

Acute guarana poisoning: report of two cases

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Abstract

Guarana (*Paullinia cupana*) is a South American plant that contains twice more caffeine compared to coffee beans, and has a stimulatory effect. Thus guarana preparations in the form of capsules, tablets, powders, teas, syrups and energy drinks contain a lot of caffeine, which can rapidly cause poisoning even when only slightly overdosed.

Caffeine poisoning may result in irritability, insomnia, anxiety, restlessness, muscle twitching, nausea or vomiting, rapid heart beat or cardiac arrhythmias, high blood pressure, sweating, diuresis and gastrointestinal disturbance.

This report presents two cases of guarana overdose with the common caffeine poisoning symptoms and signs. Guarana in therapeutic doses can exacerbate underlying cardiac disease (especially cardiac arrhythmias, coronary heart disease, heart failure) and diabetes. Furthermore, children, pregnant and nursing women should avoid guarana as well.

Treatment of guarana poisoning is symptomatic, mainly with benzodiazepines and by fluid and electrolyte substitution.

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1 Introduction

Over the last few years a marked increase in the number of patients with health problems due to overconsumption of products containing caffeine has been noticed. This has resulted from the increased offer of energy drinks, stimulants and other preparations containing caffeine (1,2). In the general population the guarana plant has become increasingly popular in various forms: capsules, tablets, powder, teas, syrups, energy drinks and vitamin drinks (1,3).

Guarana is being promoted as a natural ingredient having various effects

on memory and concentration improvement, lower degree of fatigue, increased energy and alertness, migraine pain relief, burning of body fat and on decreasing appetite. Additionally, guarana is ascribed antibacterial and antioxidative properties, therefore it is believed to have beneficial effects on numerous inflammatory diseases. For its stimulating effect it has long been used as a substitute for coffee. For all the enumerated effects it has become attractive, increasingly used, and widely known all over the world since 1958 (1,4).

Guarana, technical term being *Paullinia cupana*, is a South American climbing plant, named after the Indian tribe Guarani from the Amazon basin. It has large leaves and clusters of flowers, but it is mostly known for its brown reddish fruit containing black seeds enveloped in white coats (Figure 1) (1,5).

Active ingredient is prepared from unripe seeds extracted from fruits, shelled, and then roasted and ground; the obtained powder is modelled with water into sticks that are dried and roasted again – the product is then called *pasta guaranae* (6).

The constituent components of guarana seeds are shown in Table 1 (7). The high content of caffeine giving guarana its stimulating effects should be stressed. High doses, however, may cause health problems triggered by caffeine overdose (1).

Quite a few cases of guarana overdose have been registered worldwide (2). The purpose of this paper is to present the patients treated at the Centre of Clinical Toxicology and Pharmacology of the University Medical Centre Ljubljana for

caffeine poisoning after guarana consumption.

2 Presentation of clinical cases

2.1 Clinical case 1

In order to increase his concentration and alertness for his studies, an 18-year-old student prepared himself a drink. Instead of 1/3 of a tea spoonful he took 3–4 spoonfuls of guarana powder which corresponds to approximately 600–900 mg of caffeine or to 8–11 cups of espresso (one 60-ml cup of espresso contains about 80 mg of caffeine) or to 2–3 litres of energy drink (100 ml of energy drink contains about 30 mg of caffeine). Less than two hours after drink intake, restlessness, strong heart beat, excessive sweating, headache, abdominal distension, and diuresis occurred. Examination at the internal medicine clinic of the Emergency Service, University Medical Centre Ljubljana, revealed increased heart rate (120 beats per minute), increased blood pressure (150/90 mm Hg) and slightly widened pupils, other parameters were normal. ECG showed a borderline prolonged QTc interval (464 ms), whereas laboratory tests showed a slightly decreased potassium concentration (3.7 mmol/L). The patient was otherwise healthy not taking any medications.

He was admitted to the ward where he received diazepam 5 mg perorally, other therapeutic measures were not required. The next day he was free of any subjective health problems, the signs of poisoning resolved and he was discharged from hospital.

Table 1: Guarana seed components (7).

Guarana seed components	Number of particles of each component (parts per million; ppm)
Caffeine	25.000–76.000
Theophylline	570
Tannin	85.000–120.000
Theobromine	200–400
Fats	<30.000
Proteins	<98.600
Resin	<70.000
Starch	50.000–60.000
Adenine, guanine, hypoxanthine, choline, D-catechin	>100.000



Figure 1: Guarana fruit (27).

