Case Report

Propofol suppresses ventricular arrhythmias: a case report of acute caffeine intoxication

Shinya Terashima,[1] Takashi Muroya,[2] Hitoshi Ikegawa,[2] Kentaro Kajino,[2] Kazuhito Sakuramoto,[2] Rintaro Yui,[2] Masanobu Kishimoto,[2] Hiroki Takahashi,[2] Mari Nakajima,[2] Fumiko Nakamura,[2] Yasushi Nakamori,[1] and Yasuyuki Kuwagata[2]

[1]*Department of Emergency and Critical Care Medicine, Kansai Medical University Medical Center, Moriguchi, and* [2]*Department of Emergency and Critical Care Medicine, Kansai Medical University Hospital, Hirakata, Japan*

Background: Caffeine is widely used as a stimulant drug throughout the world, and fatal arrhythmia is a known side-effect. We experienced a patient with caffeine intoxication causing fatal arrhythmias who was successfully treated with the infusion of propofol.

Case Presentation: A 27-year-old woman was transferred to our hospital with nausea and poor general condition after intentional ingestion of 23.2 g of caffeine tablets. She was in cardiac arrest due to ventricular fibrillation just before hospital arrival. Advanced life support including defibrillation was started immediately, and we succeeded in resuscitating her 23 min later. Although she suffered from polymorphic ventricular premature beats and frequent transition to ventricular fibrillation, propofol administration converted her from a ventricular arrhythmia to sinus rhythm.

Conclusion: We report this case focusing on the cardiovascular effects of propofol and the lipid sink phenomenon. As a result, propofol could have the potential to suppress ventricular arrhythmias.

Key words: Caffeine, intoxication, intralipid, propofol, ventricular fibrillation

INTRODUCTION

CAFFEINE IS A natural alkaloid and the most widely used central nervous system stimulant drug in the world. In recent years, overexposure to caffeine from energy drinks or supplements has become a worldwide social problem, and case reports of caffeine intoxication are also increasing.[1] Clinical symptoms of caffeine intoxication include headache, nausea, vomiting, fever, dizziness, tinnitus, anxiety, irritability, insomnia, and seizures. In some cases of severe caffeine intoxication, fatal cardiac arrhythmia including supraventricular and ventricular tachyarrhythmias have been reported. Fatal arrhythmias are considered the most common cause of caffeine-related deaths,[2] and although some patients have been rescued by percutaneous cardiopulmonary support or emergency hemodialysis, there are only a few facilities with such abilities.[3] We report a patient with caffeine-induced fatal arrhythmias who responded to propofol used for sedation.

Corresponding: Shinya Terashima, Department of Emergency and Critical Care Medicine, Kansai Medical University Medical Center, 10-15 Fumizono-cho, Moriguchi, Osaka 570-8507, Japan. E-mail: marimogakkai324@gmail.com
Received 18 Dec, 2019; accepted 16 Apr, 2020

CASE REPORT

A 27-year-old woman with a 5-year history of anorexia nervosa was transferred to our emergency department with nausea and poor general condition. When her father came home, he found her complaining of malaise and nausea, so he called an ambulance. She was found with many press-through packs of caffeine tablets equivalent to a total dose of 23,200 mg. In the ambulance, her consciousness decreased rapidly, and she developed tonic seizures that progressed to cardiac arrest just before arrival at the hospital. Her electrocardiogram (ECG) on hospital admission showed ventricular fibrillation (VF). Cardiopulmonary resuscitation including defibrillation and tracheal intubation was begun, and after 23 min of advanced life support therapy, return of spontaneous circulation (ROSC) was achieved. After ROSC, the ECG showed a pattern of polymorphic ventricular premature beats (Fig. 1, ECG 1) and frequent transition to VF. The patient was admitted to the intensive care unit and treated with 300 mg amiodarone. Stomach pumping and

