

Review Article

Cardiac arrest: a case-based review

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BACKGROUND: Coffee is commonly consumed among young people in China. However, consumers are rarely aware of physically adverse effects as a result of excessive consumption of caffeine.

DATA SOURCES: A literature search using multiple databases was performed for articles published with concentration on meta-analyses, systematic reviews, and randomized controlled trials.

RESULTS: Excess coffee consumption is also a risk of primary cardiac arrest especially in young people. Treatment modalities include activated charcoals, beta-blockers, vasopressin and hemodialysis when necessary.

CONCLUSION: Coffee consumers should be advised not to routinely take more than moderate coffee.

KEY WORDS: Cardiac arrest; Coffee; Young people

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INTRODUCTION

A population-based case-control study has proposed that excessive coffee consumption is related to a higher risk of sudden cardiac death.^[1] Moreover, a few case reports described that even drugs and energy drinks which contain massive caffeine could induce cardiac arrest. The internationalization and modernization of China are accompanied by a changing life style. More and more Chinese young people prefer to drink cups of coffee daily instead of tea. However, neither coffee consumers nor primary healthcare workers are well aware of that massive coffee intake might be associated with cardiac arrest in young people. There are few reports about cardiac arrest followed by heavy coffee intake in China.

Caffeine is a natural alkaloid methylxanthine which is recognized to be responsible for coffee toxicity.^[2] On average, a five-ounce cup (150 mL) of percolated or drip coffee contains 120 mg caffeine, and a cup of espresso contains 80 mg caffeine. Moderate caffeine consumption

isn't unhealthy, and high usual caffeine (more than 5 cups per day) is believed to moderately account for an elevated risk of primary cardiac arrest.^[3] However, coffee consumption more than 10 cups per day is an independent risk indicator for sudden cardiac arrest.^[1] Severe overdose may be accompanied by ventricular arrhythmias, ventricular fibrillation and finally circulatory collapse.^[3]

Thereafter, we reported a case in which a young healthy man without any cardiovascular diseases suffered from multiple life-threatening cardiac arrests after excess consumptions of coffee for a long time, and survived without any uncomfortable complaints. Moreover, we reviewed the toxic kinetics, clinical manifestations and treatment strategies of caffeine overdose.

CASE REPORT

A 24-year-old man suddenly collapsed when he was having coffee in a coffee house. First-aid paramedics arrived soon and found him in ventricular fibrillation

(VF). An effective cardiopulmonary resuscitation was performed including two 200 J biphasic direct-current shocks and 1 mg adrenalin as an adjuvant. The patient was restored to sinus rhythm and transferred to the hospital for further treatment. However, he received chest compression and 3 mg atropine because of a short period of asystole during the ambulance transport, and restored to sinus rhythm again with a systolic blood pressure at 100 mmHg. He went into another VF in the hospital and received a second successful defibrillation.

The patient denied having any previous episodes of chest pain or syncope. There was no family history of premature coronary disease, sudden cardiac death or unexplained syncope. No alcohol misuse or illicit drug use was present. He drank 15–20 cups of coffee daily.

Glasgow Coma Scale on admission was 6–7. The patient was intubated and hemodynamically stable. No remarkable abnormalities were found by physical examination. An initial electrocardiograph (ECG) showed a sinus rhythm and a slight widened QTC at 432 ms without any ischemic changes. Chest-ray showed a normal cardiac silhouette and no signs of pulmonary venous congestion. Abnormal findings from laboratory tests included an elevated level of troponin I (225 ng/L; reference range, <15 ng/L) and a relatively lowered potassium level (3.4 mmol/L; reference range, 3.6–5.4 mmol/L). The initial arterial blood gas was deranged with metabolic acidosis (pH at 7.225 and PaCO₂ 43 mmHg). Unfortunately, a blood sample for caffeine analysis was not taken at that time.

The patient was closely monitored for 24 hours without any further treatment, and was extubated without any obstacle. Thereafter, he was discharged with no complaints.

After a follow-up for 2 months, the patient remained physically well with ECG showing sinus rhythm and no S-T segment deviation. A specific advice suggested that less than 3 cups of coffee was proper for him.

