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Case Report

A Case of Severe Theophylline Toxicity and its Management

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ABSTRACT

Background: Theophylline poisoning can lead to toxic effects on multiple organ systems. Management of theophylline overdose focuses on stabilizing cardiovascular and pulmonary function, gastrointestinal decontamination to interrupt continued absorption, and minimizing end-organ effects. This report presents a case of theophylline overdose with hemodynamic instability and metabolic derangements, along with a review of the literature to update the management of theophylline toxicity.

Case presentation: An 80-year-old Indian gentleman presented with giddiness and vomiting after the deliberate ingestion of 20 tablets of theophylline. Serum levels confirmed severe theophylline poisoning, correlating with clinical manifestations. The patient was resuscitated and subsequently given supportive care.

Conclusion: Theophylline poisoning should be treated appropriately and promptly. Initial treatment for hypotension consists of rapid infusion of isotonic saline or balanced crystalloid solution. Multi-dose activated charcoal for the elimination of drugs should be administered in severe theophylline poisoning.

Keywords: Theophylline poisoning; Arrhythmias; Metabolic derangements; Multi-dose activated charcoal

INTRODUCTION

Theophylline is utilized as a bronchodilator for patients with asthma or Chronic Obstructive Pulmonary Disease (COPD) and as an agent to treat apnea and bradycardia in premature neonates. It acts as an antagonist, exhibiting adrenergic activity and phosphodiesterase inhibition at toxic levels. As a plant-derived alkaloid, theophylline shares chemical similarities with caffeine and has up to 100% oral bioavailability, with a small volume of distribution of approximately 0.5 L. Peak serum concentration is typically reached in 1-2 h, although it can vary up to 8 h in sustained-release preparations. The half-life at therapeutic concentrations is approximately 5 h in adults; however, this changes from first-order to zero-order kinetics at increased concentrations. Acute toxicity can occur with ingested doses as low as 7.5 mg/kg, with manifestations ranging from mild symptoms such as metabolic abnormalities, tremors, and vomiting to severe outcomes, including seizures, hypotension, and arrhythmias [1,2]. Chronic toxicity poses a risk for cardiovascular and neurological manifestations, particularly in patients with increased serum theophylline concentration following minimal dose increments [3,4].

Over the past eight years, reported cases of theophylline exposure in the United States have declined significantly, correlating with the decreasing therapeutic use of the drug. Most exposures occur unintentionally, primarily in patients over 20 years of age, with oral overdoses of sustained-release formulations being the most frequently reported [5,6].

The management of theophylline toxicity focuses on addressing cardiovascular, neurological, and metabolic manifestations, emphasizing the timely use of elimination enhancement. This is determined by signs of poisoning following acute overdose and physical findings in chronic overdoses [7].

CASE PRESENTATION

An 80-year-old gentleman with a past medical history of COPD and left inguinal hernia was brought to the hospital by ambulance services. He presented with giddiness and vomiting

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after deliberately ingesting 20 tablets of theophylline extended-release preparation. Upon arrival at the emergency department, his vital signs were as follows: blood pressure of 70/40 mm Hg, heart rate of 144 beats per min, respiratory rate of 18 cycles per min, and oxygen saturation of 97% on room air. Examination revealed an alert patient with an irregularly irregular pulse. Auscultation of the lungs indicated normal bilateral vesicular breath sounds with no adventitious sounds. Notably, his left inguinal hernial orifice was remarkable for an indirect hernia. An electrocardiogram showed atrial fibrillation with rapid ventricular response at 144 bpm (Table 1). Capillary blood glucose was elevated at 313 mg/dL, with urine testing negative for ketone bodies.

Blood investigations	Results
Urea	49 mg /dL
Creatinine	1.57 mg /dL
Sodium	131 meq/L
Potassium	3.24 meq/L
Calcium	8.74 mg /dl
Magnesium	1.73 mg /dl

Table 1: Laboratory investigations conducted during the study.

