Acta Anaesthesiol Scand 2010; **54**: 521–523
Printed in Singapore. All rights reserved

ACTA ANAESTHESIOLOGICA SCANDINAVICA
doi: 10.1111/j.1399-6576.2009.02201.x

Case Report

A case of fatal caffeine poisoning

T. Rudolph and K. Knudsen
Department of Anesthesia and Intensive Care, Sahlgrenska University Hospital, Gothenburg, Sweden

Caffeine is a natural alkaloid methylxanthine that is found in various plants such as coffee or tea. Symptoms of a severe overdose may present with hypokalemia, hyponatremia, ventricular arrhythmias, hypertension followed by hypotension, respiratory failure, seizures, rhabdomyolysis, ventricular fibrillation and finally circulatory collapse. A 21-year-old woman called for the ambulance herself soon after the ingestion of about 10,000 mg of caffeine. At the arrival of the ambulance, the patient went into cardiac arrest almost immediately. After a total resuscitation period of 34 min including seven counter-shocks and 2 mg epinephrine, the patient was stable enough to be transferred to the hospital. The patient soon went into VF again and received two more counter-shocks and 1 mg epinephrine and finally an intravenous bolus dose of 300 mg amiodarone. The initial arterial blood gas showed pH at 6.47, lactate at 33 mmol/l and potassium level at 2.3 mmol/l. Unfortunately, no blood samples for caffeine analysis were taken. Three days after hospital admission, the patient developed myoclonus, which did not respond to medical treatment. Excessive intake of caffeine may produce arrhythmias and pronounced hypokalemia and ensuing ventricular fibrillation. In case of counter-shock-resistant VF, it can be necessary to give an early loading dose of amiodarone. Furthermore, it may be beneficial to replace the potassium as early as possible. Epinephrine and buffer solutions used during resuscitation may further decrease blood potassium levels and should be administrated cautiously. Epinephrine can be replaced by other vasopressor drugs, such as vasopressin without effects on β-receptors.

Accepted for publication 1 December 2009

Caffeine is a natural alkaloid methylxanthine that is found in various plants such as coffee or tea.[1] It has been used since ancient times as a mild stimulant psychoactive drug and belongs together with alcohol and tobacco as the most common legal addictive substances.[2] The pure substance is sold over-the-counter as a tablet against physical and mental fatigue and is included in some cold remedies.[1,2] Caffeine is also used as a component in some analgesics and in the treatment of apnea in premature infants.[3]

However, despite its wide-spread use, severe caffeine poisoning is rare.[4–7] Ingestion of 20 mg/kg is considered as toxic, 150–200 mg/kg may be lethal. Symptoms of an overdose include headache, nausea, vomiting, hyperventilation, dizziness, anxiety, tinnitus, tremor, excitation, tachycardia and increased urinary output.[4–7] Severe overdose may present with hypokalemia, hyponatremia, ventricular arrhythmias, hypertension followed by hypotension, respiratory failure, seizures, rhabdomyolysis, ventricular fibrillation (VF) and finally circulatory collapse. We describe a case with profound hypokalemia and multiple ventricular fibrillation where circulation was stabilized after repeated counter-shock defibrillations and the administration of amiodarone.

Case

A 21-year-old woman called for the ambulance herself soon after the ingestion of about 100 caffeine tablets, each containing 100 mg resulting in a total amount about 10,000 mg of caffeine. At the arrival of the ambulance, the patient was awake but went into cardiac arrest almost immediately. Cardiopulmonary resuscitation (CPR) was promptly commenced by the ambulance personnel by mechanical mask ventilation and external heart compressions. The initial electrocardiogram (ECG) showed ventricular fibrillation. During a resuscitation period of 10 min, the patient received five counter-shock defibrillations after which spontaneous circulation returned. The patient then was intubated and ventilated by the endotracheal tube. Two minutes later VF returned, which required two more counter-shock

