HeartRhythm

The Official Journal of the Heart Rhythm Society, The Cardiac Electrophysiology Society, and The Pediatric & Congenital Electrophysiology Society

Heart Rhythm Society SM

Sudden cardiac arrest occurring in temporal proximity to consumption of energy drinks

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ABSTRACT

BACKGROUND Energy drinks potentially can trigger life-threatening cardiac arrhythmias. It has been postulated that the highly stimulating and unregulated ingredients alter heart rate, blood pressure, cardiac contractility, and cardiac repolarization in a potentially proarrhythmic manner.

OBJECTIVE The purpose of this study was to describe our experience regarding sudden cardiac arrest (SCA) occurring in proximity to energy drink consumption in patients with underlying genetic heart diseases.

METHODS The electronic medical records of all SCA survivors with proven arrhythmias referred to the Mayo Clinic Windland Smith Rice Genetic Heart Rhythm Clinic for evaluation were reviewed to identify those who consumed an energy drink before their event. Patient demographics, clinical characteristics, documented energy drink consumption, and temporal relationship of energy drink consumption to SCA were obtained.

RESULTS Among 144 SCA survivors, 7 (5%; 6 female; mean age at SCA 29 ± 8 years) experienced an unexplained SCA associated temporally with energy drink consumption. Of these individuals, 2 had long QT syndrome and 2 had catecholaminergic polymorphic ventricular tachycardia; the remaining 3 were diagnosed with idiopathic ventricular fibrillation. Three patients (43%) consumed energy drinks regularly. Six patients (86%) required a rescue shock, and 1 (14%) was resuscitated manually. All SCA survivors have quit consuming energy drinks and have been event-free since.

CONCLUSION Overall, 5% of SCA survivors experienced SCA in proximity to consuming an energy drink. Although larger cohort studies are needed to elucidate the incidence/prevalence and quantify its precise risk, it seems prudent to sound an early warning on this potential risk.

KEYWORDS Sudden cardiac arrest; Energy drinks; Caffeine; Genetic heart disease; Long QT syndrome; Catecholaminergic polymorphic ventricular tachycardia; Idiopathic ventricular fibrillation

(Heart Rhythm 2024;■:1–6)

Introduction

The energy drink market in the United States has been growing consistently over the past few years. Most of these beverages claim to contain natural ingredients, classifying them as dietary supplements rather than medications, and, as such, monitoring of these products or manufacturerers by the US Food and Drug Administration (FDA) is not required.[1]

With emerging brands targeting younger age groups, energy drinks have become the second most consumed supplement, following multivitamins, among adolescents and young adults.[2] According to a Statista report, the energy drink industry generated nearly $14 billion in revenue in 2021, with *Red Bull* and *Monster* maintaining market leadership, with newer contenders such as *Reign* entering the top 5 best sellers.[3,4]

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https://doi.org/10.1016/j.hrthm.2024.02.018
1547-5271/$-see front matter

These beverages contain caffeine ranging from 80 to 300 mg per serving, compared with 100 mg in an 8-oz cup of brewed coffee.[5–7] However, most of these energy drinks contain other stimulating ingredients in addition to caffeine that are unregulated by the FDA, such as taurine and guarana. The industry's growth has raised concerns about the potential combined effects of caffeine consumption and additional unregulated ingredients in these beverages.

Previous studies have shown a potential correlation between high caffeine consumption (>10 cups of coffee per day) and sudden cardiac arrest (SCA).[8,9] Individuals with genetic heart diseases (GHDs) already have an increased risk for SCA and sudden cardiac death, especially those with long QT syndrome (LQTS), catecholaminergic polymorphic ventricular tachycardia (CPVT), and idiopathic ventricular fibrillation (IVF). The surge in popularity of energy drinks, increasing levels of caffeine content per serving, and presence of several unregulated ingredients raise concern about their use in patients with GHDs. Our study aimed to investigate whether there exists a potential temporal association between energy drink consumption and the risk of cardiac events, specifically SCA, among patients with an underlying GHD.

