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Systematic Review of Energy Drinks and QTc Prolongation

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Abstract

The importance of healthcare providers educating the public regarding the consequences of energy drink consumption is critical as energy drink popularity and consumption continues to rise. The purpose of this systematic review is to add to the research that proves the correlation between energy drink consumption and cardiovascular disease. Energy drinks are a contributing factor to cardiovascular disease which is the number one cause of deaths globally. The four studies reviewed in this systematic review demonstrate a statistically significant correlation between energy drinks and QTc prolongation. Further research is needed to have a better understanding of the correlation between energy drinks and its negative effects on people's health and wellbeing. Health care providers will have another resource to continue to educate patients regarding cardiovascular disease risk and prevention.

Introduction

As much as 30-50% of adolescents and young adults consume energy drinks[1]. Adverse effects of energy drinks include jitteriness, palpitations, difficulty concentrating, abdominal discomfort, seizures, diabetes, cardiac abnormalities, and death [2,3,4]. These adverse reactions arise primarily from their caffeine content[5]. Energy drinks vary widely in the amount of caffeine they contain, ranging from 50mg to more than 500 mg per can or bottle[2]. For comparison, the caffeine content of a 6 oz cup of brewed coffee varies from 77 to 150 mg[2]. The U.S. Food and Drug Administration (FDA) limits the amount of caffeine in soft drinks because they are categorized as food[3]. However, energy drinks are classified as dietary supplements and are not required to report caffeine content on their products. Caffeine alters various electrolytes, which can lead to cardiovascular events including cardiac arrest[6,7] According to the World Health Organization, more people die annually from cardiovascular disease than from any other cause[8]. The function of the heart is to constantly pump blood, which contains oxygen and nutrients through the arteries and into the heart muscle[9]. A cardiovascular event is any interruption of this blood flow that will lead to heart muscle injury[9].

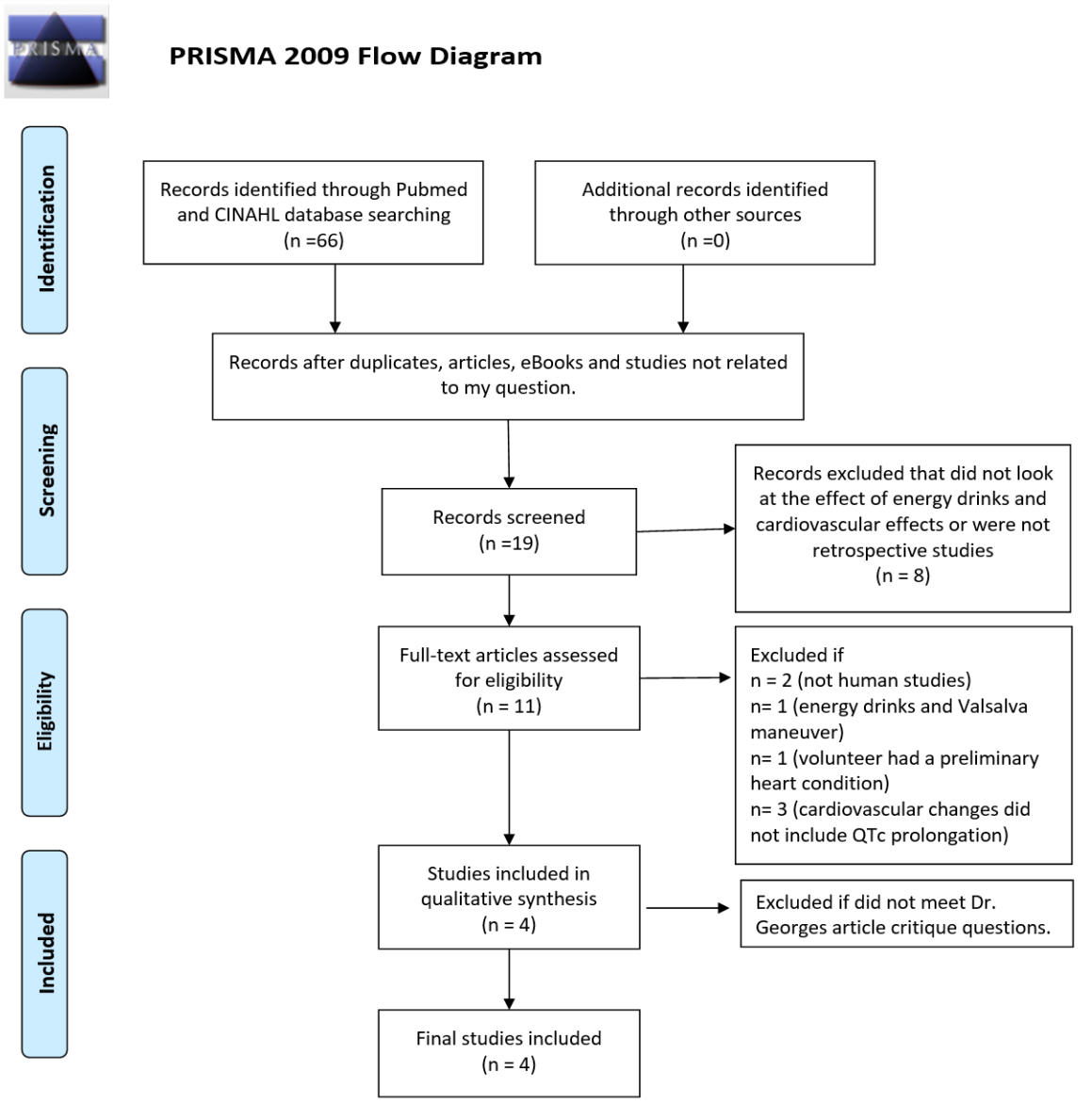
The popularity and frequency of energy drink consumption coupled with lack of public education about their potential adverse effects create an environment for harm. Therefore, it is imperative that healthcare providers educate patients and communities about the safety risks of energy drinks. The need to investigate the deaths of young adults associated with energy drink consumption is critical to gain a better understanding about their risk for toxicity. Further research will enhance patient education regarding the adverse effects of energy drink consumption, especially excessive consumption.