defibrillations. After a total resuscitation period of 34 min including seven counter-shocks and 2 mg epinephrine, the patient was stable enough to be transferred to the hospital for further treatment. During an ambulance transport of 10 min, the patient went into VF again and received two more counter-shocks and 1 mg epinephrine and finally an intravenous bolus dose of 300 mg amiodarone. Because of a short period of pulseless electrical activity, the patient received external heart compressions by a mechanical compression device Lucas-pump TM2, (Jolife Corp., Lund, Sweden). She arrived at the hospital circulatory stabilized with a sinus rhythm and a systolic blood pressure at 120 mmHg but went into VF again after 15 min and received one more successful defibrillation. The initial arterial blood gas was severely deranged with pronounced metabolic acidosis, pH at 6.47 and serum lactate at 33 mmol/l. Sodium bicarbonate and tris buffer solutions were administrated in a total amount of 500 ml corresponding to 280 mmol of buffer. Despite metabolic acidosis, the potassium level at arrival was remarkably low at 2.3 mmol/l. Unfortunately, a blood sample for caffeine analysis was not taken. The patient was transferred to the intensive care unit and 3 h after cardiac arrest hemodialysis was installed via a central hemodialysis venous catheter. Hemodialysis continued for 2 h to remove the caffeine from the blood compartment. An external cooling device was initiated to protect from further hypoxic brain damage. Circulation was stabilized with an intravenous administration of small doses of phenylephrine to maintain a systolic blood pressure above 100 mmHg. No further arrhythmias were observed with a continuous infusion of amiodarone at 37.5 mg/h. An ECG showed a sinus rhythm at 110 b.p.m. with a right bundle branch block. Potassium substitution was administrated at 15–25 mmol/h intravenously. The patient developed moderately elevated troponine-T and CK-MB blood values indicating minor myocardial damage. On the first day, the amount of urinary production increased to >18 l (sic). This extreme urinary output required large amounts of isotonic fluid replacement with Ringers lactate and sodium chloride (9 mg/ml). The urinary production then decreased gradually over the following days and reached normal values on the fourth day. A total of 370 mmol of potassium chloride was administrated on the first day, 7 mmol on the second, 167 mmol on the third, 131 mmol on the fourth and 120 mmol on the fifth day. In total, 795 mmol of potassium was given over 5 days, averaging 159 mmol/day. Three days after hospital admission, the patient developed myoclonus, which did not respond to medical treatment. A neurological examination revealed irreversible anoxic brain damage and after 5 days all treatment was terminated and the patient was transferred to a palliative ward. She died of pneumonia 11 days after the primary caffeine poisoning.

Discussion

Caffeine is related to the methylxanthines theophylline and theobromine that occur naturally together with caffeine.[1,2] In moderate doses, caffeine acts as a competitive antagonist on adenosine receptors.[5,8] Adenosine acts via specific receptors and is found all over the human body but plays a particular role both in the brain modulating systems including the sleep–awake cycle and in the heart acting as a negative inotropic and chronotropic substance. In higher doses, caffeine acts as an inhibitor of the intracellular enzyme phophodiesterase, which converts cyclic AMP into the non-cyclic form.[9] By this action, caffeine interacts with the sympathetic nervous system causing prolonged and intensified β-receptor activation with positive inotropic and chronotropic effects.[9] In very high and toxic doses, caffeine directly releases calcium from intracellular stores, which may increase the susceptibility for arrhythmias.[10]

In our case, the patient ingested as much as 10 g of caffeine. This excessive dose resulted in repeated ventricular fibrillation resistant to electrical defibrillation, probably due to a blockade of cardiac adenosine receptors and intense β-receptor activity. The blockade of cardiac adenosine receptors can lead to tachycardia and arrhythmias, whereas the β-receptor stimulation by the circulating epinephrine has numerous effects, most important is the increased chronotropy and dromotropy with an increased heart rate and conductivity. Stimulation of enzymes such as integral membrane protein sodium–potassium-ATPase lowers plasma potassium levels.[11] This stimulation results in a potassium shift from the blood to intracellular compartments making the membrane potential more negative, which increases the risk for ventricular arrhythmias.

In our case, once ventricular fibrillation occurred it was difficult to regulate by counter-shock defibrillations as the underlying pathophysiological process continued. The risk for arrhythmias may be increased and hypokalemia worsened by the administration of epinephrine and buffer solutions during resuscitation.

Stabilization of circulation was achieved first after an administration of the antiarrhythmic drug amiodarone. Possibly, the administration of unselective β-blocking agents such as propanolol also might be beneficial in this situation.[12,13]

CPR due to severe caffeine intoxication may be one of the rare occasions where potassium substitution could be considered already in the pre-hospital setting, in case all other possibilities have failed. Finally, removal of the trigger caffeine from the patient's blood compartment by hemodialysis contributed to further stabilization in our patient. Hemodialysis was terminated as the patient herself began to produce a high urinary output. An increased urinary production may here be explained by the diuretic effect of the remaining caffeine in combination with whole-body cooling and anoxic brain damage resulting in diabetes insipidus. In this secondary phase, it was important to follow and replace the loss of fluid and potassium to prevent from further arrhythmias.[14] The potassium replacement was remarkably high with the administration of 370 mmol during the first day and a total of 795 mmol over 5 days.

