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Methylphenidate Overdose Causing Secondary Polydipsia and Severe Hyponatremia in an 8-Year-Old Boy

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Objective: Attention deficit hyperactivity disorder (ADHD) is an increasingly common diagnosis of childhood that manifests with symptoms that affect cognitive, academic, behavioral, emotional, and social functioning. There are a multitude of pharmaceutical therapies to choose from when managing this condition, and though many studies on the safety and efficacy of these medications have been published, adverse effects still occur.

Case: This case discusses a previously healthy 8-year-old boy who had been prescribed 20-mg lisdexamfetamine dimesylate for ADHD however mistakenly took his brother's 36-mg methylphenidate extended-release tablets, resulting in hyperhidrosis, excessive thirst, polydipsia, and combative behavior that began within 3 hours of ingestion. He was evaluated at a community hospital emergency department and given lorazepam due to agitation and combativeness before discharge. However, he returned with hypothermia, hyponatremia, and status epilepticus resulting in intubation. Patient was transferred to our facility where a computer tomography of his head was negative and hyponatremia was corrected with 3% NaCl saline solution. A lumbar puncture was performed due to temperature instability before starting broad-spectrum antibiotics. Cerebrospinal fluid findings were normal, and he was extubated at 18 hours postingestion. Patient was discharged home after 3 days with no residual symptoms.

Discussion/Conclusions: Though both lisdexamfetamine dimesylate and methylphenidate are widely used among pediatricians today for treatment of ADHD, reports of life-threatening water intoxication as a result of overdose is rare. Studies have reported that severe 3,4-methylenedioxymethamphtamine toxicity in adults is associated with syndrome of inappropriate diuretic hormone (SIADH) secretion, hyponatremia, and seizures, along with serotonin-induced transient elevation in antidiuretic hormone. Adult schizophrenics who receive psychostimulants have also been shown to develop polydipsia with hyponatremia. Although the use of psychostimulants in adult schizophrenic patients has been studied, literature on toxicity and effects in the pediatric psychiatric population is scarce. We would suggest that this patient's polydipsia and hyponatremia are most likely a result of his ingestion of a toxic dose of a long-acting agent known to cause secondary psychosis.

Key Words: attention deficit hyperactivity disorder, lisdexamfetamine, hyponatremia, polydipsia

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Methylphenidate (MPH) is a piperidine-derived central nervous system stimulant drug that has become the primary drug of choice, along with other amphetamine class drugs, among pediatricians in treating attention deficit hyperactivity disorder (ADHD) in children. The extended-release tablet preparation of MPH is coated with immediate-release MPH that works on an osmotic pump mechanism resulting in drug release over a 10-hour period.[1] Methylphenidate exhibits similar activity to that of other amphetamines and acts primarily through dopamine uptake blockade in contrast to the catecholamine release of amphetamines. Methylphenidate has also been shown to indirectly augment the activity of serotonin, an area that is researched in psychiatry today.[2]

The most common side effects of MPH include insomnia, abdominal pains, headaches, and anorexia. However, severe and adverse toxicities may occur, including bruxism, confusion, disoriented behavior, and aggression. These side effects are more likely to occur if the patient consumes more than the maximum dose specified.[3] Multiple case studies have been published detailing the consequences of an overdose with MPH. A case report in 2010 presents a 17-year-old teenage girl that ingested a single dose of 270 mg of short-acting MPH in an attempted suicide, but consequently had no cardiac or neurological toxicity.[3] A similar case report presents a 14-year-old teenage girl who ingested 21 tablets of 54 mg long-acting MPH within an hour, also in an attempted suicide. This patient showed only increased sympathomimetic symptoms and psychopathological findings. Among the behavioral manifestations, she experienced extreme thirst and consumed an increased amount of water.[4]

