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Energy-Drink and Adverse Kidney Function: A Review of Public Health Concern and Ethical Issue

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Abstract

Best evidence to acclaim the reviewed effects, needs sufficient trials to support the linkage of incidents of adverse kidney function with the ingestion of the drink. This study aimed to conduct a review of current studies determining adverse kidney function caused by ingestion of energy-drink. Electronic academic database of Cochrane, PubMed, CINAHL, and MEDLINE were searched for relevant studies. A systematic review of English articles published from December 1988 to December 2020 was conducted. All study design was included. A Prisma-flow diagram was applied.

Nutritional ingredients, clinical parameters from urine and blood reported kidney function were summarized. The outcomes were condensed into four main interests: ingredients of energy-drinks, intensity and duration of ingestion, and ethical issue.

Adverse kidney function was found among adults with excessive ingestion of energy-drink.

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Introduction

Energy-drink consumption has become a health issue, primarily of the adolescent and adult male population. History of energy-drinks begun in Austria, where in 1987 the first was produced, and another was released one decade later in the USA. Recently, this beverage has become increasingly popular worldwide. In the US, an estimated 2.3 billion people ingested energy-drinks in 2005 and nearly three-fold of the previous population did in 2010[1]. This massive consumption of energy-drink represents the lower nutritional literacy of a common society, combined with an unquestioned belief in the claims made by the manufacturers [2]. Energy-drinks are marketed on their ability to boost performance, productivity, and concentration [3]. Hence, the society perceive them to be a healthier alternative to drugs due to the supposed functional ability of the drink [4].

Energy-drinks have been banned in several countries due to health problems such as on cardiovascular system. A study on the effect of ingesting energy-drinks on kidney function is becoming interesting to be conducted since the number of unknown etiologies or causations of chronic kidney disease (CKD)[5]. Post-authorization safety (PAS) studies reported that the major cause of kidney failure is the use of drugs, supplements, herbs, and the consumption of nephrotoxic foods and beverages. Not only Indonesia, another country with a huge population such as India has also been a potential target market for energy-drinks. Thus, the two countries are the major energy-drinks' market for both international and local brands [6,7].

Kidney disease has been reported as an important contributor to morbidity and mortality from non-communicable diseases [8]. Hence, all promotion and prevention strategies on CKD need to be actively addressed to meet the UN's Sustainable Development Goal target to reduce premature death before 2030 [8]..Concerning the above expression, any effort to reduce the risk of CKD needs to be initiated by way of increasing public concern on the effect of ingesting energy-drink.

Undoubtedly, it is the natural ingredient contained in energy-drinks that successfully

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attracts the public to become fearless of the negative effects. For ages, Ginseng, royal jelly, Ginko Biloba, and Guarana have been acknowledged as herb benefits to the health [9]. In the year 1994, the Dietary Supplement and Education Act classifies products containing herbs and other natural ingredients as supplements rather than as drugs. Consequently, this regulation allows manufacturers to side-step/dodge disclosure of the dose of the main element contained in their products. Over the last few years, there has been a growing body of literature about significant adverse health events subsequent to the ingestion of energy-drinks. Also, several health problems caused by ingesting energy-drinks [10] such as sleep pattern alteration and insomnia, cognitive and behavioural disorder , liver [11], cerebrovascular , and cardiovascular dysfunctions [12] have been discovered.

Concerning the safety, FDA recognized that there is possibility for some fatalities to have occurred due to intensive and prolonged energy-drink consumption [13]. However, scientific supports on consumption of energy-drinks have not been linked with potential renal problems as well as no current review about its impact on kidney function has been published. For now, there are millions of persons consuming energy-drinks probably because of being unaware of the kidney damaging effects associated with that habit. Therefore, this study aims to explore the published articles that have reported adverse kidney function caused or induced by ingestion of energy-drinks.

Materials and methods

The articles studied were collected from academic database such as Cochrane, PubMed (Medline), CINAHL (EBSCO), and MEDLINE (EBSCO), and they were those published from December 1988 to December 2020. There were 303 publications found, but this review considered only the free type of articles with full access, that is those not requiring passwords or subscription. Three reviewers participated in the literature search independently, while manual cross-checking was performed and duplicates were excluded, but only the articles published in scientific journals were included.

