an impaired kidney function or kidney disease.

The creatinine level was evaluated in rat. Our results showed that energy drink cause a higher increase in creatinine level compared to energy drink.

Creatinine, a chemical waste product in the blood is eliminated mainly from the filtration process in the kidneys, if there is damage to the kidneys then there is a decrease in GFR followed by an increase in creatinine levels.

The mean creatinine in the energy drink group was 2.05 mg / dl and mean creatinine level in the coffee group was 1.861 mg / dl. The post hoc test showed that there was a significant difference (p>0.05) due to the administration of energy drinks in the energy drink group and coffee group increased creatinine levels. This is in line with the finding of a study conducted by Babu 2008 stating that energy drinks and coffee both contain caffeine consumed to increase concentration and reduce drowsiness.

Caffeine is the main composition of energy drinks responsible for this effect. Caffeine also has harmful effects that can damage the body organs especially in the kidneys.

There was a significant difference in creatinine level between coffee group and distilled water group. This might have been due to the difference in caffeine that can increase the creatinine levels. Caffeine causes an increase in blood pressure, heart rate, and affects on the kidneys. This increase leads to an increase in afferent pressure (blood pressure before entering the glomerulus). A long term glomerular damage may lead to kidney function disturbance. The administration of caffeine at a dose of 2.16 ml has been shown to cause renal tubulointerstitial diseases.

One of the main limitations of our was that is that we did not evaluate caffeine concentration. Both Energy drink and Coffee treatment showed a an effect on kidney function parameter. In the this investigations, Energy drink was seen to cause higher increase in creatinin compared to coffee suggesting that energy drink cause more harm to the renal function compared to coffee.

**Conclusion**

This present study showed that the energy drinks and coffee can increase creatinine levels. The results of this study indicate that energy drink and coffee consumption can affect kidney function. Future research investigating the chemical substance responsible for the effect of energy drink and coffee on parameter of renal function would improve our understanding.

**Acknowledgments**

This work was supported by Faculty of Medicine, UNISSULA.
References: