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증 례

Rhabdomyolysis and Acute Renal Failure Following an Intentional Overdose of Stacker 3 (A Caffeine-Containing Weight-Reduction Supplement)

Mi Jin Lee, M.D.

Department of Emergency Medicine, College of Medicine, Konyang University, Daejeon, Korea

"Stacker 3" is one of the most popular caffeine-containing weight-reduction supplements and it has ephedra-free properties as "Stacker 2 Ephedra-Free" in many countries, including Korea. We describe here a 26-year-old woman who took an acute intentional overdose of "Stacker 3" (approximately 50 capsules, total amount: 25 grams, as caffeine 250 mg/kg) and who had delirium, rhabdomyolysis and acute renal failure. She had to be treated by forced diuresis and urine alkalinization, and she subsequently recovered. This is the first such case report in the medical literature.

Key Words: Poisoning, Caffeine, Stacker 3, Rhabdomyolysis, Kidney Failure

Background

Recently, weight-loss and changing of body shape are some worldwide-trends. Many potentially toxic dietary supplements are available over the counter and unregulated by FDA (Food and Drug Administration) or KFDA (Korean Food and Drug Administration). "Stacker 3" (NVE Pharmaceuticals®, Andover, NJ, USA) provides the fat burning and weight-reduction properties. Each "Stacker 3" capsule contains 250 mg of caffeine, and another 250 mg of caffeine-containing kola nut, green tea, and guarana, and multiple other ingredients include chitosan, gelatin, dextrose, stearic acid, magnesium stearate, titanium dioxide, etc. Side effects may include palpitation, nausea, weakness, dizziness, severe headache, and shortness of breath[1,2]. Additionally, "Stacker 3" improves mental alertness, increases energy and stamina. So it widely used in younger men and women, it may be exposal conditions for many overdose or poisoning.

"Stacker 3" is one of the most popular caffeine-containing weight-reduction anorexiants in many countries, so many consumers and physicians likely consider caffeine to be a relatively safe drug. Because case reports of Stacker 3 poisoning in humans are rare, we describe a cases of "stacker 3" poisoning complicated with renal and CNS side effects and compare these with other literature reports.

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책임저자: 이 미 진
대전광역시 서구 가수원동 685
건양대학교 의과대학 응급의학교실
Tel: 042) 600-9119, Fax: 042) 600-9026
E-mail: emmam@catholic.ac.kr

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Case Report

A 26-year-old woman (49.5 kg weight) was admitted to the emergency department complained with mental confusion, agitation, nausea, and irritability. According to her sister, she had taken "Stacker 3" for weight reduction for two weeks, but she ingested approximately 50 capsules (total amount 25 grams, as

caffeine 250 mg/kg) of "Stacker 3" with suicide ideation 2~3 hours ago (Fig. 1). During this 3-hour period, there was no evidence of seizure activity as witnessed by her sister. On admission, she was confused (Glasgow Coma Scale 13), anxious, and diaphoretic with blood pressure 137/70 mm Hg, heart rate 139 beats/minute, respiratory rate 24 breaths/minute, and O2 saturation 98% on room air. There was no sign of injury on physical examination. On neurologic examination, she was irritable and violent. Speech was incomprehensible. She was disoriented to time and place. Both pupils were 4 mm in diameter, equal and reactive to light. Auscultation of her chest revealed clear breath sounds and tachycardia. Her abdomen was soft and non-tender with audible bowel sounds. All of her pulses were palpable. Her skin was clammy with moist axilla. Testing of her cranial nerves was intact, and clonus wasn't elicited. Initial body temperature was 37.4°C, but 36.5°C was measured and sustained within normal range without anti-pyretics after 1 day.

Fig. 1. The photograph of "Stacker 3". This bottle belonged to patient's own. Each "Stacker 3" capsule contains 250 mg of caffeine, and another 225 mg of proprietary mixtures include kola nut, chitosan, green tea, and 25 mg tri-guarcinia complex

Gastric lavage, activated charcoal and IV Normal saline bolus were instituted. Initial laboratory data were unremarkable for sodium 139 mEq/L, potassium 3.4 mEq/L, urine nitrogen 14 mg/L, creatinine 0.9 mg/L, bicarbonate 17 mEq/L, anion gap 22, and glucose 252 mg/dL, except for a slightly increased plasma creatine kinase (CPK) activity (281 U/L; reference <145 IU/L). Urine drug screen tests of BZP and TCA, serum ethanol level were all negative. The initial electrocardiogram showed sinus tachycardia (139 bpm). A subsequent emergency echocardiogram revealed no evidence of heart failure or wall motion abnormality. Three hours after admission, the patient had regained full consciousness, and her blood pressure and tachycardia steadily improved. But, laboratory data (obtained 10 hours after ingestion) were as follows: plasma CPK, 7,890 U/L, with a CK-MB fraction of 0.7%; creatinine 1.54 mg/dL (ref. <1.2 mg/dL); AST 288 U/L (ref. <36 U/L); ALT 57 U/L (ref. <38 U/L). Plasma bilirubin and alkaline phosphatase were within the normal ranges. She had to be treated by

