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EGD for Refractory Toxidromes: Is It Time to Add to the Algorithm?

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Abstract

Toxic ingestions are an increasing concern among pediatric patients in the United States. Less common, but troubling, are those patients with persistent toxicity symptoms despite stabilization, resuscitative, and decontamination efforts. We report a case of refractory serotonin toxicity in an adolescent for whom endoscopic removal of medication remnants led to the resolution of his clinical course. A 14-year-old male patient with anxiety and depression, treated with escitalopram and clonidine, presented to an outside hospital (OSH) emergency department (ED) with tonic-clonic seizure activity and altered mental status. Non-contrast head computed tomography (CT), complete blood count, and basic metabolic panel were unrevealing. Repeated seizure activity that occurred in the OSH ED prompted transfer to a tertiary pediatric care facility for ongoing management. Based on the constellation of symptoms (tachycardia, muscle rigidity, and lower extremity clonus) and his medication history, there was concern for serotonin toxicity. His clinical course worsened, despite treatment with midazolam and cyproheptadine, requiring intubation for respiratory failure. Because of his refractory symptoms and concern for ongoing medication side effects, on hospital day 4, he underwent an esophagogastroduodenoscopy (EGD), which revealed 20 partially digested pills firmly adhered to the gastric mucosa. The pill fragments were removed and whole bowel irrigation was started, and the patient improved rapidly, allowing for extubation within 24 hours. An EGD is not routinely used for the management of toxic ingestions. In addition to this case, evidence from prior case reports supports the judicious use of EGD as a diagnostic and therapeutic decontamination modality for severe toxicities.

Keywords

adolescent, ingestion, serotonin toxicity, esophagogastroduodenoscopy

Introduction

Toxic ingestions are common in the pediatric population and vary greatly based on age, type of ingestion, and clinical outcome. More than 2 million ingestions were reported to the American Association of Poison Control Centers in 2019 and, of those, nearly 60% were among children or adolescents <20 years of age.[1] Complicating this statistic is the rise of suicide as the second leading cause of death in children 10 years of age and older in the United States, with poisoning among the top 3 means of suicide.[2] The introduction of novel pharmaceutical formulations and administration routes, as well as changing trends in drugs of abuse, have contributed to the complexity involved in caring for patients with toxic ingestions.

Basic principles of managing a pediatric ingestion involve early recognition, acute resuscitation, decontamination, utilization of antidotes and/or enhanced elimination modalities, and supportive care. Among decontamination modalities, the more commonly referenced methods include activated charcoal (AC), gastric lavage, and whole bowel irrigation (WBI). Less commonly described techniques include endoscopic or surgical removal of the xenobiotic. The American Academy of Pediatrics (AAP) and American Academy of Clinical Toxicology (AACT), together with the European Association of Poisons Centres and Clinical Toxicologists, continue to independently review the data and update their positions on the more common gastrointestinal (GI) decontamination modalities.[3-5] At this time, no

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professional organization has reviewed the literature for endoscopic removal of xenobiotics nor made recommendations on the utility of this intervention.

Endoscopic decontamination may be a helpful adjunct in the management of refractory or severe ingestions. Multiple case reports have documented that protracted toxic exposures contribute to significant morbidity and potential mortality.[6-8] Compounding this issue, the more common methods of GI decontamination are sometimes ineffective and/or complicate the clinical picture due to unintended side effects. Here, we describe a case of refractory serotonin toxicity that ultimately resolved following endoscopic removal of medication remnants.

Case

A 14-year-old male patient with a history of anxiety and depression, being managed on fluoxetine and clonidine, was transferred from a community emergency department (ED) after initial evaluation for seizure-like activity, altered speech, and aggression at school. A non-contrast head CT, complete blood count, and basic metabolic panel were all normal. He became aggressive and had 2 generalized tonic-clonic seizures. He received haloperidol, diphenhydramine, and lorazepam for agitation and seizure control and was transferred to the pediatric ED at a tertiary care hospital.

His vital signs upon arrival were heart rate (HR), 135/min; blood pressure (BP), 130/56 mm Hg; pulse oximetry was 99% in room air, and T 36.7°C. He was initially agitated and disoriented with 5 mm and reactive pupils, hyperreflexia with 8 beats of bilateral lower extremity clonus, muscle rigidity, and dry lips and skin. He had a negative urine drug screen, normal acetaminophen and salicylate concentrations, and an elevated creatinine kinase (CK) level of 522 U/L. Given the acuity of the presentation, constellation of symptoms, and medication history, a presumptive diagnosis of serotonin toxicity was made.[9,10] He was admitted to the pediatric intensive care unit (PICU), given intravenous fluids, and a midazolam infusion was started for agitation.

