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An old drug having found a new home, consideration for new sources of intoxication: A case report

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Abstract

Background: Patients presenting with altered level of conciseness are a part of everyday practice in the emergency department. With many presentations due to structural, organic and psychiatric causes. Drug intoxication is a common precipitant of altered mentation with mixed and unknown overdoses posing a unique challenge. The astute emergency physician endeavors to identify the culprit agent, as some agents have specific antidotes that alter patients' outcomes, while others can have an expected course of general medical support till resolution.

Objectives: In our case report we discuss a patient presenting with altered level of conciseness, from a likely mixed ingestion that does not demonstrate expected recovery and the clues that suggest an alternative toxin. We as well briefly discuss the diagnostic approach and evidence of treatment modalities of this intoxication. We also shed light on a potential new source of drug intoxication in communities.

Methods: A single descriptive case report with a search of Medline, Pubmed for similar cases of which two similar cases have been reported [i, ii]

Keywords: Coma, Altered level of consciousness, Barbiturates, Overdose, Phenobarbital, Emergency Department (ED), Intensive Care unit, Veterinary

Introduction

Patients presenting with altered level of conciseness are a part of everyday practice in the emergency department. With many presentations due to structural, organic and psychiatric causes. Drug intoxication is a common precipitant of altered mentation with mixed and unknown overdoses posing a unique challenge. The astute emergency physician endeavors to identify the culprit agent, as some agents have specific antidotes that alter patients' outcomes, while others can have an expected course of general medical support till resolution.

Case Report

A 67-year-old woman was brought to a rural emergency department after being found unresponsive by her husband. The patient was in her usual state of health when she had gone to bed. Her husband found her unresponsive that evening. He then pulled her to the floor and started cardiopulmonary resuscitation (CPR), as he thought she was not breathing. she vomited during the process. When emergency medical services arrived and assessed the patient, they found she had a palpable pulse. Her vital signs then were a heart rate of 50 beats per minute, a systolic blood pressure of 100 mm HG, a low and shallow respiratory rate, a saturation of 87% on room air and her pupils were noted to be small. The paramedics also reported an empty fluoxetine pill bottle at her bedside. She was brought to the emergency department where her hemodynamics remained unchanged having been bagmask ventilated intermittently in transport. Her vital signs at initial emergency department assessment were a temperature of 36.4 Celsius, a regular pulse of 51beats per min, a respiratory rate of 8 breaths per minute, a blood pressure of 104/80mm HG and an oxygen saturation of 100 percent with a non-rebreather mask applied, her blood glucose level was 120 mg/dL. On physical exam her pupils were dilated and nonreactive, she had a negative oculocephalic reflex ''doll's eye reflex'' and no response or posturing to painful stimuli to any limb. Her breathing was shallow with gurgling breath sounds and decreased air entry to the left upper lobes. An oral airway was inserted; with no reaction, to facilitate suctioning the patient. Her head had no signs of trauma, her abdomen was noted to be distended presumed due to bag masking ventilation. No comment was made of the patient's skin moisture, muscle tone or extremity reflexes as part of a comprehensive overdose exam. As part of her management in the emergency department the patient was

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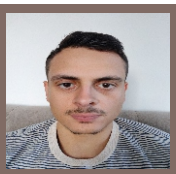

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intubated without the use of a paralytic or sedative, due to low her low Glasgow Coma Score (GCS) and concern for airway patency. Her secondary exam was unremarkable with no signs jaundice, pallor or trauma on assessment. A bedside cardiac ultrasound was done demonstrating grossly normal function of the heart. The patient also underwent a contrast computed tomography (CT) scan of her brain, chest, abdomen and pelvis which did not demonstrate any contributory findings.

The patient's past medical history was significant for fibromyalgia, bipolar disorder and post-traumatic stress disorder, and documentation of prior psychiatric admissions due to prescription medication intentional overdose. Her medication reconciliation indicated the patient had access to fluoxetine, diazepam and 'Tylenol3' (acetaminophen/codeine).