2.2 Clinical case 2

A 23-year-old man was consuming preparations for fitness containing guarana over one week. Additionally, he was extremely physically active that week. After one week he felt nauseous, had irregular and strong heart beat, felt squeezing chest pain with tingling on both sides of the body lasting for some seconds. He did not report any other problems. ECG showed a slowed down heart rhythm and non-specific elevation of the ST segment in leads V₂-V₄. Additionally, an ultrasound scan of the heart and chest roentgenogram were made revealing no abnormality. Toxicological analysis of biological samples was not made. The problems resolved in approximately two hours after the occurrence of symptoms; ECG normalized. The patient was advised to discontinue using the preparations that may trigger heart rhythm problems (caffeine, theine, guarana and other stimulants).

There have been two cases of attempted suicide with guarana overdose in combination with other psychoactive substances treated. In these two cases, poisoning with other substances was

predominant; guarana was just a supplement to overdosing.

3 Discussion

The effect of guarana is mostly related to caffeine activity. Guarana contains twice as much caffeine as coffee beans (guarana seeds contain 2–4.5 % caffeine, coffee beans 1–2 % only). Guarana seeds contain numerous other substances, mostly theophylline and theobromine that increase caffeine activity. Due to conjugation of caffeine with tannins that form hardly soluble complexes, caffeine from guarana is released into the blood circulation much more slowly than caffeine from coffee. Therefore, its effect is more steady and long lasting; it perseveres for about 6 hours (1,8,9).

In therapeutic concentrations, caffeine inhibits adenosine receptors, thus increasing adenylate cyclase activity and plasma cAMP concentration, which leads to increased activity of the sympathetic nervous system, and this increases the release of neurotransmitter transporters, catecholamines in particular. The systemic vascular resistance and blood pressure increase, and alertness, vigilance and concentration are more intense (1). Also, caffeine increases the synthesis of thromboxane and inhibits thrombocyte aggregation (10). Blocking adenosine receptors on juxtaglomerular cells in the kidney, it affects increased renin release, which further increases angiotensin and aldosterone concentrations. This usually results in diuresis (1).

Adrenaline and caffeine act synergistically in increasing metabolism which affects weight loss. In the liver, an additional amount of sugar is released into the blood circulation and the body gets more energy. Besides, caffeine activates hormone-sensitive lipase in the adipose tissue thus stimulating lipolysis.

Additionally, it stimulates peristalsis and the activity of gall bladder, which results in quicker dissolution of fats, in increased concentrations of free short-chain fatty acids in the large intestines which may lead to diarrhoea, nausea, abdominal cramps and dehydration (11).

In toxic concentrations caffeine competitively inhibits phosphodiesterase, therefore its effects are more markedly expressed. Due to inhibition of this enzyme in vascular smooth muscle cells, the amount of cAMP increases, which increases the renin production and inhibits thrombocyte aggregation, but simultaneously the calcium sensitivity of the contractile apparatus is decreased. This is the cause of vasodilatation (1,10).

In addition, due to the activation of the sympathetic nervous system caffeine impairs the endothelial function, which is the reason for decreased flow-mediated dilatation (12).

Caffeine also affects calcium release from endothelial cells, which causes increased nitric oxide synthesis, which further affects vasodilatation at simultaneous increased cardiac muscle contraction (13).

Ingestion of caffeine overdose is manifested by the following signs and symptoms: restlessness, insomnia, anxiety, fatigue, muscle twitches, nausea or vomiting, accelerated heart beat or arrhythmia, elevated blood pressure, facial

flushing, excessive sweating, diuresis, irritability of the intestines with frequent defecation (Table 2). Should the patient have at least 5 of the enumerated signs and symptoms, the diagnosis of poisoning with caffeine is in place (14,15,16). As the cases we managed presented with most of the enumerated symptoms and signs, we presume that caffeine poisoning occurred, although toxicology analysis of caffeine in the blood was not made.

In excessive doses, caffeine affects cardiac conduction and refractoriness unfavourably; repolarisation of the heart is prolonged as well. This may lead to acute cardiomyopathy, heart arrest, coronary vasospasm, myocardial infarction, increased heart rate, but mainly to cardiac rhythm irregularities, atrial fibrillation in particular (1,5,15). A case of atrial and ventricular fibrillation due to guarana overdose, i.e. caffeine overdose has been described (17,18). Electrocardiogram revealed a prolonged QTc interval, which was found also in one of our patients. Unfavourable effects on the heart action, on the heart rhythm in particular, are exerted by hypocalcaemia, revealed by laboratory tests in one of our cases. Caffeine increases both water elimination from the body and renin release, which leads to increased aldosterone release in the body, therefore potassium loss with urine occurs (19).

