Red Bull®: Red flag or red herring?

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One of the most disquieting events in modern medicine was the realization that a huge variety of drugs used also for non-life-threatening disorders such as antihistaminics or antibiotics - all blockers of the \( \text{IKr} \) current - can trigger life-threatening cardiac arrhythmias resulting in drug-induced long QT syndrome (LQTS) [1,2]. We have recently demonstrated that almost one-third of drug-induced LQTS occurs in subjects carrying disease-causing mutations for congenital LQTS [3], thus confirming earlier observations [4,5]. The emerging concept is that these arrhythmic events are not occurring randomly but are more likely to develop in apparently healthy individuals who, however, have a genetic predisposition to react to, say, \( \text{IKr} \) blockers. However, it was totally unforeseen that such substances that we may eat or drink could have similar potentially dangerous effects.

During the last 15 years there has been an explosion in the use of “energy drinks” (EDs), the best known probably being Red Bull® and Monster®. Scattered reports, mostly of mere anecdotal value, have flourished linking these EDs to serious arrhythmias in subjects without a history of heart disease [6] and to the unmasking of congenital LQTS [7]. So far, however, there has not been a study specifically designed to test the effects of these EDs in subjects carrying mutations causing congenital LQTS.

In this issue of the Journal, Dr. Gray and the expert group led by Dr. Semsarian present the first study aimed at assessing the cardiovascular responses to EDs in 24 patients with LQTS [8]. The patients were randomized to drink either one can of Red Bull® at time 0 and a second one 30 min later or two cans of a control drink. After 1 week they were given the alternate drink. In this way all subjects served as their own controls. The dose was relatively modest, as indicated by the fact that while blood pressure increased by a mean of 7–8 mmHg heart rate remained essentially unchanged. What matters, though, is the fact that 3 (12.5%) patients had an increase in their QTc ≥50 ms. This is a clinically relevant increase in the QT interval, especially in consideration that these were LQTS patients, and thus expected to have a prolonged QT intervals to begin with. As analogy, the guidelines for LQTS indicate that whenever mexiletine shortens the QTc by at least 40 ms it should be added to beta-blockers for chronic therapy [9].

The article by Gray et al. [8] is not without weaknesses which, however, do not limit the importance of its warning. The study population is rather small and, above all, the dose of Red Bull® was low. It is common knowledge that, especially teen-agers, when they take EDs tend to do it “big way”, like the infamous “six pack” of beer, and frequently mix them with various types of alcohol. This implies that whatever the “true” effects of EDs, Gray’s study is likely to underestimate them. In other words, with the doses of EDs used, the most likely thing was to see... nothing. By contrast, 3 of these 24 subjects, several of whom had a normal or borderline QTc (and were, thereby, at very low risk) showed a significant lengthening of the QT interval.

When something, in this case EDs, is ingested by millions of individuals all over the world a percentage such as 12.5% is no longer small, and the findings deserve careful consideration. In these situations it is important to preserve common sense. One should avoid spreading unjustified alarms and fears but, at the same time, one should not push the dust under the carpet and ignore potential dangers. Mike Ackerman’s group has already, and wisely, called attention to the possibility that EDs could unmask a latent or not yet diagnosed LQTS [7]. The initial concern was, and logically so, that EDs could be proarrhythmic because of caffeine and taurine, and this may apply to anyone with an electrically unstable heart or ischemic heart disease. The study by Gray et al. raises a different, and worse, concern; namely that in patients with LQTS these drinks could lead to a further QT prolongation. This obviously has the potential for triggering life-threatening arrhythmias and leads to the next issue, namely what is the probability that a LQTS subject may drink an ED?

Here what matters is the prevalence of LQTS which, based on evidence, is 1 per 2000 live births [10]. This figure, however, relates to the patients who have a clearly prolonged QT interval and does not include those who carry a LQTS-causing mutations but have a normal or borderline QT interval. This is a large number, close to 30% of those with a clearly prolonged QT interval. When this fact is combined with the evidence that majority of LQTS patients destined to become symptomatic has the potential for triggering life-threatening arrhythmias and leads to the next issue, namely what is the probability that a LQTS subject may drink an ED?

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It is equally wrong to spread unjustified concerns and to ignore warning signs. The report by Gray et al. (2017-in this issue) [8] comes after several smaller signals that EDs have the potential of favoring cardiac arrhythmias and provides a first, very tentative and potentially misleading, quantification of the numbers at risk. Its merit is in making impossible now to bury the question. A larger study with a somewhat different design is now warranted. The possibility that these drinks might be harmful for LQTS patients, which would imply the need to inform about this contraindication, has to be tested. In science and in medicine hypotheses need to be properly tested to be either confirmed or dismissed.

Disclosures

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References