

Unusual association of diseases/symptoms

Caffeinated energy drink intoxication

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Summary

In recent years an increasing number of different energy drinks have been introduced to provide an energy boost. They contain high levels of caffeine and other additives that act as stimulants. Several recent studies present that energy drinks could increase the risk of seizures, acid-base disorders and cardiovascular events. The authors report a 28-year-old man who was brought to the emergency room after sudden onset of tonic-clonic seizures and metabolic acidosis after drinking several cans of a caffeinated energy drink. The authors believe that this clinical picture was caused by caffeine intoxication from an energetic drink causing a syndrome of catecholamine excess. The patient was discharged within a week with no complaints and no neurological signs. Finally, recognising the features of caffeine intoxication and its potential health consequences may be especially relevant when treating younger persons who may be more likely to consume energy drinks.

BACKGROUND

In recent years, a number of different energy drinks have been introduced to provide an energy boost or as dietary supplements. They contain high levels of caffeine as well as other additives, such as taurine, ginseng and carnitine that act as stimulants. Some energy drinks contain up to 500 mg of caffeine.¹ Most consumers are unaware of the caffeine content or about the potential dangers.

The Food and Drug Administration² does not currently require energy drinks to display warnings or limit the amount of caffeine they can contain. However, a report published in the journal *Drugs and Alcohol Dependence* in 2009 calls for warnings to be added about the potential health risks energy drinks could pose.³ According to these researchers at Johns Hopkins University, the labels of popular energy drinks, such as Red Bull, should contain warnings about the amount of caffeine they contain and the potentially harmful effects they could cause. In fact, Canada requires labels indicating that Red Bull should not be mixed with alcohol and that maximum daily consumption not exceed two cans (8.3 oz).⁴ Moreover, this energy drink is restricted in Norway and prohibited in France, Uruguay and Denmark because of health risks listed on its cans.³

A recent study conducted by the Cardiovascular Research Centre at the Royal Adelaide Hospital in Australia⁵ found that energy drinks could lift the risk of cerebrovascular accidents and myocardial infarctions by increasing platelet aggregation and decreasing endothelial function, especially when combined with any predisposition to cardiovascular disease, stress or high blood pressure.

The objective of this report is to describe a case of caffeine intoxication from an energy drink acting as a trigger of epileptogenesis in a patient with a previous cerebrovascular accident. The authors also present a literature review of potential health problems caused by caffeinated energy drinks.

The authors think it is important for clinicians to be familiar with the potential health consequences associated

with the use of energy drinks. Recognising the features of caffeine intoxication, withdrawal and dependence may be especially relevant when treating younger persons who may be more likely to consume energy drinks.

CASE PRESENTATION

A 28-year-old man was brought to the emergency room of our hospital after sudden onset of tonic-clonic seizures. The patient had no history of head trauma and denied experiencing any seizure-provoking factors, such as sleep deprivation, illicit drug or recent alcohol abuse, fever or infection. His friends reported that he had drunk several cans (about 6) of a caffeinated energy drink ('Redbull') together with coffee in 4 h.

He had a past history of heroin and cocaine consumption, chronic hepatitis C, severe mitral insufficiency and post-infectious endocarditis. His occupational history was also investigated. He had been living in a recovery and rehabilitation centre for 2 years and he was working in an 'action against hunger' (based in resettlement back into society) when he suddenly developed generalised tonic-clonic seizures with subsequent loss of consciousness. The seizure lasted about 10 min and the patient remained unconscious for a period of time.

On admission, the patient was stuporous, in a post-ictus state, with eye opening in response to verbal command, no verbal response and withdrawal response to pain (Glasgow Coma Scale 8).

The blood pressure was 160/70 mm Hg, heart rate 170/min, respiratory rate 30/min and tympanic temperature 38.4°C. Pulse oxymetry revealed oxygen saturation 48%.

Chest examination was clear. Cardiac auscultation revealed regular heart sounds with a grade 4/6 pansystolic murmur best heard at the apex with radiation into the axilla. The rest of the examination was unremarkable.

About 15 min after admission, the patient developed rapid hypoxia and deterioration of consciousness and became unresponsive. He immediately convulsed in a tonic-clonic way with drooling for several minutes. Arterial

carbon dioxide tension (PaCO₂) was 90 mm Hg, oxygen tension (PaO₂) 40 mm Hg, pH 6.8, with non-measurable plasma bicarbonate and lactic acid >15 mmol/l.

