

treating severe caffeine poisoning through an assessment of caffeine clearance (CL). Here we discuss two cases of severe caffeine poisoning; one patient was treated by HD and the other by CHP.

The patient in Case 1 was a 24-year-old male (height, 170 cm; weight, 65 kg, non-smoker) who ingested six cans of Monster Energy® (852 mg caffeine) and 60 tablets of Estaron Mocha® (6000 mg caffeine), to a combined total of 6852 mg caffeine in a suicide attempt and was transported to our hospital. On arrival (3 h after drug ingestion), the patient vomited repeatedly and presented with irritation and shivering. He exhibited tachycardia (110 bpm), hypercreatininemia (509 U/L), hypokalemia (2.4 mmol/L), and leukocytosis (22,440/μL). Serum caffeine concentration was 87.2 mg/L, as determined by liquid chromatography–tandem mass spectrometry using 3200QTRAP® (AB SCIEX, Framingham, MA, USA) and the Prominence® LC system (Shimadzu Corporation, Kyoto, Japan). Because he had ingested a lethal concentration of caffeine (>80 μg/mL) [3], HD was performed for 4 h at a blood flow rate (Q_B) of 200 mL/min and dialyrate flow rate (Q_D) of 500 mL/min, during which clinical signs and symptoms improved dramatically. One hour after HD, he became calm and his nausea and shivering subsided. Serum caffeine concentrations in the pre-HD column/post-HD column were 76.3/19.6 mg/L (0 hour period after beginning HD), 57.3/5.5 mg/L (1 hour period), 49.4/10.6 mg/L (2 hour period), 31.7/8.9 mg/L (3 hour period), and 27.3/8.2 mg/L (4 hour period). The following day, he was transferred to the Department of Psychiatry for mental evaluation and treatment.

The patient in Case 2 was a 24-year-old male (height, 164 cm; weight, 63 kg, non-smoker) who ingested 80 tablets of Estaron Mocha® (8000 mg caffeine) in a suicide attempt and was transported to our hospital. On arrival (7 h after drug ingestion), he vomited repeatedly and was agitated. He complained of nausea, epigastric discomfort, and peripheral numbness. He was tachycardic (136 bpm), and exhibited tachypnea (72 breaths/min), hyperglycemia (217 mg/dL), leukocytosis (24,310/μL), and metabolic acidosis (pH, 7.26; PaCO₂, 20.9 mm Hg; PaO₂, 30.1 mm Hg; BE, −17.5 mmol/L; and HCO₃[−], 9.5 mmol/L). Serum caffeine concentration was 76.2 mg/L as determined by gas chromatography–mass spectrometry (GC–MS) using QP-2020® (Shimadzu Corporation, Kyoto, Japan). Given the near lethal caffeine concentration (>80 μg/mL) [3], CHP was performed for 4 h with a Q_B of 150 mL/min, during which his clinical signs and symptoms improved notably. Immediately after CHP, he was calm without nausea and metabolic acidosis disappeared. Serum caffeine concentrations in the pre-CHP column/post-CHP column were 79.5/4.0 mg/L (0 hour period after beginning CHP), 61.2/0 mg/L (1 hour period), 42.3/4.5 mg/L (2 hour period), 32.7/0 mg/L (3 hour period), and 19.4/0 mg/L (4 hour period). On hospital day 3, he was discharged with no sequelae.

CL of caffeine were calculated using the following formula reported by Hirata et al. [4]:

$$CL_{HD \text{ or } CHP} = \left\{ \frac{C_{pre-column} - C_{post-column}}{C_{pre-column}} \right\} \times Q_P$$

Q_P (plasma flow rate) is calculated as Q_B during HD or CHP (mL/min) × {100–Hematocrit (%)}

As calculated from the above equation, CL_{HD} was 79.3–102.3 mL/min and the corresponding CL_{CHP} value was 67.4–75.5 mL/min. When comparing CL by column, CL_{HD} was higher than CL_{CHP} at all assessed time points. This suggests that removal efficiency is high with HD, likely due to the ability to adjust the Q_B during the procedure. Since internal circuit pressure of CHP increases readily, increases in Q_B over 150 mL/min are difficult. Therefore, HD was found to demonstrate higher estimated caffeine clearance, mainly due to a higher Q_B during the procedure.

It is well known that complications such as thrombocytopenia [5] occur at a much higher frequency with CHP than with HD. In Case 2, blood platelets decreased, from 297,000/μL to 122,000/μL during CHP.

There is a significant cost difference between CHP and HD in that the activated carbon column used for HP is roughly 100 times more

expensive than the column used for HD in Japan (approximately 2000 yen vs 130,000 yen).

Considering the number of associated complications (e.g., thrombocytopenia), higher costs, fewer skilled experts, and lower clearance rate of CHP, HD may be the preferred procedure for treating severe caffeine poisoning.