Treatment with respiratory support, the anti-arrhythmic drug amiodarone and aggressive potassium substitution stabilized the circulation adequately in this severely poisoned patient. There was no need for any inotropic or vasopressor drugs once the arrhythmias were converted to a sinus rhythm except for the initial administration of small amounts of phenylephrine. Unfortunately, anoxic brain damage did prevent from a successful outcome in this previously healthy young woman. As caffeine blood samples were not taken, it is uncertain to what extent the high urinary output was due to the remaining caffeine that could have been eliminated further with continued hemodialysis.

Conclusion

Excessive intake of caffeine may produce a life-threatening condition with arrhythmias and pronounced hypokalemia and ensuing a risk for ventricular fibrillation. In case of counter-shock-resistant ventricular fibrillation, it can be necessary to give an early loading dose of amiodarone already at the pre-hospital setting. Furthermore, it may be beneficial to replace potassium as early as possible. Epinephrine and buffer solutions used during resuscitation may further decrease blood potassium levels and should be administrated cautiously. Epinephrine can be replaced by other vasopressor drugs, such as vasopressin without effects on ß-receptors. Finally, it is necessary to monitor plasma potassium levels frequently and plasma caffeine values to avoid a risky progress in the post-resuscitation period.

Acknowledgements

None of the authors consider they have a conflict of interest.

References

1. Abbott PJ. Caffeine: a toxicological overview. Med J Aust 1986; 145: 518–21.
2. Rogers PJ, Richardson NJ, Elliman NA. Overnight caffeine abstinence and negative reinforcement of preference for caffeine-containing drinks. Psychopharmacol 1995; 120: 457–62.
3. Bauer J, Maier K, Linderkamp O, Hentschel R. Effect of caffeine on oxygen consumption and metabolic rate in very low birth weight infants with idiopathic apnea. Pediatrics 2001; 107: 660–3.
4. Holmgren P, Nordén-Pettersson L, Ahlner J. Caffeine fatalities, four case reports. Forensic Sci Int 2004; 139: 71–3.
5. Mrvos RM, Reilly PE, Dean BS, Krenzelok EP. Massive caffeine ingestion resulting in death. Vet Hum Toxicol 1989; 31: 571–2.
6. Kerrigan S, Lindsey T. Fatal caffeine overdose: two case reports. Forensic Sci Int 2005; 153: 67–9.
7. Shum S, Seale C, Hathaway D, Chucovich V, Beard D. Acute caffeine ingestion fatalities: management issues. Vet Hum Toxicol 1997; 39: 228–30.
8. Biaggioni I, Paul S, Puckett A, Arzubiaga C. Caffeine and theophylline as adenosine receptor antagonists in humans. J Pharmacol Exp Ther 1991; 258: 588–93.
9. Forth W, Henschler D, Rummel W, Starke K. Allgemeine und spezielle Pharmakologie und Toxikologie, 7th edn. Heidelberg: Spektrum Akademischer Verlag, 1998.
10. Forman J, Aizer A, Young CR. Myocardial infarction resulting from caffeine overdose in an anorectic woman. Ann Emerg Med 1997; 29: 178–80.
11. Holstege CP, Dobmeier S. Cardiovascular challenges in toxicology emergency. Med Clin North Am 2005; 23: 1195–217.
12. Price KP, Fligner DJ. Treatment of caffeine toxicity with esmolol. Ann Emerg Med 1990; 19: 44–6.
13. Knudsen K, Heath A. Role of extracorporeal drug removal in acute theophylline poisoning. Med Toxicol 1987; 2: 294–308.
14. Holstege CP, Hunter Y, Baer AB, Savory J, Bruns DE, Boyd JC. Massive caffeine overdose requiring vasopressin infusion and hemodialysis. J Toxicol Clin Toxicol 2003; 41: 1003–7.

Address:
Kai Knudsen
Department of Anesthesia and Intensive Care
Sahlgrenska University Hospital
S-413 45 Gothenburg
Sweden
e-mail: kai.knudsen@aniv.gu.se