Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Hypercoagulability after energy drink consumption

*Matthew J. Pommerening, MD, Jessica C. Cardenas, PhD, Zayde A. Radwan, MD, Charles E. Wade, PhD, John B. Holcomb, MD, and Bryan A. Cotton, MD, MPH**

Department of Surgery and the Center for Translational Injury Research, The University of Texas Health Science Center, Houston, Texas

ARTICLE INFO

Article history:
Received 3 January 2015
Received in revised form
6 May 2015
Accepted 11 June 2015
Available online 18 June 2015

Keywords:
Energy drink
Coagulation
Hypercoagulability
Platelet aggregation
Thrombosis

ABSTRACT

Background: Energy drink consumption in the United States has more than doubled over the last decade and has been implicated in cardiac arrhythmias, myocardial infarction, and even sudden cardiac death. We hypothesized that energy drink consumption may increase the risk of adverse cardiovascular events by increasing platelet aggregation, thereby resulting in a relatively hypercoagulable state and increased risk of thrombosis.

Methods: Thirty-two healthy volunteers aged 18–40 y were given 16 oz of bottled water or a standardized, sugar-free energy drink on two separate occasions, 1-wk apart. Beverages were consumed after an overnight fast over a 30-min period. Coagulation parameters and platelet function were measured before and 60 min after consumption using thrombelastography and impedance aggregometry.

Results: No statistically significant differences in coagulation were detected using kaolin or rapid thrombelastography. In addition, no differences in platelet aggregation were detected using ristocetin, collagen, thrombin receptor–activating peptide, or adenosine diphosphate –induced multiple impedance aggregometry. However, compared to water controls, energy drink consumption resulted in a significant increase in platelet aggregation via arachidonic acid–induced activation (area under the aggregation curve, 72.4 U *versus* 66.3 U; $P = 0.018$).

Conclusions: Energy drinks are associated with increased platelet activity via arachidonic acid–induced platelet aggregation within 1 h of consumption. Although larger clinical studies are needed to further address the safety and health concerns of these drinks, the increased platelet response may provide a mechanism by which energy drinks increase the risk of adverse cardiovascular events.

1. Background

In the last two decades, energy drinks have become increasingly popular in the United States. In 2007, just 10 y after the introduction of Red Bull to the United States, the energy drink market expanded to over 500 brands, comprising over 62% of the national beverage market. Sales have increased at an exponential rate, and as of 2013, Americans spend nearly $20 billion consuming <290 million gallons of "performance-enhancing" beverages annually [1,2]. Much of their success

Presented at the Thrombosis and Hemostasis Summit of North America in Chicago, Illinois, April 10th, 2014.

* *Corresponding author*. Center for Translational Injury Research, The University of Texas Health Science Center, 6410 Fannin St, UPB Suite 1100.20, Houston, TX 77030. Tel.: +1 713 500 7313; fax: +1 713 500 0683.
E-mail address: bryan.a.cotton@uth.tmc.edu (B.A. Cotton).

0022-4804/$ – see front matter © 2015 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jss.2015.06.027

has been attributed to their clever and aggressive marketing strategies toward adolescents and young adults [2,3]. It is estimated that 34% of 18–24 year old males drink energy drinks on a regular basis, and up to 51% of college students drink at least one energy drink per month as an energy boost for studying, partying, or simple day-to-day activities.

In recent years, there has been increasing concern regarding the safety of energy drinks. Energy drinks have been anecdotally linked with several adverse cardiovascular events, including arrhythmias, myocardial infarction, and sudden cardiac death [4–6]. Although no causal association has been made, consumption of these beverages has been implicated in over 18 deaths and as many as 30 filings of serious injury, and the Food and Drug Administration has formally opened an investigation into the safety of these products [7–9].

Although the mechanisms are unknown, health risks associated with energy drinks may be related to hypercoagulable changes resulting in increased risk of thrombosis. In surgical and trauma patients, hypercoagulable changes are a normal response to tissue injury; however, they also significantly increase the risk of venous thromboembolism [10–15]. Thromboembolic complications remain among the leading causes of postoperative morbidity and mortality, yet the underlying mechanisms are poorly understood and predicting thromboembolic events remains a challenge [16]. We hypothesized that energy drinks induce coagulation changes that result in a relative hypercoagulable state.