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Methamphetamine psychosis: Lack of association with stimulant prescription ADHD medications



Methamphetamine use is increasing nationwide [1]. Recently, cases of methamphetamine psychosis have been increasing in frequency in Montgomery County, Ohio, with up to 40% of methamphetamine users affected [2,3]. Methamphetamine psychosis is characterized by hallucinations, uncontrolled movements and potential violent behavior, and in a subset of patients may result in recurrent psychotic episodes [4]. Poison death

review data for Montgomery County shows increasing methamphetamine associated overdose deaths, nearly doubling between 2016 and 2017 [1].

We hypothesized that the increase in the diagnosis and prescriptions for Attention Deficit Hyperactivity Disorder (ADHD) over the past several years may be contributing to the observed increasing rates of methamphetamine psychosis in our area [5]. This study was undertaken to identify any association of methamphetamine psychosis and prior prescriptions for stimulant ADHD medications.

In this retrospective study, eligible participants included patients with a diagnosis of methamphetamine overdose or psychosis between 10/2016 to 12/2017. This study was reviewed and approved as exempt research by the Wright State University Institutional Review Board. Methamphetamine toxicity or psychosis was confirmed. The prescription history of these patients was accessed using the prescription drug monitoring program (PDMP). The system extracts prescription data for the past 2 years from the date in which the chart was accessed. The amount and the date of the prescription for any stimulant ADHD medication was recorded. Following extraction of this data, patient records were deidentified and the results tabulated as described below.

Participants included 48 subjects with methamphetamine psychosis or overdose. Participants were 68% male, 92% Caucasian and ranging in age from 18 to 65 year (median 30). None of these cases had an identified prescription for stimulant medication within the most recent 2 years. Therefore, there was no association between patients presenting to the ED with signs and symptoms of methamphetamine intoxication and having received a recent prescription for any ADHD stimulant medication prior to their presentation.

Over the past decade prescriptions for ADHD medications have doubled [6]. In light of this increase, we attempted to determine whether there was an association between methamphetamine overdose and a recent prescription for an amphetamine based ADHD medication. We were concerned that, not unlike what was noted regarding the opiate epidemic, recent increases in the frequency of patients presenting to the emergency department may have been associated with amphetamine-based ADHD medication prescribing. However, this study did not identify any associated amphetamine prescription among ED patients with methamphetamine psychosis or overdose.

Due the limitations of the prescription drug monitoring program (PDMP) in use, remote prescriptions may not have been identified. Our study was also limited in the fact that the PDMP does not identify non-prescribed stimulant use, unauthorized use of prescription medication from another patient, or a more remote prescription history. Non-prescribed stimulant use is common among middle, high school, college, and medical students, both recreationally and as an aid in studying [7,8,9]. It is possible that recreational use of stimulants could lead to drug abuse later in life. Further directions will focus on the role of ADHD medication prescribing in childhood and early adolescence in the subsequent development of methamphetamine addiction.

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Comments on GEDI vs. CVP goal-directed fluid resuscitation for chronic obstructive pulmonary disease patients with septic shock: A randomized controlled trial



To the Editor,

We have greatly enjoyed reading the article by Yu et al. [1], which was a single-center, prospective, randomized, controlled trial (RCT) compared the effects of Global end-diastolic volume index (GEDI) vs. central venous pressure (CVP) goal-directed fluid resuscitation for chronic obstructive pulmonary disease (COPD) patients with septic shock. The authors conclude that GEDI goal-directed fluid resuscitation shows better clinical effects compared to CVP for COPD patients with septic shock.

We would like to add several appreciations. First, the author defined a targeted endpoint CVP of 12 mmHg based on the 2008 SSC guidelines. [2] However, the 2008 SSC guidelines recommended a targeted endpoint CVP of 15 mmHg in patients with mechanical ventilation, not 12 mmHg for mechanical ventilation decreasing venous return. The normal range of GEDI is 680–800 ml/m² [3]. The low targeted endpoint CVP of 12 mmHg could result in lower fluid volume and higher norepinephrine dosage. Second, the main endpoints were fluid volume, NE dosage, ICU mortality rate, blood lactate clearance rate and ICU length of stay. Nevertheless, it is common for sample size to be based on the primary outcomes alone. The author did not explain the calculation of sample size (71 patients). Blood lactate clearance rate could assess the mortality rate of patients with sepsis shock during hospitalization with high specificity and sensitivity [4]. Thus, I suggest that the author could define blood lactate clearance rate as the only primary outcome and calculate the sample size based on it. Fourth, the lack of blinding could lead to observer bias in length of ICU stay and duration of mechanical ventilation. At last, according to 2008 SSC guidelines, [1] norepinephrine and dopamine were recommend as the first vasopressors agent, epinephrine should be the first alternative agent when septic shock is poorly responsive to them and dobutamine was recommend in patients with myocardial dysfunction. Hence, the types and doses of total vasopressors administration not just norepinephrine should be provided.

Abbreviations: GEDI, Global end-diastolic volume index; CVP, central venous pressure; COPD, chronic obstructive pulmonary disease; RCTs, random, controlled trials.