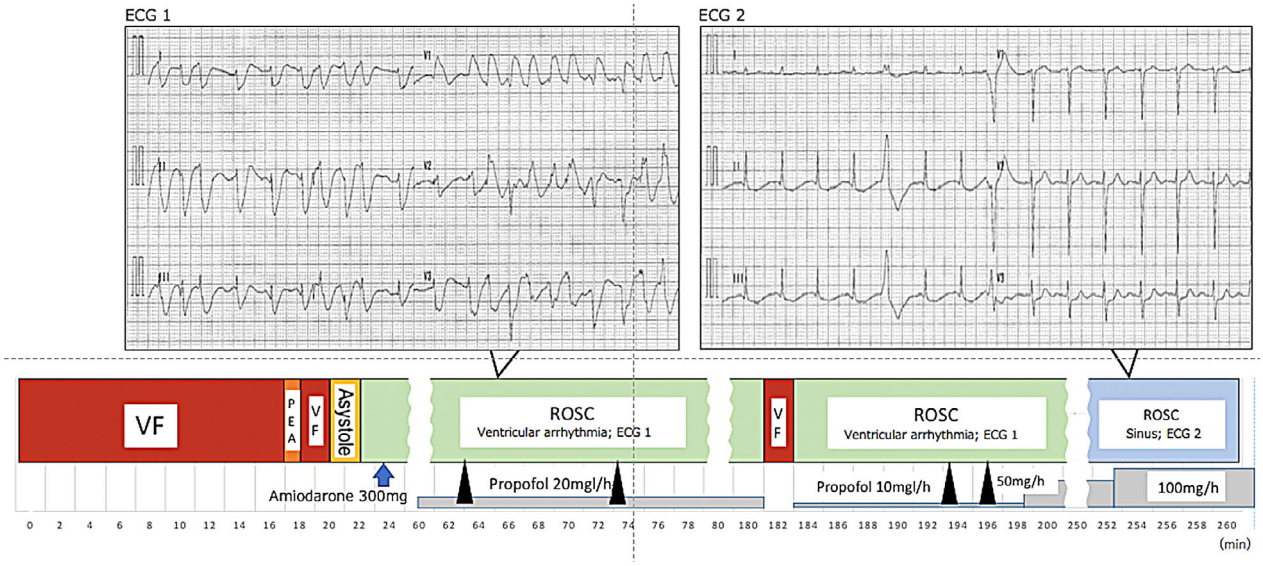

Fig. 1. Clinical course of a 27-year-old woman who intentionally ingested 23.2 g caffeine tablets. Cardiopulmonary resuscitation including defibrillation and tracheal intubation was started, and after 23 min of advanced life support, she was resuscitated. We began propofol (20 mg/h) infusion for her restlessness. After we administered a bolus of propofol (▲), her electrocardiogram (ECG) converted from a ventricular arrhythmia (ECG 1) to sinus rhythm (ECG 2). The same episode was repeated several times, and continuous infusion of propofol was gradually increased to 100 mg/h. After that, her cardiovascular condition improved, and ventricular arrhythmia did not reappear. PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation.

activated charcoal were also administered. Laboratory examinations on arrival revealed hypokalemia (2.3 mEq/L) and an elevated white blood cell count (18,100/mm^3). Arterial blood gas values under intubation revealed lactic acidosis: lactic acid, 16.5 mmol/L; pH 7.089; pCO_2, 31.4 mmHg; pO_2, 31.4 mmHg; and base excess, −19.6 mmol/L. Other blood test values, including electrolyte concentrations, hepatic enzymes, renal function values, and creatine kinase were within their normal ranges. Although we cannot test for caffeine blood levels at our hospital, we diagnosed caffeine intoxication as the cause of the fatal arrhythmias based on a series of clinical findings. As we began to prepare venoarterial extracorporeal membranous oxygenation, the patient became restless with intense movements. We thus administered i.v. propofol at 20 mg/h (0.48 mg/kg) for sedation. After giving a propofol bolus of 30 mg (0.7 mg/kg), the patient's ECG changed from ventricular arrhythmia to sinus rhythm (Fig. 1, ECG 2). This same episode recurred several times, and continuous infusion of propofol was gradually increased to 100 mg/h (2.3 mg/kg). After that, her cardiovascular condition improved, no ventricular arrhythmias reappeared, and she did not require hemodialysis treatment. The total dose of propofol until improvement to sinus rhythm was approximately 140 mg over 4 h. The patient's clinical course is shown Figure 1. The patient was extubated on the 4th hospital day and discharged on the 13th hospital day without neurological impairment.

DISCUSSION

CAFFEINE (1, 3, 7-trimethyxlaniline) is sold as a nervous system stimulant that can be conveniently bought in drug stores.[1] In recent years, energy drinks that include large amounts of caffeine have become very popular among young adults and adolescents.[1] The maximum plasma concentration is reached within 30–60 min after consumption.[4] In our case, the patient initially talked to her father, but then her consciousness decreased rapidly, and it is assumed that she was found within several tens of minutes after ingesting the caffeine. In a review of adverse cardiovascular events associated with caffeine or energy drinks, there are reports of atrial arrhythmias, VF, ST elevation, and QT prolongation.[5] Arrhythmias are considered the most common cause of death.[3,5] In our case, the patient ingested 23 g caffeine and developed VF at hospital admission. She was resuscitated after 23 min in cardiac arrest, but her ECG showed polymorphic ventricular premature beats and frequent transition to VF. Although we prepared to initiate venoarterial extracorporeal membranous oxygenation, the polymorphic premature ventricular rhythm returned to sinus rhythm right