The bibliographies of the articles were searched for pertinent publications and web resources. The title, abstract, or text of the articles was searched using the terms “energy-drink”, “caffeinated drinks”, and “caffeinated sports drinks” alone and in various combinations. The 303 pertinent or important publications were further screened for studies on the health effects of energy-drink using the following inclusion criteria: *“written in English”, “published in a scientific journal”, “described the case of an adverse kidney function”, and “supported by clinical test to present/examine the kidney-function”*.

The excluded publications were letters to the editor; short communications; images; features such as news in scientific journals, newspapers, or online resources; popular media reports; animal and human studies in a small sample size; and studies that are either indirectly related to the health effects of energy drinks or are associated with the composition/manufacturing process of the drinks.

The studies that did not meet the above criteria were excluded from the review and analysis, but some were used as references and considered in the discussion section of this review, and each of them addressed one or more outcomes. Several excluded studies were used in the results and discussion section to sharpen the findings, while appraisal/ verification and synthesis of evidence were performed. Study quality was assessed using two evaluation tools, namely Joana Brigg Institute (JBI) critical appraisal checklist for randomized controlled trials and Center for Evidence-Based Management (CEBma) critical appraisal of a case study. A Prisma-flow diagram was applied to map the number of records identified, included, excluded, and the reasons for exclusions. The search and selection processes were illustrated following the Prisma guidelines [14] as can be seen in figure 1.

Analysis

I.S and I.Y.W independently identified the brand, dose, and clinical report for non-experimental and experimental studies on energy-drinks in full text, and grouped according to the content. For example, the brand of energy-drinks as written on the paper, the content, the dose, demographic characteristics, and clinical test to assess kidney function.

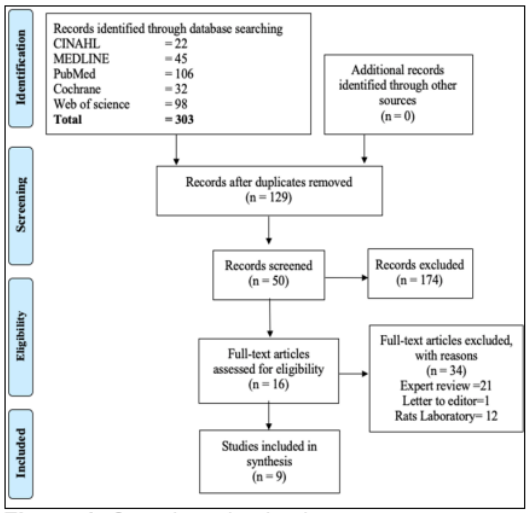

Figure 1 Search and selection process

Brand	Nutritional Information retrieved from the study
Assault®	▪ Branched-Chain Amino Acids =6 g ▪ Creatine =5 g ▪ β-alanine = 4 g ▪ citrulline malate=1.5 g ▪ caffeine=300 mg ▪ Citrulline malate =15mg ▪ Creatine=15mg ▪ βAlanine=4g ▪ Caffeine=300g
Neon Volt®	▪ NA*
Red Bull®	▪ (250 mL can, 110 Cal)
Five Hour Energy®	▪ Taurine ▪ Glucuronic acid ▪ Caffeine ▪ Other substances in small 1.93 fl. oz. container.
NA* Brand	▪ Taurine ▪ Caffeine
NA* Brand	▪ Caffeine ▪ Taurine ▪ Inosite ▪ Glucuronolactone
NA* Brand	▪ Per serving (8 oz. or 240 ml) ▪ Taurine1000 mg ▪ Guarana seed 100 mg ▪ extract Caffeine 80 mg ▪ Glucuronolactone 50 mg ▪ L-carnitine 25 mg ▪ Vitamin B8=25 mg ▪ Vitamin B3=20 mg ▪ Vitamin B6 2mg ▪ Vitamin B12=2 mcg ▪ B2=3.4 mg ▪ Vitamin B5=10 mg

Table 2. The Brand and the nutritional information.

