Energy Drinks: Another Cause of QT Prolongation?

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Since the first product appeared on US shelves in 1997, the caffeinated energy drink market has grown dramatically, with an estimated annual revenue of $10 billion in 2018. Advertising for products such as Red Bull, Monster, and Rockstar emphasizes claims of enhanced energy level, mental focus, and physical performance. This marketing strategy resonates with teenagers and young adults, the dominant consumer group for these products. As the energy drink market has grown, so too has awareness of their health risks.[1,2] Between 2004 and 2014, 34 deaths linked to energy drinks were reported to the US Food and Drug Administration, and serious adverse events described in the literature include cardiac arrest, myocardial infarction, atrial fibrillation, and seizures.[3] Despite multiple articles in the medical literature and lay press describing the risks of energy drinks, especially when combined with alcohol, growth of this industry shows little sign of slowing.

Although the health risks of energy drinks have been widely recognized, the mechanism responsible for the cardiovascular complications associated with them remains uncertain. The acute hemodynamic effects of energy drinks in healthy volunteers have been well described: a modest increase in systolic and diastolic blood pressure (in the range of 3–5 mm Hg) with little change in heart rate. Although transient hemodynamic changes of this degree are unlikely to be harmful in the young consumers of energy drinks, the rapid ingestion of a large volume by a susceptible individual may result in potentially more dangerous changes. In this issue of the *Journal of the American Heart Association* (*JAHA*), Shah and colleagues[4] test the hypothesis that energy drinks can cause QT-interval prolongation, a well-recognized risk factor for ventricular arrhythmias. Previous small studies of the electrocardiographic effect of energy drinks, some lacking a placebo control, have reached conflicting conclusions. Using a double-blinded crossover trial design, the effect of 2 different caffeinated energy drinks and a caffeine-free placebo drink on the QT interval was assessed in healthy volunteers with a normal QT interval at baseline. Both energy drinks produced an average maximal increase in heart rate–corrected QT interval (QTc) of 18 to 20 ms that persisted up to 4 hours after consumption. In contrast, the placebo drink was followed by only a small transient increase in QTc. Although no subject developed a QTc >500 ms, both energy drinks resulted in QTc prolongation >50 ms in 2 subjects, a range clearly associated with increased risk of arrhythmia. The effect of the energy drinks on blood pressure and heart rate was similar to that observed in previous studies.

In the drug development world, the US Food and Drug Administration would require extensive safety testing before approval of a drug that caused this degree of QT prolongation in a "thorough QT/QTc study." Whether classified as beverages or dietary supplements, energy drinks require no such safety evaluation. It is sufficient to declare that the individual ingredients are "generally recognized as safe." Safety testing is not required to determine whether the combination of several ingredients that are each generally recognized as safe results in a not-so-safe concoction.

The electrocardiographic effects of caffeine, the main ingredient in energy drinks, have been extensively studied; there is no convincing evidence that caffeine alone causes QTc prolongation.[5,6] Ginseng, added to many of these products for its purported energy-boosting properties, has been reported to cause QT prolongation, but in a direct comparison of a ginseng-containing energy drink with the same amount of ginseng alone, ginseng had no effect on QT interval.[7] In the concentration found in energy drinks, none of the other common ingredients, such as taurine, guarana, L-carnitine, yohimbine, sugars, and B vitamins, is known to cause QT prolongation. Although the observation by Shah et al[4] that the 2 different energy drinks had the same effect on QTc suggests that this may be a class effect, there are >100 different products on the market, each with a

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proprietary combination of ingredients. A conclusion about a possible class effect would at least require knowing about differences in the composition of the 2 products tested.

So, does energy drink–induced QT prolongation pose a serious health risk? The most obvious at-risk group would be those with a genetic long-QT syndrome (LQTS); a health risk in this group is supported by 2 case reports and a small clinical trial. A previously healthy 22-year-old woman experienced cardiac arrest after drinking 6 cans of energy drink over 4 hours.[8] The initial ECG showed torsade de pointes, and her QTc shortly after arrival was prolonged at 526 ms, normalizing to 419 ms over the next few days. Subsequent genetic testing confirmed LQTS-1. In a similar case, a 13-year-old girl who presented with chest pain and palpitations after consuming an energy drink had a prolonged QTc interval on admission (561 ms) that fully normalized by the next day.[9] Genetic testing again confirmed LQTS-1. Finally, in a randomized, placebo-controlled study of subjects with familial LQTS, the QTc interval increased by >50 ms after energy drink in 3 of 24 patients.[10] Perhaps some of the cardiac arrests linked to energy drinks were the result of unmasking a previously undiagnosed genetic ion channelopathy.