DISCUSSION

Severe coffee poisoning is rare worldwide even coffee is such a popular drinking.^[4–7] We have postulated a possible role of excess consumption of coffee in triggering the life-threatening cardiac event described above and make a brief review.

Toxic kinetics and pharmacokinetics

Caffeine is well-absorbed following oral ingestion, and metabolized in the liver by demethylation with a half life of 3–10 hours. The molecular weight of

caffeine is 194 KDa. A mean plasma protein binding ratio of caffeine is 36%, and a volume of distribution is about 0.6–0.8 L/kg.^[8] Its peak plasma concentration is achieved 30–60 minutes after ingestion.^[8] An ordinary coffee consumption may be a modest protective effect against some diseases including certain types of cancer. However, caffeine toxicity usually becomes apparent at various concentrations over 30 mg/L.^[8] Fatal doses have been suggested to be above 6.5 g in adults.^[9–11]

The most important mechanism involving caffeine is to activate adenosine receptors, and thus increase activities of neurotransmissions of acetylcholine, epinephrine, dopamine and glutamate.^[12,13] Adenosine receptors are found throughout the body including the neural, cardiovascular, respiratory, renal and gastrointestinal systems as well as in adipose tissues.^[14]

Furthermore, caffeine exhibits as a competitive antagonist of the benzodiazepine receptors, inhibits phosphodiesterase and acetyl cholinesterase, sensitizes dopamine receptors, and increases renin activity.^[12,13] Moreover, it is estimated that caffeine increases fat utilization and decreases glycogen utilization.^[15]

Caffeine and the cardiovascular system

As a naturally occurring xanthine derivative related to theophylline, caffeine plays a potential role in the cardiovascular system. It competitively inhibits adenosine receptors^[11] and induces catecholamine release.^[16,17] It also makes smooth muscle randomly contract and/or relax by increasing intracellular calcium in myocytes released from the sarcoplasmic reticulum.^[12,16,17]

The role of caffeine in triggering arrhythmia has been well established.^[8,12,16,17] The blockade of cardiac adenosine receptors leads to tachycardia and arrhythmias, whereas the activated beta-receptors by the circulating epinephrine increase chronotropy and dromotropy with an increased heart rate and conductivity.^[18] The arrhythmia most commonly observed in caffeine overdose is sinus tachycardia. Moreover, heavy caffeine intake might result in repeated ventricular fibrillation which is resistant to electrical defibrillation.

The excessive caffeine also stimulates integral membrane protein sodium-potassium-ATPase which lowers plasma potassium levels. Therefore, it results in a potassium shift from the blood to intracellular compartments, makes the membrane potential more negative, and consequently increases the risk for ventricular arrhythmias.^[19]

The hypertension followed by hypotension is also observed in caffeine overdose. The underlying mechanism involved the pressor effect is peripheral vasoconstriction.

High-dose caffeine causes hypotension as a result of beta-adrenergic mediated vasodilation and marked tachyarrhythmia with reduced cardiac filling. Moreover, increased circulating catecholamines activate beta-2 receptors, and leads to a rise in intracellular cyclic adenosine monophosphate (cAMP). Both activation of beta-2 receptors and inhibition of phosphodiesterase lead to a prolonged effect of cyclic AMP and thus hypotension.^[20] Accompanied by the release of catecholamine, patients may present metabolic (lactic) acidosis, hypokalemia and hyperglycemia.^[14]

Caffeine with the central nervous system

Caffeine is usually applied to reduce physical fatigue and to restore alertness when drowsiness occurs. It produces increased wakefulness, faster and clearer flow of thought, increased focus, and better general body coordination.^[21] But when it is overdosed, it would cause the central nervous system over-stimulated, and thereby induce restlessness, anxiety, agitation, insomnia, psychosis, confusion and even seizure.^[22]

Because caffeine is not only water-soluble but also lipid-soluble, it easily crosses the blood-brain barrier, and acts as a nonselective antagonist of adenosine.^[15]