The patient's airway was supported with orotracheal intubation and mechanical ventilation with 100% oxygen. It is important to stress the exuberant oropharyngeal candidiasis.

INVESTIGATIONS

The laboratory exams revealed leucocytosis (23 200/μl), hyperglycaemia (220 mg/dl), serum creatinine 1.5 mg/dl, serum phosphate 7.9 mg/dl, serum magnesium 2.5 mg/dl and D-dimers 430 ng/ml. Urine screening for the presence of cocaine, opioids and benzodiazepins were negative. Screening for phenytoin, carbamazepine, tricyclics, valproic acid and phenobarbital were also negative. Blood and urine cultures were sterile.

The 12-lead ECG showed supraventricular tachycardia with a ventricular rate ranging from 130–150 beats/min.

On chest x-ray, the cardiothoracic index was augmented with clear lung fields.

One hour later, arterial blood gas analysis (with FiO₂ 1.0) revealed PaCO₂ 48 mm Hg, pO₂ 217 mm Hg, pH 6.95; HCO₃ 12 mmol/l and lactic acid 12 mmol/l.

Brain CT scan revealed chronic vascular encephalopathy with corticosubcortical atrophy with absence of acute cerebrovascular lesions.

Lumbar puncture was performed to exclude neurological lesions. Opening pressure and analysis of the cerebrospinal fluid were normal.

Transthoracic echocardiogram revealed severe mitral regurgitation and mild tricuspid regurgitation, left ventricular and atrial dilatation, mild pulmonary hypertension, normal systolic function and no evidence of vegetations. These findings were confirmed by transoesophageal echocardiogram.

TREATMENT

For the control of seizures, the patient was initially treated in the emergency room with midazolam infusion with subsequent valproate infusion.

Treatment also consisted in hydration, oxygen, sodium bicarbonate for the acute control of the acidemia and paracetamol for the control of hyperthermia.

Supraventricular tachycardia showed good response to digoxin administration.

The patient was also treated for the oropharyngeal candidiasis with fluconazol.

OUTCOME AND FOLLOW-UP

The patient was transferred to the intensive care unit with successful weaning from mechanical ventilation 24 h later.

He was then transferred to the intermediate care unit with a complete control of seizures, a good clinical recovery and an improvement of the laboratory findings.

He was discharged within a week to the recovery centre. Three months after being told to abstain from consuming energy drinks, the patient claimed not to have experienced any further seizure activity.

DISCUSSION

We postulate a possible role of excessive consumption of caffeinated energy drinks in triggering the life-threatening events described in this case.

To our knowledge, this is the first case of a catecholamine shock syndrome associated to an epileptogenic process triggered by a caffeinated energy drink.

The energy drink consumed by our patient contains 80 mg of caffeine per can.⁶ He drank about six cans within 4 h together with coffee—up to 500 mg of caffeine in total.

There have been a number of case reports on hospital admissions or deaths due to caffeine toxicity, although the mechanism usually seems to be tachyarrhythmia and involves far higher doses than in this case.^{7–10}

Caffeine is a methylxanthine—part of the biochemical family that includes theophylline and aminophylline.^{10 11} Methylxanthines are associated with cardiac and central nervous system stimulation leading to their use in 'high energy' stimulant drinks.¹¹

Caffeine's primary cardiac action is a competitive antagonism of the adenosine cell surface receptor and has been shown to induce catecholamine release and to increase myocardial automaticity.^{12–14} It also causes a rise in intracellular calcium in myocytes leading to depressed left ventricular systolic and diastolic function.^{12–14} In large doses it can be profoundly toxic resulting in arrhythmia, tachycardia, vomiting, seizures, coma and death.¹⁰

The drink also contains high doses of taurine (an amino acid) and glucuronolactone (a glucose metabolite).⁶ Studies have shown that taurine has an inotropic effect on cardiac muscle similar to that of caffeine and potentiates caffeine-induced muscle contracture.¹⁵ However, few studies regarding taurine toxicity have been performed and there are insufficient data to suggest what level of taurine consumption might be unsafe.