Of course, most energy drink consumers do not have a genetic LQTS. Is there evidence that energy drink–induced QT prolongation poses a risk to these individuals? A MEDLINE search finds only a single case of torsade de pointes, the characteristic arrhythmia caused by QT prolongation, linked to energy drink consumption (ie, the young woman with LQTS-1 described above).[8] Torsade de pointes can rapidly progress to ventricular fibrillation, and it is impossible to know whether QT prolongation played a role in any of the unexplained deaths or cardiac arrests linked to energy drinks. But with millions of consumers and >20 000 emergency department visits yearly involving energy drinks, the role of QT prolongation would be more compelling if there were other reports of torsade de pointes.

Concerns about the short- and long-term health risks of energy drinks extend well beyond their effect on ventricular repolarization. These concerns have led to a wide range of recommendations, including stricter requirements for product labeling, restrictions on caffeine content, limitations on the marketing and sale to children and adolescents, and educating parents, teachers, and healthcare providers about the health risks of energy drinks. On the research front, the observation that energy drinks can cause QT prolongation, a well-established risk factor for sudden death, warrants further investigation. Which ingredient or combination of ingredients is responsible for this effect on repolarization? Do some products pose a greater risk than others? What effect does the addition of alcohol or other drugs have on the electrocardiographic effect of energy drinks? What role does QT prolongation play in the sudden deaths linked to energy drinks? Further research is not needed to support the sensible recommendation that patients with a genetic LQTS should be cautioned about the risks of energy drinks. Likewise, individuals who are taking QT-prolonging medications as well as those with coronary or structural heart disease should be advised of this risk.

Disclosures

None.

References

1. Howland J, Rohsenow DJ. Risks of energy drinks mixed with alcohol. *JAMA*. 2013;309:245–246.
2. Sports drinks and energy drinks for children and adolescents: are they appropriate? *Pediatrics*. 2011;127:1182–1189.
3. Goldfarb M, Tellier C, Thanassoulis G. Review of published cases of adverse cardiovascular events after ingestion of energy drinks. *Am J Cardiol*. 2014;113:168–172.
4. Shah SA, Szeto AH, Farewell R, Shek A, Fan D, Quach KN, Bhattacharyya M, Elmiari J, Chan W, O'Dell K, Nguyen N, McGaughey TJ, Grant D, Nasir JM, Kaul S. Impact of high volume energy drinks consumption on electrocardiographic and blood pressure parameters: a randomized trial. *J Am Heart Assoc*. 2019;8:e011318. DOI: 10.1161/JAHA.118.011318.
5. Fletcher EA, Lacey CS, Aaron M, Kolasa M, Occiano A, Shah SA. Randomized controlled trial of high-volume energy drink versus caffeine consumption on ECG and hemodynamic parameters. *J Am Heart Assoc*. 2017;6:e004448. DOI: 10.1161/JAHA.116.004448.
6. Turnbull D, Rodricks JV, Mariano GF, Chowdhury F. Caffeine and cardiovascular health. *Regul Toxicol Pharmacol*. 2017;89:165–185.
7. Shah SA, Occiano A, Nguyen TA, Chan A, Sky JC, Bhattacharyya M, O'Dell KM, Shek A, Nguyen NN. Electrocardiographic and blood pressure effects of energy drinks and Panax ginseng in healthy volunteers: a randomized clinical trial. *Int J Cardiol*. 2016;218:318–323.
8. Rottlaender D, Motloch LJ, Reda S, Larbig R, Hoppe UC. Cardiac arrest due to long QT syndrome associated with excessive consumption of energy drinks. *Int J Cardiol*. 2012;158:e51–e52.
9. Dufendach KA, Horner JM, Cannon BC, Ackerman MJ. Congenital type 1 long QT syndrome unmasked by a highly caffeinated energy drink. *Heart Rhythm*. 2012;9:285–288.
10. Gray B, Ingles J, Medi C, Driscoll T, Semsarian C. Cardiovascular effects of energy drinks in familial long QT syndrome: a randomized cross-over study. *Int J Cardiol*. 2017;231:150–154.

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