A chest radiograph was performed and was unremarkable for consolidation or congestion. Serum theophylline levels were measured due to the suspicion of theophylline poisoning. The patient's hypotension and arrhythmia were attributed to acute ingestion of theophylline overdose. He was started on intravenous fluids, completing 1 L of ringer's lactate, which improved his blood pressure to 108/60 mm Hg and reduced his tachycardia to 107 bpm. Point-of-care ultrasound revealed no concern for fluid overload, and cardiac function was normal. Considering his hemodynamic instability, he was admitted to the ICU for closer monitoring.

During his stay, he complained of abdominal pain and experienced repeated episodes of vomiting, which were treated with high-dose ondansetron (8 mg IV) and injection pantoprazole. A total of 50 g of activated charcoal was administered via a rectal tube, with multi-dose activated charcoal (25 g every 2 h) continued. Oral potassium syrup supplementation (30 mL) was given every 4 h to correct hypokalemia. A nephrology consultation was sought to consider hemodialysis due to signs of severe poisoning and acute kidney injury. Potassium levels subsequently improved to 4.71 meq/L, and serum theophylline levels measured 26 mcg/L. As blood pressure, heart rate, and electrolytes normalized with no seizure episodes, the patient was transferred to a step-down unit.

Upon discharge, the patient was advised to follow up in the outpatient department. As features of obstructed inguinal hernia were absent, elective hernioplasty was planned after a pre-anesthetic evaluation. The patient was discharged with stable vital signs.

RESULTS AND DISCUSSION

Theophylline poisoning can lead to multisystem toxic manifestations, with potential death resulting from intractable ventricular arrhythmias [3]. Immediate management often targets life-threatening complications, particularly in acute overdose cases. Major toxicity, such as seizures, is significantly correlated with serum theophylline concentration in patients with acute overdose, while chronic intoxication may pose a risk for life-threatening events, even without elevated peak levels [4].

Hypokalemia

Hypokalemia arises from catecholamine excess and is rapidly reversible through appropriate enhancement of theophylline elimination. Potassium supplementation is suggested for hypokalemic patients with serum potassium <3 mEq/L or with ventricular arrhythmias. Monitoring of serum potassium levels is essential, as total body potassium depletion may not be significant in these cases.

Vomiting

Persistent vomiting is common in theophylline poisoning and must be controlled to allow for multiple-dose activated charcoal administration [8]. High-dose ondansetron is recommended for managing emesis in these patients, potentially supplemented by metoclopramide [7].

Ancillary testing

In patients with acute theophylline overdose, levels should be measured every two hours until peak concentration is achieved, then every four hours for up to 24 h. In chronic cases, daily monitoring is advised until clinical signs resolve [9].

Management of cardiovascular instability

Hypotension resulting from theophylline overdose is primarily due to beta-adrenergic stimulation and vasodilation. Rapid infusion of isotonic saline is recommended for initial treatment [7]. Avoiding selective beta-adrenergic agonists, as many cardiovascular derangements are caused by beta-2 stimulation, is essential.

Decontamination

Theophylline binds well to activated charcoal, and its clearance is enhanced with multiple-dose activated charcoal administration [10]. Gastric emptying methods, such as lavage or emesis, have not demonstrated clinical benefits and pose risks [3].

CONCLUSION

In conclusion, severe theophylline poisoning should be identified early, and appropriate treatment should be initiated promptly. Multi Dose Activated Charcoal (MDAC) should also be considered and administered in cases of severe theophylline poisoning. Given the declining but still significant use of theophylline, especially in regions with limited access to newer bronchodilators, emergency physicians must remain vigilant. Awareness of theophylline's pharmacokinetics and potential

toxicity is significant, as the rapid progression from mild symptoms to severe complications can occur. Staying informed about the management of theophylline overdose not only improves patient outcomes but also enhances overall public health efforts to address poisoning incidents effectively.

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