Berger and Alford⁹ postulate that, in physiologically predisposed individuals, a combination of excessive ingestion of caffeine-containing and taurine-containing energy drinks and strenuous physical activity can trigger serious cardiovascular events and induce myocardial ischaemia by coronary vasospasm with potentially fatal results.

In a recent study, Willoughby *et al*⁶ showed that energy drink consumption acutely increases platelet aggregation and decreases endothelial function in healthy young adults; thus, raising the risk of myocardial infarction.

Peake *et al*¹⁴ report a case of highly caffeinated drink ingestion that has precipitated a tachycardia-induced cardiomyopathy, which fully resolved on discontinuation.

The consumption of energy drinks that contain caffeine and other stimulants has also been implicated in causing adverse central nervous system effects, such as seizures and cerebral vasculopathy. According to research presented at the 59th Annual Meeting of the American Academy of Neurology, large amounts of energy drinks may induce seizures in genetically susceptible persons especially if they are taken on an empty stomach.¹⁶

In this context, it is important to point out that our patient had a cerebrovascular accident for 6 months. According to Goldstein *et al*,¹⁷ the risk of having a seizure after ischaemic stroke is 4.2% at 1 year. Late onset seizures

are thought to be caused by gliosis and the development of a meningocerebral cicatrix. Changes in membrane properties, deafferentation, selective neuronal loss and collateral sprouting may result in hyperexcitability and neuronal synchrony sufficient to cause seizures. Therefore, we postulate that catecholamine stimulation due to caffeine intoxication could have triggered an epileptogenic process in a patient with a previous cerebrovascular accident.

Kaufman and Sachdeo¹⁸ state that methylxanthines have been shown to have proconvulsive features. As such, the authors speculate that, in addition to caffeine, patients with epilepsy should avoid all unnecessary dietary sources of methylxanthines.

In addition, studies have suggested that taurine has both anticonvulsant and epileptogenic properties and excessive caffeine consumption has been shown to result in a lower seizure threshold with a dose-dependent effect.¹⁶

It is important to note that the patient had ingested the caffeinated beverages within 240 min. In this way, the total time associated with ingestion of caffeinated beverages may be pertinent to the proconvulsive effect of caffeine. In one study, the proconvulsive effect was dose dependent and lasted for at least 230 min.¹⁹

Judge²⁰ report that excessive adrenergic stimulation from caffeine may also result in hyperglycaemia, hypokalaemia, leucocytosis and metabolic acidosis. In the presence of catecholamines, β adrenoreceptor stimulation results in the hydrolysis of ATP and augments cyclic AMP activity within cells, which stimulates Na-K-ATPase and causes K⁺ ions to shift intracellularly. Excess catecholamines also stimulate glycogenolysis and the breakdown of fatty acids

resulting in hyperglycaemia and metabolic acidosis, respectively.²⁰ They also suggest that intoxication with an agent that causes hyperadrenergic stimulation should be strongly suspected in a patient who has the aforementioned laboratory abnormalities and a sympathomimetic toxidrome.²⁰

The most important measures in treating caffeine-induced metabolic acidosis are to recognise and treat the underlying cause and to provide excellent supportive care, including close observation, airway control, fluid resuscitation and oxygen therapy. For that reason, it is important a complete occupational and past history.

As a solitary case, the findings from this case cannot be generalised. Further limitations include the lack of caffeine blood levels and the lack of quantitative myoclonic frequency.

Competing interests None.

Patient consent Obtained.

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Learning points

- ▶ The consumption of caffeine and its effect on the human body is a topic of ongoing debate.
- ▶ The average consumer may unwittingly consume excessive amounts of caffeine that may lead to adverse physiological side effects, such as seizures and metabolic acidosis.
- ▶ Even the most astute clinician may miss caffeine excess in the differential diagnosis. Therefore, a careful patient history (including a food and beverage diary), physical examination, appropriate use of laboratory tests and a stepwise approach may be helpful in the diagnosis of caffeine excess.
- ▶ In the context of concerns reported in the media and scientific magazines in recent years, and in the presence of a plausible pharmacological mechanism, the potential dangers of these caffeinated energy drinks should be highlighted and monitoring for future adverse events should be conducted.
- ▶ Recognising the features of caffeine intoxication and its potential health consequences may be especially relevant when treating younger persons who may be more likely to consume caffeinated energy drinks.

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