Caffeine with rhabdomyolysis

Some researchers have reported that caffeine can result in rhabdomyolysis which in turn leads to acute renal failure. Actually the effect of caffeine on skeletal muscle is dose-dependent. At very high levels it potentiates intracellular calcium sequestration, prolonging the action potential and causing titanic contraction to such a degree that it ultimately impairs contractility and causes cell death.^[12]

Clinical manifestation of caffeine overdose

Symptoms due to caffeine overdose are complained as headache, nausea, vomiting, hyperventilation, dizziness, anxiety, tinnitus, tremor, excitation, tachycardia and increased urinary output.^[4-7] Moreover, caffeine toxicity may be present as hypokalemia, hyponatremia, ventricular arrhythmias, hypertension followed by hypotension, respiratory failure, seizure, rhabdomyolysis, acute renal failure due to rhabdomyolysis, ventricular fibrillation and finally circulatory collapse.^[12,13,18,23,24]

Treatment

Anti-arrhythmia

It has been recommended to treat cardiac toxicity

with beta-blockers, procainamide and lidocaine.

Procainamide suppresses phase four of the action potential of myocardial cells, reducing the automaticity of ectopic pacemakers. It is known to be effective for both supra- and ventricular tachycardias, although intravenously infusing procainamide may cause hypertension.^[9]

Beta-blockers antagonize both the cardiac and peripheral beta-receptors stimulated by caffeine, and activated beta-receptors are responsible for hypotension, hypokalaemia and hyperglycaemia which are observed in cases of caffeine overdose. Esmolol has been successfully applied as a bolus at a dose of 500 µg/kg and as a continuous infusion at a dose of 50 µg/kg, titrating up to 100 µg/kg in order to keep the heart rate from 100 to 110 beats/min. Esmolol also has a concomitant anxiolytic effect and reduces tremors.^[20]

Some researchers have found that the calcium channel blocker verapamil abolishes caffeine-induced arrhythmias in rats for a relative longer duration than that of propranolol. However, it has been indicated that propranolol is superior to verapamil for the adverse effect of hypotension.^[25] Other antiarrhythmic drugs do not display antiarrhythmic or antidotal activity and thus are not recommended for treating caffeine-induced arrhythmia. But some case reports have suggested that amiodarone is also effective.^[8,23]

Electrical cardioversion still remains a choice of treatment if the patient is hypotensive although caffeine-induced cardiac arrhythmias are more refractory to cardioversion.

Vasopressin

Vasopressin inhibits adenylate cyclase and guanylate cyclase in vascular smooth muscle. Subtypes of vasopressin receptors are located in smooth muscle cells with the ability of triggering vasoconstriction. Therefore, vasopressin may be proper for correcting caffeine-induced hypotension.^[9] Infusion rates from 0.03 to 0.07 units /min are titrated to effect. Adverse effects of vasopressin include organ ischemia, hypersensitivity, skin necrosis and rhabdomyolysis.^[19]

Activated charcoal and haemodialysis

Activated charcoal has been successfully used in treating caffeine toxicity.^[26] Caffeine overdose can be handled by hemodialysis in view of the fact that it has a molecular weight of 194 kDa, a mean plasma protein binding of 36% and a volume of distribution between 0.6–0.8 L/kg.^[8,12] It has been proved that

remarkable clinical improvement would be seen at the end of dialysis.^[8,12,23] There have been cases of severe caffeine toxicity which were treated by peritoneal dialysis although such a modality is less efficient at drug clearance than hemodialysis.^[27,28] Some researchers^[29] have suggested that charcoal hemoperfusion could be used to clear the theophylline. However, there is a solid evidence that charcoal hemoperfusion would provide increased caffeine clearance over hemodialysis.

In summary, caffeine consumption is increasingly popular in Chinese young people, and it thereby brings about an increasing risk of primary cardiac arrest. Then clinicians should understand that excessive coffee consumption may be responsible for primary cardiac arrest in clinical circumstances especially in young people. Treatment modalities include activated charcoals, beta-blockers, vasopressin and hemodialysis when necessary.

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