Currently the data that we have is inconclusive and mostly limited to case reports. Case reports by Seifert et al, and Rocco et al, reported arrhythmias as a cause of death in patients

drinking large amounts of energy drinks[1,8,10]. Other studies by Conen et al, and Shen et al, showed no significant association between energy drinks and arrhythmias[11,12]. There are, however, a variety of cardiovascular changes (cardiac rhythm changes/ EKG changes) seen in patients who consume energy drinks. Two systematic reviews by Mangi et al, and Goldfarb et al, looked at previous case reports of young adults consuming large amounts of energy drinks and their effects. They found changes that include arrhythmias, coronary vasospasm, ST elevation, prolonged QT interval, aortic aneurism dissection, cardiac arrest cardiomyopathy, acute coronary thrombosis[6,13,14]. The purpose of this report is to systematically review research published in the past two years that address the potential correlation between energy drink consumption and cardiovascular safety.

Methods

This systematic review was done in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The databases Pubmed and CINAHL were used using the following mesh terms: “energy drinks and cardiac changes”, “energy drinks and heart” “energy drinks healthy population” from 2017 to 2019. The exposure was the consumption of energy drinks and the outcome was the effects on QTc intervals on an EKG. Inclusion criteria included retrospective studies involving both sexes. Exclusion criteria included review studies, studies not conducted on humans, studies with a preliminary cardiac condition, and studies looking at other cardiovascular events not QTc prolongation.


PRISMA 2009 Flow Diagram
Identification
Screening
Eligibility
Included
Records identified through Pubmed and CINAHL database searching (n =66)
Additional records identified through other sources (n =0)
Records after duplicates, articles, eBooks and studies not related to my question.
Records screened (n =19)
Records excluded that did not look at the effect of energy drinks and cardiovascular effects or were not retrospective studies (n = 8)
Full-text articles assessed for eligibility (n = 11)
Excluded if
n = 2 (not human studies)
n= 1 (energy drinks and Valsalva maneuver)
n= 1 (volunteer had a preliminary heart condition)
n= 3 (cardiovascular changes did not include QTc prolongation)
Studies included in qualitative synthesis (n = 4)
Excluded if did not meet Dr. Georges article critique questions.
Final studies included (n = 4)

Results/Interpretation

The following formulas were used to correct for all QTc intervals for the heart rate. Kozik, et al. used Fridericia's formula. Basrai, et al. did not report what formula they used. Shah, et al. and Fletcher, at al. used the Bazett's correction formula.