Methods

In this Mayo Clinic Institutional Review Board-approved study, we performed a retrospective review of >5000 patients evaluated in the Mayo Clinic Windland Smith Rice Genetic Heart Rhythm Clinic between July 2000 and January 2023 to identify the subset of patients who survived SCA (N = 144; 51% female) with proven arrhythmias requiring resuscitation and/or defibrillation. Among the 144 SCA survivors, we identified, through extensive chart review, the subset of patients who experienced a documented sentinel event or breakthrough cardiac event (BCE) in close temporal proximity to consuming an energy drink. Sentinel events were defined as events that occurred before diagnosis, whereas BCEs were defined as events that occurred after diagnosis and treatment initiation. Electronic medical records were evaluated for patient demographics, clinical characteristics, documented energy drink consumption, and temporal relationship of energy drink consumption to SCA. Energy drink consumption was considered frequent or infrequent based on patient self-reporting. Although retrospective in nature, ascertainment of energy drink consumption was near 100% because it has been part of the senior author's (MJA) standard routine history taking since 2000. Genetic variants were classified using American College of Medical Genetics recommendation.[10]

Abbreviations

AED: automatic external defibrillator

BCE: breakthrough cardiac event

CPVT: catecholaminergic polymorphic ventricular tachycardia

FDA: Food and Drug Administration

GHD: genetic heart disease

ICD: implantable cardioverter-defibrillator

IVF: idiopathic ventricular fibrillation

LCSD: left cardiac sympathic denervation

LQTS: long QT syndrome

SCA: sudden cardiac arrest

Statistical analysis

Continuous variables are given as mean ± SD, and categorical variables are given as frequency (percentage).

Results

Among the 144 SCA survivors (73 females [51%]), 7 patients (5%; 6 female; mean age at SCA event 29 ± 8 years) had a temporal correlation between energy drink consumption and SCA (Table 1). SCA following energy drink consumption was the sentinel event in 6 patients (87%) and a BCE in the remaining patient. Following comprehensive clinical evaluation of these 7 patients, 3 (43%) were diagnosed with unexplained SCA/IVF, 2 (29%) with CPVT, and 2 (29%) with LQTS.

Three patients (43%) reported to consume energy drinks frequently, whereas the remaining 4 patients (57%) consumed them infrequently. The time span between energy drink consumption and the occurrence of the event varied from within 12 hours to immediately before the event. Various types of energy drinks were consumed, with caffeine contents ranging from 80 to >200 mg per serving. The majority of patients (6/7 [86%]) required a rescue shock for malignant arrhythmia, whereas manual resuscitation with chest compressions and precordial thump was performed on 1 patient (14%).

Following their event and subsequent clinical evaluation at Mayo Clinic, 6 of 7 patients (86%) were discharged with an implantable cardioverter-defibrillator (ICD), 2 (29%) underwent left cardiac sympathetic denervation (LCSD), and 2 (29%) were discharged on pharmacologic therapy. One of these patients (case 5) did not change her already established triple protection treatment of nadolol, flecainide, and LCSD, only changing her habits to quit both consuming energy drinks and vaping. Following their SCA, all patients ceased consuming energy drinks, were further risk-stratified, and had their disease-directed therapies optimized. They have since remained free from BCEs, with an average follow-up of 52 ± 43 months. Clinical characteristics of these 7 patients are detailed here and summarized in Table 2.

Table 1 Cohort demographics

Mean age at event (y)	29 ± 8
Female	6 (86)
Diagnosis	
IVF	3 (43)
CPVT	2 (29)
LQTS	2 (29)
Genotype positive	5 (71)
Sentinel event	5 (71)
Frequent energy drink consumption	3 (43)
Rescue shock needed	6 (86)

Values are given as n (%) or mean ± SD.
CPVT = catecholaminergic polymorphic ventricular tachycardia; IVF = idiopathic ventricular fibrillation; LQTS = long QT syndrome.

Table 2 Clinical details of SCA survivors with temporal energy drink consumption

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age at event (y)	32	37	20	28	21	42	26
Gender	F	F	M	F	F	F	F
Diagnosis	IVF	IVF	IVF	CPVT	CPVT	LQT5	LQT8
Gene	None	None	ALPK3	RyR2	RyR2	KCNE1	CACNA1C
Variant found	None	None	p. Arg1547Thr	p. Arg3734Cys	p. Ser2246Leu	p. Asp76Asn	p. Arg858His
Variant classification	None	None	VUS	LP	P	LP	P
Therapy before event	No medications	Fexofenadine	No medications	No medications	Flecainide, LCSD, nadolol	Azithromycin, trimethoprim/ sulfamethoxazole	No medications
Sentinel event	Yes	Yes	Yes	Yes	No	Yes	Yes
Circumstances	Loss of consciousness while sleeping	Agonal breathing leading to loss of consciousness while sleeping	Syncope during exercise	Syncope while breaking up a fight at work	Syncope during an argument at work	Syncope during exercise	Loss of consciousness while sitting in the passenger seat of a car
No. of shocks needed to resuscitate	2	1	2	1	3	6	0*
Frequent energy drink consumer	No	Yes	Yes	Yes	No	No	No
Time between energy drink consumption and event	Hours before	Evening before	Before workout	Day of	Morning of	Before workout	Immediately before
Approximate amount of caffeine consumed (mg)	80	160	Unknown	200+	160	Unknown	160
Follow-p treatment	ICD	ICD, nadolol	ICD	ICD, LCSD	Flecainide, LCSD, nadolol	ICD	ICD