The patient's initial blood work demonstrated an acetaminophen level of 1140mcg/mL (0-200mcg/mL) and an otherwise normal complete blood count, renal panel, liver enzymes, anion gap, creatine kinase and coagulation profile. Her blood was negative for ethanol and aspirin. The initial arterial blood gas while on the ventilator was a PH 7.24 which a pC02 of 57 mmHg. A urine toxicology screen was performed which was positive for opiates, barbiturates, benzodiazepines and THC (Tetrahydrocannabinol). The patient was subsequently transferred to a regional intensive care unit for management of her mixed overdose, altered level of consciousness and acetaminophen toxicity. Her stay in the intensive care unit was notable for a persistently low GSC, initially thought to be due to a combination of benzodiazepine and opiate overdose with no other contributory causes. On the 3rd day due to her slow improvement and concern of hypoxic brain injury a magnetic resonance imaging (MRI) of the brain was ordered which demonstrated non-specific subtle abnormal T2 signal hyperintensity and cortical thickening involving the frontoparietal parasagittal gyri and parietal gyri bilaterally with no findings of acute brain injury. The patient's 5th day neurological exam demonstrated a low level of wakefulness with a GCS of 2T(intubated). She had regained pupil reflexes and demonstrated findings of intact brain stem function (normal doll's eyes, cough, gag and triggering of the ventilator). Her reflexes were symmetrical and intact with normal tone and no upper motor neuron findings on exam. The patient had recovered from an aspiration pneumonia at the time and had cleared her acetaminophen level after being treated with a N-acetylcysteine infusion. The reminder of the patient's lab work had remained within normal limits. The patient was booked for an electroencephalogram and planned for a lumber puncture to assess the patient's persistently low GCS, but on the 6th day the patient's partner had called into the unit stating he could not find the family dog's antiseizure medication at home and was concerned the patient had ingested it as well. The dog had been receiving phenobarbital for seizure disorder which it had suffered from for many years. A phenobarbital level was requested and returned after a few day sat 343 umol/L (60-160 umol/L). The case was discussed with the regional poison control center for consideration of enhanced elimination techniques to speed up the patient's recovery, but due to improvements in the patient's neurological status none were initiated. The patient was extubated a few days later and transferred to the psychiatry unit for evaluation of her suicidality.

Discussion

Phenobarbital, a barbiturate developed In 1912, is the oldest epilepsy medication still in use [1]. Its use has diminished over the years due to introduction of newer antiepileptics [2]. And has become less popular in the industrialized world primarily due to perceived negative side effects [3]. It still remains a popular choice in many developing countries [4], and is still endorsed by the world health organization as a first lineagent for epilepsy in the developing world [5].

Phenobarbitala sedative hypnotic, acts as a potent GABA receptor up regulator. In overdose situations it presents primarily with altered level of consciousness, respiratory depression and hypotension. It has been described as a "mimicker of brain death" in large ingestions [9]. Phenobarbitalis only partially cleared by the kidneys which makes it detectable to conventional urine toxicology screens [10], yet conventional immunoassay urine barbiturates screening has been shown to demonstrate false positive results [11]. The gold standard for the diagnosis of barbiturate toxicity is a plasma barbiturate concentration measured through Immunoassays (EIA) or gas chromatography/mass spectrometry (GC/MS) [12].

The treatment of phenobarbital and other barbiturate toxicity is mostly supportive, with its deleterious effects on the respiratory, neurological and cardiovascular systems. Phenobarbital is amenable to binding with multi dose activated charcoal, allowing enhanced elimination via urinary alkalinization. Cases of massive overdose, resulting in hemodynamic derangement or prolonged coma are most often treated with extracorporeal removal using hemodialysis and hemoperfusion [7, 13–15]. Although there is a lack of patient oriented outcomes with any of these therapeutic interventions [16].

Barbiturate toxicity is well described in the medical literature. Although its use has diminished, it should still be suspected in cases of respiratory depression and altered level of consciousness. Particularly with recent reports of intentional Phenobarbital overdose from physician prescribed medication, online black-market sellers and veterinary sources [6–8]. There are increasing reports of human ingestion of veterinary prescribed medications, such tricyclic antidepressants and phenothiazine antipsychotics [17]. Phenobarbital in pets has gained momentum for use in small animals as it is the drug of choice in the treatment of seizures for dogs and cats [18].

This case report is the 3rd, we identified after searching the medical literature of phenobarbital toxicity from prescription pet antiseizure medication [7,19]. It highlights a significant potential source of toxic exposure.

Conclusion

In cases of suspected intoxication of unknown origin, a detailed pet history could prove invaluable. Bartbiturate toxicity should still be strongly considered in the altered patient with respiratory depression, as there is an expansion of its potential sources. Although no patient centered outcomes have been demonstrated, enhanced elimination techniques have demonstrated efficacy in overdoses of phenobarbital.

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