after a bolus infusion of propofol was given for sedation. Although amiodarone might have worked, the arrhythmia improved for a few minutes immediately after administration of propofol. So, we surmised that the propofol infusion had resulted in prompt improvement of the fatal ventricular arrhythmia. We considered two hypotheses for this occurrence. First, propofol has several cardiovascular effects, such as baroreflex activity and direct peripheral vasodilatation, and it affects central sympathetic nervous system outflow, myocardial contractility, and the underlying pathophysiological state of the myocardium.[6] Although the molecular biological mechanism is unknown, there are several studies elucidating this mechanism. In animal models, propofol acts directly on the sinoatrial node and atrioventricular conduction to cause bradycardia,[6] but in human electrophysiological studies, propofol has been shown to have few direct effects on sinoatrial node activity or intra-atrial or AV conduction.[7] There are many case reports of the side-effects of bradycardia caused by propofol.[8] Some reports indicated that a centrally mediated increase in vagal tone could cause bradycardia.[4,5,7] Burjorjee and Milne reported that the bolus administration of propofol for intractable ventricular tachycardia and VF was associated with both conversion of ventricular tachycardia and suppression of further ventricular arrhythmias.[7] Similarly, in our case, propofol likely acted to stimulate vagal tone or induce sympathetic blockade to help resolve the fatal arrhythmias.

Second, propofol could have acted as an i.v. lipid emulsion. Recently, detoxification treatment for severe local anesthetic toxicity by i.v. lipid emulsion has been reported.[9] Although the exact mechanisms of action of lipid emulsion infusion are not clear, the most widely accepted mechanism is the "lipid sink" phenomenon, in which the lipid emulsion infusion creates an expanded lipid phase and extracts toxic drugs from tissues during this phase. As a result, toxic drugs cannot exert their pharmacologic actions.[9] Lipid emulsion infusion has become the first-choice treatment for local anesthetic toxicity.[10,11] Furthermore, there are some reports of successful resuscitation, suggesting the efficacy of lipid emulsion infusion in the treatment of non-local anesthetic overdoses, include caffeine intoxication.[9,12] Propofol contains 10% purified soybean oil, but the dose given in our case was less than that shown in various guidelines and case reports, so effects of the lipid sink phenomenon might not have occurred in our patient. Therefore, we considered that the cardiovascular action of propofol was effective in suppressing the ventricular arrhythmia caused by caffeine intoxication in this patient.

In conclusion, we experienced a patient in whom propofol was effective in resolving fatal arrhythmias caused by caffeine intoxication.

DISCLOSURE

ETHICS APPROVAL: THE institutional review board of Kansai Medical University Medical Center approved this study and waived the need for informed consent.

Informed consent: The patient's parent provided consent for publication.

Animal studies: N/A.

Conflict of interest: None.

REFERENCES

1 Wikoff D, Welsh BT, Henderson R, *et al*. Systematic review of the potential adverse effects of caffeine consumption in healthy adults, pregnant women, adolescents, and children. Food Chem. Toxicol. 2017; 109(Pt 1): 585–648.

2 Yamamoto T, Yoshizawa K, Kubo S, *et al*. Autopsy report for a caffeine intoxication case and review of the current literature. J. Toxicol. Pathol. 2015; 28: 33–6.

3 Ishigaki S, Fukasawa H, Kinoshita-Katahashi N, Yasuda H, Kumagai H, Furuya R. Caffeine intoxication successfully treated by hemoperfusion and hemodialysis. Intern. Med. 2014; 53: 2745–7.

4 Cappelletti S, Piacentino D, Sani G, Aromatario M. Caffeine: cognitive and physical performance enhancer or psychoactive drug? Curr. Neuropharmacol. 2015; 13: 71–88.

5 Fletcher EA, Lacey CS, Aaron M, Kolasa M, Occiano A, Shah SA. Randomized controlled trial of high-volume energy drink versus caffeine consumption on ECG and hemodynamic parameters. J. Am. Heart Assoc. 2017; 6: pii: e004448.

6 Searle NR, Sahab P. Propofol in patients with cardiac disease. Can. J. Anaesth. 1993; 40: 730–47.

7 Burjorjee JE, Milne B. Propofol for electrical storm; a case report of cardioversion and suppression of ventricular tachycardia by propofol. Can. J. Anaesth. 2002; 49: 973–7.

8 Briggs I, Heapy CG, Pickering L. Electrophysiological effects of propofol on isolated sinoatrial node preparations and isolated atrial conduction in vitro. Br. J. Pharmacol. 1989; 97: 504.

9 Fettiplace MR, Weinberg G. Past, present, and future of lipid resuscitation therapy. JPEN J. Parenter. Enteral. Nutr. 2015; 39(1Suppl): 72S–83S.

10 Cave G, Harrop-Griffiths W, Harvey M, *et al*. AAGBI Safety Guideline: Management of Severe Local Anaesthetic Toxicity. London: The Association of Anaesthetists of Great Britain and Ireland; 2010 [cited 18 Jul 2017]. Available from: https://www.aagbi.org/sites/default/files/la_toxicity_2010_0.pdf.

11 Neal JM, Bernards CM, Butterworth JF 4th, *et al*. ASRA practice advisory on local anesthetic systemic toxicity. Reg. Anesth. Pain Med. 2010; 35: 152–61.

12 Muraro L, Longo L, Geraldini F, Bortot A, Paoli A, Boscolo A. Intralipid in acute caffeine intoxication: a case report. J. Anesth. 2016; 30: 895–9.