CPVT = catecholaminergic polymorphic ventricular tachycardia; F = female; ICD = implantable cardioverter-defibrillator; IVF = idiopathic ventricular fibrillation; LCSD = left cardiac sympathic denervation; LP = likely pathogenic; LQT5 = long QT syndrome type 5; LQT8 = long QT syndrome type 8; M = male; P = pathogenic; SCA = sudden cardiac arrest; VUS = variant of uncertain significance.
*Manual resuscitation with chest compressions and precordial thump was performed.

Cardiac events temporally associated with energy drink consumption

Case 1

The first patient was a 32-year-old woman who, before her pregnancy, was a regular consumer of energy drinks but paused her consumption while pregnant. The evening before her event, she was 11 weeks postpartum and had just begun working out again. Before her workout, she consumed an energy drink. A few hours later, while in bed, she experienced SCA and was defibrillated twice. This patient was not in her usual state of health, potentially experiencing a "perfect storm" of converging confounding variables as she was postpartum, sleep deprived, and potentially undernourished. After this event, she underwent genetic testing, which revealed nothing of concern. She had no history of cardiac symptoms or events. She was diagnosed with IVF and was discharged with a subcutaneous ICD.

Case 2

The second patient was a 37-year-old woman. Her sentinel event occurred the evening after consumption of an energy drink, as she had been doing most days. A few hours after consumption, she experienced agonal breathing in the middle of the night and received a shock by first responders. She was discharged on nadolol and received an ICD. Genetic testing later revealed nothing of concern; therefore, she was diagnosed as IVF. She has not experienced further cardiac symptoms or BCEs since.

Case 3

The third patient was a 20-year-old man who typically consumed an energy drink before his workouts, which were relatively intense as he was a collegiate track and cross-country athlete. He did not report experiencing cardiac symptoms or events before his sentinel event. On the day of his

sentinel event, he collapsed in the middle of doing sprints during practice. He received 2 shocks from an automatic external defibrillator (AED), with record of asystole between the first and second shocks. Genetic testing revealed a variant of uncertain significance in ALPK3. Follow-up evaluation was unremarkable, with his stress test showing that he exercised for 18 minutes (121% of predicted) to a peak heart rate of 176 (88% of predicted) and generated a VO_2 of 60.5 (122% of predicted). There was no evidence of exercise-associated ectopy. As such, the patient was labeled as IVF and received subcutaneous ICD monotherapy. He has since returned to collegiate athletics and has remained free of cardiac symptoms and events.

Case 4

The fourth patient was a 28-year-old woman whose sentinel event occurred after she consumed "large amounts" (>200 mg) of an energy drink, as she did most days. She collapsed suddenly while breaking up a fight at work and was resuscitated via AED shock by first responders. Before this event, she did not report experiencing any other cardiac related symptoms or events. She was discharged with a secondary-prevention, dual-chamber pacemaker defibrillator and beta-blocker therapy. Genetic testing was pursued and led to a diagnosis of CPVT after a variant in *RYR2* was discovered. After evaluation at Mayo Clinic, she opted to stop taking beta-blockers due to intolerance and instead underwent LCSD and began taking flecainide. The patient has remained event-free since.

Case 5

The fifth patient was a 21-year-old woman. She experienced her sentinel event, syncope, at age 7. After this event, she was discharged on a combination treatment of nadolol and flecainide. Genetic testing was performed, and she was diagnosed with *RYR2*-mediated CPVT. While compliant with her CPVT1-directed combination drug therapy for about 10 years, she experienced an SCA and an ICD was implanted, which later was extracted due to multiple infections. At that time, she came to Mayo Clinic for evaluation. She opted for triple protection with the addition of an LCSD. Three years later, the patient had another SCA while adherent with her medications. Although not a regular consumer of energy drinks, she had consumed one the morning of her BCE. She also had been vaping the day of the event, which had become a habit for her at the time. Subsequently, she collapsed at her workplace during an argument with a coworker and received 3 AED shocks. After this incident, her course of therapy did not change, but she stopped vaping and consuming energy drinks. The patient has yet to have subsequent BCEs over these past 4.5 years of follow-up.