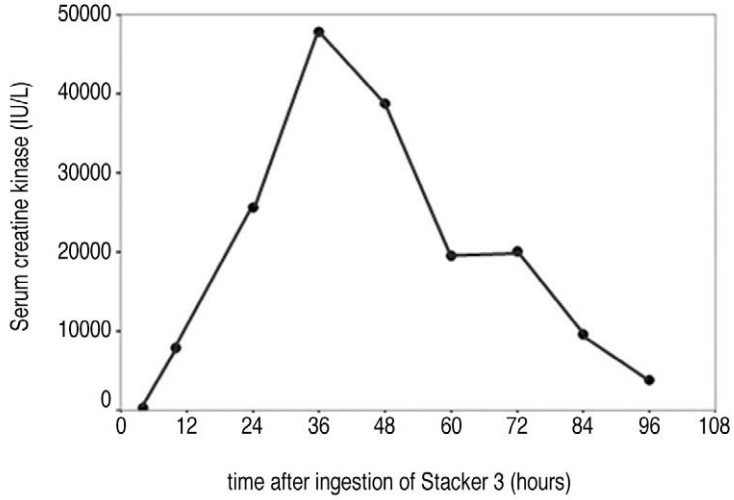

Fig. 2. Creatine kinase level-time curve after Stacker 3 overdose. CPK level (CPK peak 47,800 IU/L) decreased on HD 2 days after overdose and normalized on HD 5 days

forced diuresis and urine alkalization with mannitol and intravenous sodium bicarbonate, and together with a careful increase in the rate of intravenous fluids (200~250 mL per hour).

During the detoxification and conservative therapy, she was discovered to have acute renal failure (peak creatinine 2.37 mg/dL), with severe rhabdomyolysis (peak CPK 47,800 IU/L, Fig. 2). With aggressive supportive therapy, including urine alkalization and forced diuresis, CPK level decreased on 3 days after overdose. The patient subsequently recovered without detectable sequelae and was discharged at day 5.

Discussion

Caffeine has long been recognized as an addictive substance. A significant proportion of caffeine ingestions occurred in the context of recreational abuse or intended weight loss. The clinical consequences of caffeine ingestion were generally mild, and no patient experienced any features of severe toxicity. Mild electrolyte disturbances and palpitation were common, and resolved spontaneously without specific treatment in most cases. No effect on liver biochemistry occurred, and there was no significant effect on any of the electrocardiographic complications. These findings are reassuring from a safety perspective[3].

Many potentially toxic dietary supplements are available over the counter and unregulated by FDA or KFDA. "Stacker 3" is one of the most popular caffeine-containing weight-reduction supplement and ephedra-free properties. Side effects may include palpitation, nausea, weakness, dizziness, severe headache, shortness of breath or other similar symptoms of caffeine overdose[1-3]. Over-the-counter supplements that are used to combat fatigue typically contain 100~200 mg caffeine per tablet and doses of 32~200 mg are included in a variety of prescription drug mixtures. A small number of fatalities have been attributed to caffeine ingestion, so patients that present to hospital after acute caffeine ingestion generally required only supportive cares. Fatal caffeine overdoses in adults are relatively rare and require the ingestion of a large quantity of the drug, typically in excess of 5 grams. Ingestion of large doses, it can be profoundly toxic, resulting in agitation, ventricular arrhythmia, tachycardia, vomiting, convulsions, coma and death[4-7].

The clinical features of severe poisoning described in the literature include nausea, headache, tachycardia, neuropsychiatric manifestations, and rhabdomyolysis[3,8,9]. Our patient had similar clinical features, most of which were treated forced diuresis and urine alkalization. In a matter of consequence of our case, neuro-toxidrome and CNS effects from "Stacker 3" exposure were usually noted within 0.5~6 hours, but the onset of rhabdomyolysis, renal and hepatic failure were delayed more than 6~10 h after poisoning[8,9]. Serial monitoring of laboratory profiles of rhabdomyolysis-related renal failure, especially creatine kinase (CPK) and creatinine, is recommended in overdose of caffeine-containing weight-reduction drugs ("Stacker 3") to determine the prevalence of rhabdomyolysis and/or acute renal failure.

The clinical course suggests that "Stacker 3" toxicity injured the muscle cells, which were fragile due to result in unusually severe rhabdomyolysis. However, we were able to exclude seizure, concomitant alcohol ingestion, and long-term muscle ischemia as causes of rhabdomyolysis in this case[9-11]. So we hypothesize that Stacker 3 may have direct organ toxicity. Aggressive supportive therapy, hydration and measures to prevent renal hypoperfusion are essential to reverse acute renal failure.

There are several limitations to our case report. The first, we have not measured serum caffeine level of the patient. In the last limitation, Stacker 3 included various chemical substances and unclear ingredients. It was not enough to describe the mechanism of its renal and serious toxicities as only caffeine toxicity.

This is only the first case repot of serious renal and CNS complications due to Stacker 3. Many literatures suggest that the popular caffeine-containing weight-reduction supplements are nontoxic, however, in the light of our experience which is otherwise, we would like to exercise caution in making such statement. But, caffeine toxicity is typically mild but severe

cases (〉10 grams or 150~200 mg/kg) exhibit seizures and shock[12-16]. Therefore clinicians should be aware of the ingredients and potential lethality of unregulated weight loss products. Also, we present a case of Stacker 3 overdose that were complicated by a delayed rise in CPK and creatinine. Although the initial clinical consequences were not serious, physicians should be alerted to the possibility of delayed rhabdomyolysis or acute renal failure in patients who have taken "Stacker 3" in overdose.

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