Results

The main goal of this review was to establish what is known about the adverse effect caused by ingesting energy-drink on kidney function. Limited experimental studies published in 2 articles [15,16] were found and the remaining seven[17-23] that were also discovered were case studies with detailed information on kidney function. Detailed information on the content, the dose, demographic characteristics, and clinical test to assess kidney function as can be seen in table 1.

Nine studies reported ingestion of selected brands, six named the brand, while another three were anonymous or unidentified. Nutritional information of each brand as reported in the study and written on the label is shown in table 2.

Data (table 2) were extracted, measured, and condensed as the addressed outcomes of this review among which the 4 that were of main interest are as follow:

1. Ingredients of energy-drinks

Caffeine was founded as the first-major element discovered in the studies examined in this review. Followed by Taurine (an amino acid) , a stimulant in vitro physiological effect of this organic compound on vascular smooth muscle is potentiated or enhanced by its combination with Caffeine. This explanation tends to relate to a remarkable case of rhabdomyolysis (a disease that involves rapid disintegration of striated muscle tissue) associated with the ingestion of energy-drinks containing Taurine [23]. Selected B vitamins, namely thiamine (B1), riboflavin (B2), niacin (B3), pantothenic acid (B5), pyridoxine (B6), biotin (B7), folate (B9), and cobalamin (B12) are often added into a package of energy-drinks. Thus, medicinal plants such as Guarana and Ginseng were added and blended with Caffeine, Taurine, and B vitamins to be named as energy-drinks. Medicinal plants and unknown interactions among various stimulants in energy-drinks tend to potentiate adverse kidney events [9].

2. The intensity and duration

Ingesting energy-drinks as reported in the experimental and case studies were contrasted. In the experimental study, the researchers fully managed the dose which is connected to intensity and duration. While in the case study, individuals randomly ingested energy-drinks in a large amount for several days, week, or even a year.

3. Ethical issue

It has been acknowledged that the ethical consideration of the experimental study defines the necessity of protecting the participants [24]. Nevertheless, several case studies have provided intense public interest especially on the safety of regular ingestion of energy-drinks.

Discussion

Kidney disease has been reported as an important contributor to morbidity and mortality from non-communicable diseases [8]. Hence, all promotion and prevention strategies on CKD need to be actively addressed to meet the UN's Sustainable Development Goal target to reduce premature death before 2030 [8]. Concerning the above expression, any effort to reduce the risk of CKD needs to be initiated by way of increasing public concern on the effect of ingesting energy-drink. The debate on energy-drinks in the Europe leads to regulation and public policy of energy-drinks in another country [25]. However, the key questions that are still unanswered are whether Caffeine is solely responsible for the adverse response to excessive energy-drink consumption or whether an untoward interaction develops between Caffeine and/or Taurine, as well as one or more of the active ingredients

Primarily, a logical first step of the relationship of causal effect between energy-drinks and adverse kidney function was probably placing Caffeine or Taurine as the basic content of energy-drinks on the label. This must have been followed by additional ingredients blended into energy-drinks, sustained consumption of significant amounts for longer periods, and the speed of ingestion as reported in the cases. Note that those written above contributed to adverse kidney function. Second, the adverse effect was assumed to be caused by the lack of a standardized definition of use and limited knowledge about the effects of the various active ingredients in energy-drinks, thus, fewer experimental studies were conducted. Therefore, the fact that there was a swift change in public perception of energy-drink from harmless mild to lethal stimulant, and less understanding of the effects on kidney function is segmented. To a certain extent, raising public concern on the potential dangers caused by regular consumption of energy-drink on the kidney function is crucial.

Thus far, energy-drink is ingested continuously as the most common beverage. In order to save more lives, there is need to constantly advise on protection of ones' kidney in the target markets of energy-drinks. The public possibly underestimates or is less aware of the health effects caused by excessive consumption of energy-drinks. Even, there is tendency that they have received no sufficient information regarding energy-drinks associated with lowering kidney function. Due to this phenomenon, there is need to urgently carry out an investigation among high-risk populations such as construction workers that presumably require instant and extra energy daily, and aiding of targeted health education as well.