Case 6

The sixth case was a 42-year-old woman. Before her SCA, the patient experienced postpartum-timed syncope. After a cardiac workup, the syncope was attributed to bradycardia, and she was discharged without treatment. More than 10 years later, her sentinel event occurred following the consumption of an energy drink just before her workout. Of note, frequent consumption of energy drinks was not part of her routine, and at the time she was taking 2 different QT-prolonging antibiotics (trimethoprim/sulfamethoxazole and azithromycin) because of an infection. While cycling, she suddenly lost consciousness, fell off her bike, and struck her head. She recovered spontaneously but fainted again. She was taken to the hospital and admitted to the intensive care unit due to recurrent episodes of polymorphic ventricular tachycardia (VT). She received 6 shocks and underwent implantation of a dual-chamber pacemaker defibrillator before her discharge from the hospital. She also was placed on beta-blockers, which later were discontinued due to intolerance. ICD monotherapy then became her course of treatment. She was diagnosed with type 5 LQTS, after genetic testing revealed a known LQT5-causative variant in *KCNE1*.

Case 7

The seventh case was a 26-year-old woman. On the day of her sentinel event, she had just finished exercising; she was dieting, likely dehydrated, and consumed an energy drink. While consuming the beverage, she lost consciousness while sitting in the passenger seat of a car. She was immediately transported to the hospital, where she was successfully resuscitated manually and a prolonged QTc was recorded. The patient was discharged from the hospital after implantation of a single-chamber transvenous ICD. Genetic testing results after discharge revealed a known LQT8-causative variant in *CACNA1C*.

Discussion

The beverage industry in the United States has witnessed a significant surge in energy drink consumption over the past few years as demonstrated by a total of $58 billion in revenue at the end of 2022,[11] with *Red Bull* and *Monster* leading the industry in sales.[12] With the emergence of new energy drink brands marketed specifically toward younger generations and new ways to consume the beverages in the form of seltzers, sodas, and shots, it is reasonable to expect that consumption of energy drinks will continue to grow.

Many of these drinks purport inclusion of natural ingredients, leading to their classification as dietary supplements rather than medications. According to the National Center for Complementary and Integrative Health,[2] energy drinks are one of the most popular supplements for teenagers and young adults in the United States, second only to multivitamins. Presently, these beverages are most heavily consumed by men aged 18–34 years.[2] Because of the classification of these drinks as a supplement, the energy drink industry avoids regulation by the FDA, allowing companies to circumvent disclosure of precise caffeine content and ingredients for each serving.[1] There is growing concern that the absence of

accurate dosage information on labels may contribute to accidental caffeine overdoses, although such incidents remain rare,[13,14] while the potentially harmful effects of the remaining ingredients are largely unknown.

Energy drinks typically contain anywhere from 80 to 300 mg of caffeine in a 16-oz serving. Previous studies have shown a link between caffeine and sudden cardiac death,[8,9] with cardiac arrhythmias being the most common cause of caffeine-related deaths.[1] This raises concern about individuals already prone to cardiac arrhythmias due to an underlying GHD because they could be at higher risk for arrhythmia when consuming energy drinks.

In 2017, testing of the effect of caffeine on individuals with LQTS showed direct physiological changes within 90 minutes of consumption of energy drinks.[15] With clear changes being shown in patient blood pressure and QT interval, concern for individuals with GHDs consuming energy drinks is valid. However, many confounding variables make it difficult to establish direct causation between arrhythmias and caffeine in energy drinks, such as the overall lack of regulation of the ingredients, uncertainty in exact caffeine content, role and effects of other ingredients, and low event rate. Given these uncertainties, the question arises whether an energy drink could trigger cardiac events in individuals with GHDs.

Herein, we present 7 cases of individuals with GHDs who experienced SCA in close temporal proximity to the consumption of energy drinks. In most of these cases (4 [57%]), the individuals were not frequent consumers of high levels of caffeine. Furthermore, only 1 patient in the cohort had a previous GHD diagnosis and was receiving treatment for it. Although there seemed to be a temporal relationship between energy drink consumption and the SCA event, several of the events occurred among a myriad of potential "agitators" that also could have contributed to a GHD-associated arrhythmia, such as sleep deprivation, dehydration, dieting or extreme fasting, concomitant use of QT-prolonging drugs, or the postpartum period. As such, unusual consumption of caffeine most likely combined with other variables to create a "perfect storm" of risk factors, leading to SCA in these patients.