Although MPH has not been directly associated with SIADH or hyponatremia, it can be concluded that MPH may cause a transient elevation in antidiuretic hormone (ADH) in patients with underlying psychiatric disorders, such as schizophrenia.[5] The presence of elevated ADH levels has been clinically confirmed in 3,4-methylenedioxymethamphtamine–induced SIADH; therefore, it can be concluded that MPH or other potent serotonergic agents and serotonin reuptake inhibitors may induce psychogenic polydipsia with secondary water intoxication causing hyponatremia. In this case, we report a previously healthy 8-year-old boy with a diagnosis of ADHD who was prescribed lisdexamfetamine dimesylate, whom after accidental ingestion of MPH extended-release tablets experienced secondary polydipsia with symptomatic hyponatremia.

CASE

A previously healthy 8-year-old boy, with ADHD on 20-mg lisdexamfetamine dimesylate, presented from an outside community hospital emergency department (ED), as a direct admit to the pediatric intensive care unit (PICU) of a university hospital, with altered mental status 15 hours after accidental ingestion of his 10-year-old brother's 36 mg long-acting MPH. Before ingestion, patient was in his normal state of health. Immediately after ingestion, he had notified his parents; however, because he was acting well at the time, he was sent to school. Upon arrival to school, patient proceeded with his usual daily activities. Approximately

3 hours after the ingestion, teachers noted patient to be disoriented and extremely combative. At this time, patient was also reported to have drunk copious amounts of water. The school called the patient's mother due to his altered mental status and combative behavior. His mother then took patient to the outside hospital ED. En route to the hospital, he was still combative and demanding to drink water. On arrival he was noted, by ED personnel, to be diaphoretic, flushed, and combative to obtain water. His parent's note that he had likely drank 3 to 4 gallons of water during his time at school and in the ED. Due to his agitation, he was given a dose of lorazepam and fell asleep. He was discharged home 8 hours postingestion, but was still drowsy and without resolution of his altered mental status.

He slept through the afternoon and was difficult to arouse later that evening, reportedly having 2 episodes of urinary incontinence. At 13 hours postingestion he was taken back to the same ED and had multiple episodes of emesis. At this time, the ED was concerned the patient was in status epilepticus due to his severely altered mental status and reported tonic-clonic seizure activity lasting few minutes with bowel and urinary incontinence. He was then intubated for airway protection with etomidate and succinylcholine. He was also noted to be hypothermic with a rectal temperature of 94.8°F. Laboratory evaluation demonstrated hyponatremia with sodium of 118 and a urine drug screen positive for amphetamines. The patient was then transported to our PICU for ongoing care and diagnostics.

On arrival, patient was sedated and intubated, only withdrawing to painful stimuli, with a documented sodium of 115. He was then given 250 mL of 3% NaCl bolus, which brought his sodium to 127. Initial laboratory results, which were obtained after initial resuscitation with hypertonic saline, revealed normal urine osmolality of 450, low plasma osmolality of 246, normal urine sodium of 104, negative levels of acetaminophen and salicylate in serum. A computed tomography of the head was performed, which demonstrated no evidence of acute trauma or cerebral edema. After correction of sodium to 132, patient continued to have altered mental status. Pediatric neurology was consulted, resulting in a loading dose of fosphenytoin 20 mg/kg being given. A 24-hour EEG showed no seizure activity. Antiepileptics were discontinued. Due to temperature instability, a lumbar puncture was performed, and broad-spectrum antibiotics were initiated. After 48 hours of negative cerebrospinal fluid findings, antibiotics were discontinued. 18 hours postingestion, patient was more alert and had significant improvement in mental status therefore was extubated. Patient was then transferred out of PICU to the progressive care unit postextubation. By 36 hours postingestion, the patient had returned to neurocognitive baseline. Patient was observed overnight for 24 hours with no further interventions. Patient was discharged home 60 hours postingestion with no residual sequelae.