2. Methods

2.1. Selection of participants

Healthy adult volunteers between the ages of 18 and 40 y were recruited to participate in the study. Subjects were required to have consumed at least one energy beverage in the past 12 mo without adverse effects to participate. A screening questionnaire was used to evaluate for exclusion criteria, which included use of aspirin, clopidogrel, or any other anticoagulant within 14 d, evidence of acute illness or infection, pregnancy, or significant history of cardiovascular disease and/or diabetes mellitus. The questionnaire also screened for recent use of oral contraceptives and nonsteroidal anti-inflammatory drugs. All subjects were required to fast overnight and refrain from consuming caffeine, alcohol, and nonsteroidal anti-inflammatory drugs for a minimum of 24 h before participation in the study. The Institutional Review Board at the University of Texas Health Science Center at Houston approved this study (HSC-GEN-13-0177).

2.2. Study protocol

Following informed consent, blood samples were drawn from eligible subjects on two separate laboratory visits a minimum of 1-wk apart from each other. On the first visit, subjects were randomized to receive 16 oz of a sugar-free energy drink or 16 oz of bottled water as a control, which was consumed over a 30-min period. Antecubital venipuncture using a 21-gauge butterfly needle was performed immediately before and 60 min after consumption of the energy drink or water control. The process was then repeated 1-wk later with the beverage not consumed during the first visit. The energy drink chosen for the study contained a total of 140 mg of caffeine content and an "energy blend" containing undisclosed amounts of taurine, *Panax ginseng* extract, L-carnitine, glucuronolactone, inositol, and guarana extract. Coagulation changes were measured using kaolin thrombelastography (TEG) and rapid thrombelastography (rTEG), and platelet function was measured using multiple electrode impedance aggregometry (Multiplate; Roche Diagnostics GmbH, Mannheim, Germany).

2.3. Laboratory measurements and processing of specimens

2.3.1. Thrombelastography

The activated clotting time on rTEG (normal range, 0–118 s) is the time in seconds between the initiation of the test and the initial fibrin formation and is increased with factor deficiency and decreased with enzymatic hypercoagulopathy [17]. The *r*-value (reaction time, min) is also another representation of the time to the beginning of clot formation. The alpha angle, (normal range, 66–82°) is the angle between the tangent line drawn from the base horizontal line to the beginning of the cross-linking process and represents to mean rate of thrombin generation, which directly influences the conversion of fibrinogen to fibrin and thus clot formation. Therefore, an increased alpha angle represents an increased rate of clot formation, as would be seen in hyperfibrinogenemia. The maximal amplitude (MA; normal range, 54–72 mm) is the greatest amplitude of the tracing and reflects platelet and fibrinogen contribution to clot strength. High MA values correspond with states of platelet hypercoagulability. The G-value (normal range, 5.3–12 K dyn/cm^2) is a measure of absolute clot strength (both enzymatic and platelet contributions) and is increased in hypercoagulable states. Percent fibrinolysis at 30 min (LY30; normal range, 0.0%–7.5%) represents the percent amplitude reduction at 30 min after MA and reflects the degree of fibrinolysis.

All TEG specimens were run on a TEG 5000 thromboelastograph (Haemoscope Corporation, Niles, IL). TEG was performed as previously described [17]. Briefly, anticoagulation was reversed by the addition of calcium chloride to citrated whole blood in the TEG cup. Kaolin and tissue factor were added to initiate coagulation as per manufacturer's instructions for performing rTEG. Quality controls were performed on the TEG analyzers every 8 h per the package insert from the Haemonetics Company (Braintree, MA).

2.3.2. Platelet aggregation

While TEG is a global measure of the kinetic processes involved in coagulation, including platelet activation, impedance aggregometry specifically measures coagulation as it relates to platelet function. After the addition of a platelet activator to whole blood, activated platelets adhere to two pairs of sensor wires made of highly conductive copper electrodes, which are silver-coated. Platelet aggregation between the sensor wires increases the electrical resistance between the wires, resulting in a change in impedance to the electrical signal. Increased impedance implies increased platelet