

Clinical Research: Open Access

Case Report

Volume: 2.2

Open Access

Acute Renal Failure and Death after Misuse of Concentrated Anhydrous Caffeine as A Pre-Work Out Supplement By Athletes

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Introduction

Caffeine is a naturally produced xanthine stimulant that has become nearly ubiquitous in society: widely available in common beverages such as coffee, tea and sodas that are consumed by a large portion of the population on a daily basis [1]. In addition to these "low dose" beverage forms of caffeine, higher concentrations of caffeine formulations have become more common such as "energy drinks", caffeine pills and "energy shots" [2,3]. In a 2 year period, 4854 exposures to caffeine-containing energy drinks were reported to US poison centers [4]. From 2005 to 2011, there was a 20 fold-increase in the number of emergency department visits due to energy drink ingestion [3]. These higher concentration caffeine products can produce significant morbidity but are rarely fatal [4]. Life threatening effects and fatalities have been reported, but these severe cases followed massive ingestions due to substance abuse or suicidal efforts [5-17]. However, the risk of ingesting toxic levels of caffeine due to unintentional misuse of caffeine products has now been heightened by the availability of highly concentrated caffeine powders purchased online [18,19]. The significant difference in dose, between the former available concentrations in milligrams and the newly concentrated forms in grams, puts the user at significantly increased risk for accidental overdose.

We report a series of caffeine cases where concentrated caffeine was misused for athletic performance and body build purposes with severe or fatal outcome. None of these cases are intentional overdose or intent to self-harm.

Case History

Case 1

An 18 year old previously healthy, honor roll wrestler was discovered dead in his bedroom by his brother. He was found with emesis and believed to have had a seizure. A bag of powdered anhydrous caffeine was found in the bedroom with the decedent. Post mortem investigation reported it was a common practice of the decedent to use caffeine as a "pre-workout" supplement. Further investigation revealed he had recently purchased the powdered caffeine online. The decedent had no previous medical problems or medication/drug use and no recognized or reported psychosocial stressors. No foul play or attempt at self-harm was suspected, Autopsy revealed no undiagnosed metabolic or apparent neurologic disorders, no structural heart defects or other anatomic cause of death. Post mortem toxicology showed blood caffeine 100 mg/L. No other drugs were detected. Cause of death was ruled accidental by the county coroner on autopsy

Received date: 07 Apr 2016; **Accepted date:** 18 Apr 2016; **Published date:** 22 Apr 2016.

Citation: Burns G, Spiller HA, Pruchnicki, Siegel E, Casavant MJ (2016) Acute Renal Failure and Death after Misuse of Concentrated Anhydrous Caffeine as A Pre-Work Out Supplement By Athletes. Clin Res Open Access 2(2): doi <http://dx.doi.org/10.16966/2469-6714.115>

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and was attributed to caffeine overdose causing cardiac arrhythmias and probable seizure in an otherwise healthy male.

Case 2

A 53 year old, previously healthy male, presented to the emergency department (ED) 26 hours after ingesting approximately "1 tablespoon" of caffeine powder purchased online (estimated dose 9,600 mg). The powder was identified as Hard Rhino pure anhydrous caffeine (Hard Rhino has since discontinued its anhydrous powder formulation). The label of this bottle stated that the serving dose was "1/16th of a teaspoon, or 50 mg. His symptoms began approximately 30 minutes after ingestion. On presentation to the ED he reported continuous and persistent vomiting, diarrhea, abdominal pain, headache and increased agitation with anxiety. Initial lab results were remarkable for acute kidney injury (AKI) with a BUN of 38 mg/dL and creatinine of 3.30 mg/dL and a creatine phosphokinase (CPK) level of 10,096 IU/L. He was hospitalized for ten days, with progressively worsening acute kidney injury with an increase in creatinine to 6.6 mg/dL and transient oliguria. Anxiety and persistent psychomotor agitation resolved after 3 days. At the time of discharge, his rhabdomyolysis had resolved with his CPK level dropping to 358 IU/L and his AKI had resolved with a serum creatinine of 1.6 mg/dL. When questioned about the large dose he ingested, he replied that "I use a lot of caffeine and thought it wouldn't be a problem." On the container, the recommended serving size of the caffeine powder was "between 50 to 200 mg", with directions stating this translated to 1/64 of a teaspoon to 1/16 of a teaspoon.

Case 3

A 23 year old male with no past medical history ingested 1 to 2 "teaspoons" (estimated 3 to 6 gm based on label concentration of 50mg 1/16th teaspoon) of powdered anhydrous caffeine he had purchased online before beginning a regular workout session. He was not caffeine naive and regularly used over-the-counter stimulants as a workout supplement. While still at home he began having persistent nausea, vomiting, abdominal pain, agitation and muscle jerking. Sixteen hours post ingestion he presented to the ED with sustained nausea, vomiting and palpitations. Significant laboratory abnormalities were a white blood cell count of 26,000/c/mL, potassium 2.9 mEq/L, BUN 21 mg/dL, creatinine 1.6 mg/dL and CPK 706 IU/L. Over the next three days he exhibited laboratory findings consistent with mild rhabdomyolysis with a peak CPK of 3,297 IU/L. Rhabdomyolysis corrected completely with aggressive intravenous hydration.

Caffeine Source	Caffeine Tablet "No Doz"	Black Tea	Coca-Cola	Red Bull Energy Drink	Starbuck's Drip Coffee "Pike's Place"	Hard Rhino powder
Dose per Milliliter	N/A	0.12-0.41 mg	0.095 mg	0.32 mg	0.63 mg	640 mg
Dose Per Serving	200 mg	20-70 mg	34 mg	80 mg	415 mg	50 mg
Recommended Serving Size	1 tab	177 mL (6oz)	355 mL (12oz)	250 mL (8.5oz)	660 mL (20oz)	1/64 th teaspoon

Table 1: Caffeine levels per milliliter in commonly available over-the-counter products

Discussion

Caffeine is an almost ubiquitous stimulant consumed daily by a significant number of adults and children around the world, and represents a multi-billion dollar market in the US economy. It is generally considered safe by the typical consumer, but has been labeled as a category 3 on the FDA Generally Recognized as Safe (GRAS) list, which means the FDA has insufficient data available for sufficient classification. Additionally it is widely abused by fitness enthusiasts as a legal over-the-counter performance enhancing drug [21]. But many consumers appear to be unaware of the significant disparity between the concentrated doses available in the powdered formulations and other forms/sources of caffeine (Table 1).

The disparity has led to unintentional ingestions of near lethal doses of 150 mg-200 mg/kg. Renal failure and death has been reported in intentional caffeine overdoses in patients with suicidal ideation [18,20]. Our cases represent acute kidney injury and death after ingestion of super-concentrated anhydrous caffeine powder with recommended dosing of 1/16th teaspoon being used specifically as a work-out supplement in caffeine tolerant individuals.

These powdered formulations may be especially dangerous due to their rapid absorption. With lower traditional concentrations of caffeine, during misuse or abuse, the onset of the side effect of spontaneous emesis may serve to limit the amount of caffeine consumed. While concentrated powders may result in absorption of toxic doses prior to onset of vomiting, leading to toxic and even lethal serum concentrations.

Conclusion

Concentrated forms of anhydrous caffeine are now available in doses >10-fold more concentrated than traditional caffeine sources. Consumers and providers need to be aware of the potentially life threatening complications that can occur from ingestion of seemingly small doses of these powders. A high-index of suspicion for severe complications should be considered by physicians when caring for ill patients with a history of ingestion of anhydrous caffeine powders.

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