Nevertheless, although energy drinks cannot be confidently deemed the sole contributor of cardiac arrest in these individuals, the temporal association of energy drink consumption to their event should not be taken lightly. In fact, along with general lifestyle recommendations that we provide patients with a GHD after an event (staying hydrated, QT drug avoidance), we believe that a cautionary note regarding energy drink consumption is warranted. Individuals with GHDs should monitor energy drink consumption, especially in combination with other potential risk factors in their daily life that could trigger an event. Certain steps can be taken by individuals diagnosed with GHDs to help minimize the risk of an event occurring. This can include consuming no more than the recommended amount of caffeine each day and ensuring proper nutrition and hydration.

We previously reported a case study of an individual who consumed an energy drink and her LQT1 substrate subsequently was unmasked. We concluded that the caffeine was potentially acting like epinephrine during stress testing.[16] As previously reported by Schwartz and Dagradi,[17] we are calling attention to the potential risks that energy drinks can have on individuals with genetic variants leading to prolonged QT intervals, and we encourage the FDA to look into this potential connection. Although there is no evidence suggesting that all individuals diagnosed with GHDs should completely avoid caffeine, these events should serve as an early warning about the potential dangers associated with irregular consumption of energy drinks for individuals with GHDs.

Study limitations

Because this is a small cohort at a single center, we have to show appropriate restraint to draw conclusions about the direct effects that energy drinks may have on individuals with GHDs. Furthermore, Mayo Clinic is a tertiary/quaternary referral center for patients with GHDs. Even though our reported event rate is low, this still could be an inflated number because of the selection bias of patients seen at the Windland Smith Rice Genetic Heart Rhythm Clinic. Additionally, due to the retrospective nature of this study design and the fact that consumption was evaluated solely by chart review, energy drink use has not been captured in a standardized manner. This ascertainment bias is less likely because all patients were evaluated by a single genetic cardiologist (MJA) who inquired about energy drinks and other potential triggers in all SCA survivors over these past 20+ years through routine history taking. Nevertheless, it is possible that additional patients might have had an event related to energy drink consumption. It also makes it difficult to estimate overall energy drink consumption in our population. In fact, the patients included in this study were limited to those whose events occurred in close temporal proximity (within 12 hours) to their energy drink consumption and for whom this was noted in their evaluation of circumstances of the SCA event. There could be other patients in this cohort who consume energy drinks regularly without an impact on their cardiovascular health of whom we are unaware. Finally, information on potential confounding variables was limited in this study. The energy drinks likely contributed to a perfect storm of risk factors leading to SCA and were not the sole contributor. Further research is required to continue examining the effects of energy drinks on individuals with GHDs, considering the amount of caffeine, days of consumption, and other variables to determine what aspect of the energy drink is dangerous, if any.

Conclusion

Among the individuals evaluated at our clinic, 5% of SCA survivors consumed one or more energy drink before their event. Although the event rate is low, energy drinks could be triggering SCA in individuals with GHD, and an early warning should be made about the potential risks of these drinks in these patients. Patients should be educated on minimizing their consumption of energy drinks, and the FDA should be urged to provide guidelines about the proper and safe use of these drinks.

Funding Sources: This work was supported by the Mayo Clinic Windland Smith Rice Comprehensive Sudden Cardiac Death Program to Dr Ackerman and the Mayo Clinic Center for Translational Science Activities (CTSA) through Grant Number UL1TR002377 from the National Center for Advancing Translational Sciences (NCATS), a component of the National Institutes of Health (NIH).

Disclosures: Dr Ackerman is a consultant for Abbott, BioMarin Pharmaceuticals, Boston Scientific, Bristol Myers Squibb, Daiichi Sankyo, Illumina, Invitae, Medtronic, Solid Biosciences, and UpToDate. Dr Ackerman and Mayo Clinic have license agreements with AliveCor, Anumana, ARMGO Pharma, Pfizer, and Thryv Therapeutics. However, none of these entities were involved in this study. All other authors have no conflicts of interest to disclose.

Authorship: All authors attest they meet the current ICMJE criteria for authorship.

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