Numerous cases of cardiac problems accompanied by epileptic seizures, delirium, irritability, restlessness, frightfulness have been registered (20). Caffeine is a psychoactive substance that can be manifested as agitation, aggressive behaviour, and inclination to suicidal behaviour.

It is estimated that adverse effects will occur at a daily dose exceeding 250–300 mg. A potentially lethal caffeine dose ranges between 10 and 14 g (150–200

Table 2: Effects of low and high doses of caffeine (14,15,16).

Caffeine dose	Caffeine effect
Low dose	insomnia, restlessness, increased alertness, lower degree of fatigue, muscle twitches, accelerated heartbeat tachycardia, increased blood pressure, diuresis, fast digestion
High dose	nausea, vomiting, irregular heartbeat, headache, anxiety, low blood pressure, accelerated breathing, paraesthesia in the hands and around the mouth, inhibited thrombocyte aggregation, epileptic seizures

mg/kg body mass); it depends on the individual's sensitivity to caffeine, smoking, age and health condition. Although 10 g of caffeine corresponds to 100 cups of coffee, quite some death cases have been reported (21).

The consequences of acute guarana/caffeine overdose have been described so far. However, unwanted side effects have been observed also with frequent ingestion of high doses of caffeine which leads to resistance of the organism to high doses. Should a sudden cessation of daily caffeine ingestion occur, withdrawal syndrome would occur within 12–24 hours with a headache, nausea, nasal discharge, fatigue, sleepiness, depression, aversion to work; which may persist up to one week (22).

Guarana ingestion may lead to deterioration of some chronic diseases; special attention should be paid to heart diseases, existing high blood pressure, glaucoma. In diabetic patients additional disorders with glucose regulation may occur since guarana increases glucose concentration in the blood. Regular control of blood sugar level and adaptation of treatment for insufficient effect of anti-diabetic drugs are required. Also, special attention is required with blood clotting disorders as caffeine in guarana slows down thrombocyte aggregation and blood clotting process. Caffeine accelerates calcium and potassium excretion from the body through the kidneys, which is unfavourable in patients with osteoporosis as this further worsens their bone condition. Pregnant and nursing women are advised not to consume guarana/caffeine to prevent negative effects on the newborn (14). Also, guarana consumption is not recommended before and/or during physical activity for additional load on the heart. Caution is needed with adolescents; due to their lower body mass, the effects of caffeine are more ra-

pid and pronounced than in adults; the consequences may be lethal (23). Due to stimulant consumption in children and adolescents poor sleeping habits have been observed that bring along other long term consequences such as growth and developmental disorders, concentration problems, tiredness in school and poorer school achievements (24). Studies have shown that in children caffeine preparations do not increase momentary cognitive abilities and concentration as in adults but have rather negative effects. Caffeine exerts negative effects on brain development, particularly on orbitofrontal cortex and temporal lobe where many adenosine receptors are located. Children also tend to gain body mass at a slower pace, have poor eating habits and are prone to risky and impulsive behaviour (25)

For interaction of guarana with some medications the effect of the latter may be diminished. Simultaneous intake of guarana and different stimulants (amphetamines, cocaine, adrenaline) results in the increased activity of the nervous system, which may lead to serious health problems. Interestingly, the reported cases of guarana intake are often connected with simultaneous intake of other risk substances. Simultaneous intake of guarana and alcohol is quite frequent, a particularly dangerous combination as caffeine masks the subjective perception of alcohol activity. An individual thus has a feeling that he may consume more alcohol than usually, which is tricky as this increases the harmful effect of alcohol on the body and on risky behaviour. The same is true of combination of energy drinks and alcohol. Alcohol is also known to inhibit the metabolism of caffeine, therefore its half life is prolonged (1,23,25).

The diagnosis of guarana/caffeine poisoning is based on medical history and

clinical picture, and is to be confirmed by toxicological blood analysis with gas chromatography and mass spectrometry (22).

The therapy within the first hour after guarana consumption includes gastrointestinal decontamination with activated charcoal. In life-threatening poisoning, caffeine can be removed from the body with haemodialysis. Further treatment is symptomatic, mainly with benzodiazepines (restlessness), parenteral hydration and electrolyte substitution (22,26).

4 Conclusion

In Slovenia, not many cases of guarana overdose have been registered, but due to widespread use of stimulants, an

increase is expected. Generally, guarana is presented as a most healing substance without harmful effects. However, it is necessary to stress that it contains a high dose of caffeine, which may quickly cause poisoning. Among the most life-threatening symptoms of caffeine poisoning are arrhythmias and epileptic seizures. To avoid health problems it is necessary the public be informed of the danger of guarana overdose, also via clear indications on the product.

The patients approved the publication of the present article.

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