Table 2. Results of EKG change

Author/Year	Study Type	Sample Size	Caffeine Amount	QTc Prolongation	P value
Kozik, et al. 2018	Retrospective observational	23	Two 16oz energy drinks (320mg)	423, ± 22.74 ms to 503, ± 24.56.	P <0.001
Basrai, et al. 2019	Randomized control trial	38	One commercial energy drink (320mg)	393.3 ± 20.6 to 400.8 ± 24.1 ms	P <0.01
Shah, et al. 2019	Randomized control trial	34	Two 16oz energy drink A or B (304,320 mg)	413.7 ±11.1 to 412.9 ±13.9, 412.3 ±15.8 ms	P <0.001
Fletcher, et al. 2017	Randomized control trial	18	32 oz energy drink (320mg)	0.44±18.4 to −10.4±14.8 ms	P= 0.02

Kozik, et al. reported QTc interval prolongation in 23 healthy individuals post consumption of energy drinks baseline = 409, ± 16 ms; PC = 423, ± 24 ms. Basrai, et al. reported QTc interval prolongation in 38 healthy individuals 1-hour post consumption of energy drinks (393.3 ± 20.6 to 400.8 ± 24.1 ms. Shah, et al. reported the maximum change from baseline in QTc interval prolongation for drink A, drink B, and placebo +17.9±13.9, +19.6±15.8, and +11.9±11.1 ms, respectively. Baseline for drink A =412.9, drink B= 412.3 and placebo= 413.7 Fletcher, at al. reported a significant difference in the baseline QTc interval two hours after energy drink consumption and caffeine respectively 0.44±18.4 ms, −10.4±14.8 ms. All four studies showed a statistically significant correlation between energy drinks and QTc prolongation.

Discussion

In these four studies the correlation between energy drinks and significant QTc interval prolongation is established. QTc interval prolongation is a risk factor for cardiovascular events. Two previous systematic reviews by Mangi et al, and Goldfarb et al, looked at the effects of energy drinks and found the following cardiovascular changes: 5 atrial arrhythmias, 5 ventricular arrhythmias, 1 QT prolongation, 4 ST-segment elevations, 3 aortic dissections, and 2 cardiac arrest cases[13,14]. QTc prolongation can lead to torsade des pointes, ventricular fibrillation, and sudden cardiac death[19]. Normal QT interval is below 400 to 440 milliseconds (MS)[20]. QTc prolongation of >450ms in men and >470ms in women is associated with a three-fold increased risk for sudden cardiac death[21]. Energy drinks are also a risk factor for cardiovascular events such as hypertension, diabetes, increased heart rate, and blood vessel

constriction which contribute to cardiovascular disease[1,22,23]. Further studies are needed to have a better understanding of these cardiovascular changes.

Limitations

This systematic review contains several limitations. The sample size for all studies reviewed was relatively small and results were, therefore, not broadly generalizable. The studies vary in their study designs. Basrai, et al. did not include a control group for comparison. Fletcher, at al. compared energy drinks to regular caffeine and used the regular caffeine as their "control group". Therefore, they did not have a baseline for comparison. These studies did not investigate the different doses of caffeine in energy drinks or investigate the other ingredients in energy drinks. Future studies with larger clinical trials controlling for these limitations are warranted to have a more complete understanding of the effects of energy drinks in larger sample sizes. That will make the studies become representative of the global population, provide a thorough comparison between different doses of caffeine, and reveal possible effects of the different ingredients within energy drinks. Doctors, researchers, and public health experts have joined forces to pressure the FDA to act on energy drinks to protect adolescents from the possible risks of consuming these drinks[24].

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