Conclusions

There is need to include the patient's status of energy-drinks consumption in the health assessment of decreasing kidney function. Haven learnt from the reviewed case studies, it is a need to elevate public awareness, to pay attention to, and be proactive about this growing, and preventable kidney toxicity.

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Declaration of Interest

The authors have declared that no conflict of interests exist.

Author/ Study design/ Country	Reports/Treatments	Clinical laboratory findings
[16] ▪ Experimental study design ▪ Double-blind RCT ▪ USA	Treatment: 1. Ingested one full scoop (46gram) supplementation every day for 28 days either 20minutes before exercise 2. Supplementation marketed as Assault® (Denver, CO.USA) contained BCAA (6gram). Creatine (5g), ß-Alanine (4gram), Citrulline malate (1.5 gram), and Caffeine (300mg)	Blood urea nitrogen: ▪ pre-supplementation =13.12±2.55mg/dL ▪ post supplementation =15.24±4.47 mg/dL
[15] ▪ Experimental study design ▪ A double-blind ▪ USA	Treatment: 1. Normal Calorie Red Bull® (250ml, 110Cal) 2. Low-Calorie Red Bull® (250ml, 10Cal) Control: High-Calorie Placebo (250, 110 Cal)	Urine formation rate and urine specific gravity were also not changed for the groups examined
▪ [23] ▪ Case study ▪ A male 17-years-old ▪ Germany	Ingesting 3-4 cans = 1.93 fl. oz each day for 3-4 months	Blood sample test: ▪ Serum Urea=64 mg/dL ▪ Serum Creatinine=6.9 mg/dL ▪ Creatinine clearance 7.4 mL/min
[17] ▪ Case study ▪ A male 30-years-old ▪ UK	Drinking up to 12 250ml cans of Red Bull® per day, consuming an estimated daily total of 960 mg caffeine in the days preceding on the admission.	Blood samples test's: ▪ Creatinine =1205 μmol/L ▪ (eGFR)= 4mL/minute
[18] ▪ Case study ▪ A male 17-years-old ▪ USA	Consuming 3 L of energy-drink (ED) in combination with 1 L of vodka amounting to 4600 mg of taurine and 780 mg of caffeine.	Laboratory test: ▪ Serum Urea=64 mg/dL ▪ Serum Creatinine=6.9 mg/dL ▪ Creatine Clearance=7.4 mL/min
[19] ▪ Case study ▪ A female 25-years-old ▪ Spain	Consuming 500-700ml Energy-drinks and 1 L of caffeinated soda	Blood sample test: ▪ Creatinine=192.72 mg/dL ▪ Urea=920 mg/dL Urinalysis after 18 hours later: ▪ Sodium= 25.3 mEq/L ▪ Potassium= 6.2 mEq/L ▪ Creatinine= 266.27 mg/dL ▪ Urea= 642 md/dL
[20] ▪ Case study ▪ A male 40-years-old ▪ USA	Regularly ingesting 2-3per week @100-120 oz of Red Bull®	Blood sample test: ▪ Creatinine Clearance= 17 mL/Min ▪ Serum Creatinine= 5.5 mg/dL ▪ BUN= 108 mg/dL
[21] ▪ Case study ▪ A male 25-years-old ▪ USA	Drinking Five Hour Energy® drink in frequent 3-4 1.93 fl. oz. bottles each day. The last intake was 3 bottles before the onset of symptoms. Drank 2.5 bottles of the drink the night before the presentation. The individual has been consuming Five-Hour Energy shots for the past 3-4 months, with increasing intake over the past 1.5 months.	Blood sample test: ▪ BUN=12 mEq/L ▪ Creatinine= 0.7 mEq/L
[22] ▪ Case study ▪ A female 60-years-old ▪ USA	Weeks before admission, the appetite had declined and substituted with minimal intake five to six cans of a 16-fluid ounce sugar-free ED daily.	Blood sample test's: ▪ Creatinine (Cr) 2.83mgDL ▪ BUN 18mgDL ▪ eGFR 17 ml/minute/1.72m^2

Table 1. The summary of the experimental and case studies included in the review.

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