DISCUSSION

The American Psychiatric Association states in the Diagnostic and Statistical Manual of Mental Disorders that 3% to 7% of school-aged children have ADHD.[6] Rates of ADHD diagnosis increased an average of 5.5% per year from 2003 to 2007.[7] As of 2007, parents of 2.7 million youth ages 4 to 17 years (66.3% of those with a current diagnosis of ADHD) report that their child was receiving treatment for the disorder.[8] The majority of children with ADHD who are treated pharmacologically receive stimulant medication, MPH being the most commonly prescribed.[9] A study done in 2002 showed there was a significant increase in overall rate of stimulant medication use by children between 1987 and 1996. Stimulant use increased from 0.6 to 2.4 per 100 children and adolescents, with the rate of stimulant use highest among boys and children aged 6 to 14 years. The use of MPH has increased substantially in the Unite States since its approval by the Food and Drug Administration in 1955.[10] In 1998, a retrospective review of all reports of MPH exposure to a certified regional poison information center was conducted. With a reported 113 short-acting and long-acting MPH human exposures, majority of exposures in children younger than 12 years involved unintentional ingestion of a sibling's medication, self-administration of an excessive therapeutic dose, or the administration of an inadvertent dose given by a caregiver. Results suggested that in the 0- to 5-year age group, the mean exposure was 13.6 mg (0.94 mg/kg), with clinical effects of drowsiness or hyperactivity occurring in 16% of exposures. In the 6- to 12-year age group, the mean exposure was 26.8 mg (0.89 mg/kg), with clinical effects including drowsiness, hyperactivity, and hyperventilation, occurring in 30.8% of exposures. Though recommended pediatric dosing is 1 mg/kg, the review suggested that doses up to 40 mg in the 0- to 5-year age group and up to 80 mg in the 6- to 12-year age group were well tolerated without significant adverse sequelae.[11]

In our case, the patient weighed 23 kg and ingested a medication he had not been previously had exposure to at more than the recommended dose of 1 mg/kg (36 mg). After his ingestion of approximately 1.5 mg/kg, he subsequently experienced psychosis causing secondary polydipsia and severe hyponatremia due to excess water intake. It is however difficult to say whether this is an effect of immediate overdose or exacerbation of chronic amphetamine use. Our patient had findings similar to SIADH, however, given that patient was in his normal state of health before ingestion along with evidence of altered thirst mechanism, it can be concluded patient subsequently had psychogenic polydipsia. Though initial laboratory findings were obtained after resuscitation with hypertonic saline, patient was still noted to be hyponatremia with high urine output of 5 mL/kg per hour, also consistent with water intoxication. Studies and multiple case reports in the pediatric population in United Kingdom have shown that psychotic side effects appeared to be related to the use of long acting preparation of MPH.[12] Though stimulant-induced psychosis is known to occur, the secondary polydipsia and severe hyponatremia associated are yet to be reported. A study in 1997 suggested that psychotic exacerbations are associated with enhanced ADH secretion in schizophrenic patients associated with polydipsia and hyponatremia, thereby placing them at increased risk of life-threatening water intoxication.[5] We conclude that this patient's polydipsia and hyponatremia are most likely a result of his ingestion of a toxic dose of a long-acting agent known to cause secondary psychosis.

CONCLUSIONS

In terms of addressing amphetamine safety, a major limitation is the paucity of information available to determine a therapeutic mg/kg dose of extended-release MPH. There are no studies known that differentiate between immediate-release, sustained-release, or extended-release preparations. Consequently, determining which specific symptoms were associated with any weight-based dosage range is not possible. This limits the ability to determine if there is a threshold dose at which toxicity is likely to occur. Though there is an abundance of data in the adult population, literature on toxicity and effects in a pediatric population remains scarce. To decrease this limitation, outcomes of intentional and unintentional exposures to MPH with adverse effects need to be reported. In addition, pediatricians need to be educated on rare but possible effects of psychosis induced polydipsia and hyponatremia. This

will allow for careful monitoring when prescribing different stimulant medications with different side effects in 1 household.

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