Letter to the Editor

Fatal cardiac arrhythmia following voluntary caffeine overdose in an amateur body-builder athlete

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A R T I C L E   I N F O

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Dear Editor,

Caffeine (1,3,7-trimethylxanthine, CAS 58-08-2) is one of the most commonly consumed substances in the world and is well known to have extensive effects on physiological functions, especially on the cardiovascular system. We report a fatal cardiac arrhythmia following voluntary caffeine overdose in an amateur body-builder athlete.

A depressive 44-year-old male presented itself to the local emergency department after having intentionally ingested a huge amount (10 g) of pure anhydrous caffeine (1,3,7-trimethylxanthine). Initial physical examination noted a sweaty, trembling and tachypneic patient. Vital signs revealed a blood pressure of 123/83 mm Hg, heart rate of 75 beats per minute and oxygen saturation 100% on ambient air. Five minutes later, a cardiac arrest due to ventricular fibrillation (VF) occurred. Despite 30 min of effective cardiopulmonary resuscitation following most recent guidelines, the patient remained in refractory VF. After multidisciplinary discussion, the patient was transferred in a tertiary university center and assisted by arterio-venous extracorporeal membrane oxygenation (ECMO) device 120 min after the collapse (no flow: 0 min, low flow: 120 min). Initial laboratory investigation showed abnormal findings including elevated white blood cell count of 14.740 G/L, lowered potassium level (2.6 mmol/L; reference range [RR], 3.5–5.0 mmol/L) and elevated glycemia (4.02 g/L; RR, 0.70–1.10 g/L). Rhabdomyolysis was suggested by elevated creatine kinase (CK, 9040 UI/L; RR, <171 UI/L) and cardiac damages by elevated cardiac enzymes: Troponin I (31.01 μg/L; RR, <0.04 μg/L) and CK-MB (346 UI/L; RR, <24 UI/L). A toxicology screening was performed and revealed markedly elevated levels of caffeine in the blood sample (190.0 mg/L; therapeutic range, 5–20 mg/L; toxic, >50 mg/L). No drug of abuse was found in urine. Under ECMO device, a high volume (35 mL/kg/h) continuous veno-venous hemofiltration (CVVHF) was immediately started to clear caffeine in the blood. Caffeine persisted as toxic blood levels (145.2 mg/L initially and 130.1 mg/L after 2 h of CVVHF). The patient died in refractory shock state 13 h after the voluntary ingestion of pure anhydrous caffeine and 4 h after being under arterio-venous ECMO.

Originally a plant derivative alkaloid, caffeine is the most methylated xanthine with numerous pharmacological actions, especially on the cardiovascular system and the central nervous system. Caffeine is structurally similar to adenosine and its main action is the competitive inhibition of adenosine receptors (especially A2a). This action leads to an increase of catecholamine release through the inhibition of phosphodiesterase activity and the increase of cAMP and intracellular calcium concentration. Caffeine also exaggerates β-1 adrenergic receptor effects and sensitizes dopamine receptors. Major result of all those changes is a variable alteration of smooth muscle contraction as supported by some studies showing caffeine-induced vasoconstriction of coronary arteries [1–3]. Therefore, there have been a few case reports of coronary artery vasospasm with abnormal electrocardiogram (ECG) concerning ST elevation myocardial infarct and elevated cardiac enzymes following caffeinated ‘energy drinks’ ingestion [4,5]. The patient’s clinical state
Caffeine is also well known as a trigger for ventricular arrhythmias sometimes leading to cardiac arrest [6,7]. Putative mechanisms have not yet been fully elucidated. The increasing cytosolic calcium level due to caffeine intoxication shortened refractory periods of the right atrium, the atrio-ventricular node and the right ventricle with a prolonged left atrial refractory period. This calcium overload may lower the arrhythmogen threshold. Moreover, caffeine inhibits endogenous adenosine receptors and enhances endogenous catecholamines concentrations. Among the possible other causes in triggering or worsening the arrhythmia, hypokalemia and concomitant illicit stimulants consumption (especially cocaine) should be regarded with caution. Hypokalemia can favor arrhythmia such as VF. The cause of the patient’s hypokalemia remains unclear but is often described in case of caffeine intoxication and may have contributed partially to the intractable VF. Moreover, the negative result on the patient’s drug test makes the role of other illicit stimulants an unlikely cause for the VF.

In humans, blood concentration greater than 50 mg/L is generally considered as toxic and lethal dose is thought to be 100 mg/L even if the correlation between concentration and clinical effects is quite poor [8,9] due to inter-patient variability, tolerance, and/or pre-existing disease states. Most published cases report ECG ischemic changes or arrhythmias in relation to excessive caffeine use based upon a history of such consumption but without toxicological evidence (blood or urine) [4–6]. Moreover, reports of fatal caffeine intoxications with toxicological evidence are essentially available on the base of post-mortem analysis (autopsy), thus without arguments for any cardiac arrhythmia or ischemia [8,9]. Our case reports a massive ingestion followed by refractory VF and death with the toxicological evidence of caffeine intoxication (190.0 mg/L) supporting an obvious causal relationship. Given these specificities of caffeine poisoning, the usual guidelines for cardiopulmonary resuscitation could be not appropriated. Alpha-adrenergic agonist or vasoressin should be preferred to epinephrine or norepinephrine in order to avoid a superimposed beta-adrenergic stimulation in case of refractory hypotension. Hypokalemia correction should be a priority. Brief duration of action β-blocker as esmolol should be considered to avoid the recurrence of ventricular arrhythmias after effective recovery of cardiac function. Finally, in case of massive ingestion, haemodialysis enhances caffeine clearance [10] whereas multiple-dose activated charcoal could play an important role to limit caffeine absorption.

Body-builders are well known to suffer from altered perception of body image often leading to unhealthy eating, exercise habits or even drug-taking. Caffeine has been removed from the list of prohibited substances in sport, but remains on a monitoring program run by the World Anti-Doping Agency and numerous athletes entertaining a hope of enhancement of their performance, still have excessive caffeine consumption. This case report emphasize that prescribed medications can be misused, especially in some sports activities, and thereby sometimes leading to dramatic condition. Physicians must therefore be very attentive and adequately identify any request suggestive of performance enhancing request.

The patient described ingested massive amount of caffeine followed by VF and death with toxicological evidence of caffeine intoxication supporting a strong causality between both events. Intensivists and emergency physicians should be aware of the increasing incidence of misused caffeine in amateur sports activities in case of unusual intractable ventricular arrhythmias with an unclear context. The knowledge of its specific pathophysiology may improve management and may avoid fatal issue.

References