The patient remained nonverbal and altered with persistent muscle rigidity despite benzodiazepine therapy and had a peak in his CK concentration of 1923 U/L on hospital Day (HD) 2. Cyproheptadine was started in light of these refractory symptoms. Despite these additional measures, on HD 3, he had increased work of breathing, worsening tachycardia, hypertension, and hyperthermia. He was endotracheally intubated for hypoxemic respiratory failure, midazolam infusion was escalated, and antipyretics were administered.

Given the refractory and worsening toxicity, he underwent an esophagogastroduodenoscopy (EGD) on HD 4. Twenty foreign bodies, with textured white outer coating and green gelatinous inner material, were found in and adhered to the gastric fundus. Removal of all the visualized foreign bodies was accomplished with a retrieval basket (Image 1). Due to the inability to visualize distal to the duodenum, WBI with polyethylene glycol was initiated. Within hours of EGD, the patient had increasing awareness and purposeful movements and was extubated less than 24 hours later. Gas chromatography–mass spectrometry analysis of the gelatinous gastric material found a mixture of bupropion, fluoxetine, and cyproheptadine. The patient made a full recovery and was transferred to inpatient psychiatry care on HD 7.

Image 1. Foreign bodies removed from patient, with EGD retrieval basket.

Discussion

An EGD is not a routinely utilized treatment method for the management of toxic ingestions. Our illustrative case demonstrates the utility of EGD, particularly in the case of prolonged toxicity and in which continued absorption is suspected. Our decision to proceed with EGD was based on prior experience with refractory and progressive toxicity in a teenager who was found to have a large intragastric mass of charcoal mixed with intact and fragmented tablets. The case reports from both adult and pediatric literature have discussed the role of EGD for drug elimination in the setting of protracted clinical courses that did not respond to the more commonly used GI decontamination methods.[6,11] This is further supported by unfortunate reports of fatal ingestions that, upon autopsy, found retained medication in the GI tract despite traditional decontamination attempts during resuscitation efforts.[8]

A variety of risk factors can predispose to prolonged toxicity: medication formulation, decontamination modalities in-and-of themselves, underlying medical disorders, and novel drug delivery techniques. Extended-release medication

technology ensures slow release of medications often through outer coatings that are insoluble at lower pH environments. These can aggregate and form a gel-like layer in the stomach, predisposing to the formation of a pharmacobezoar.[12] In addition, delayed gastric motility, due to an underlying medical condition or medication side effect, plays a role in absorption following an ingestion. Confounding these issues are the complications that can arise from common decontamination modalities.[3-5] Pharmacobezoar formation and gastric outlet obstruction due to adherence to AC can prevent gastric emptying and therefore prolong medication exposure. Finally, relatively newer considerations in cases of sustained and/or severe toxicities include novel drug delivery methods (eg, parachuting, packing, or stuffing). Body packers and stuffers consume drugs for the purpose of moving drugs from one point to another and avoiding arrest or detection, respectively. Alternatively, parachuting (aka bombing) is the method of wrapping a drug in a material that will dissolve or unravel in the GI tract allowing for absorption for either delayed rapid uptake or sustained-release effect. A unifying characteristic inherent to the varying methods of alternative drug ingestion is the use of a foreign material for drug packaging and/or delivery. Depending on the amount of drug and the type of material used for packaging, complication risk may increase for GI obstruction or perforation, altered drug metabolism, decreased efficacy of decontamination modalities, and the potential for airway complications.

An EGD is an invasive procedure and the risks should be weighed against the benefits of its utility on a case-by-case basis. The risk of worsening toxicity or mortality were drug packaging or delivery methods to be damaged in the process of performing an EGD should be carefully considered. An EGD, in an intensive care unit (ICU) setting, with an intubated, appropriately sedated, and closely monitored patient, in general, has a good safety profile. The use of an EGD in our case highlights some of the factors that should be considered when managing patients with refractory toxidromes. In our case, there was concern for an alternative drug delivery method due to the presence of the thick, white coating on the outside of the partially digested pill fragments (Image 2). As aforementioned, additional factors to consider include extended-release medication formulations, the use of AC, and delayed gastric motility due to underlying medical condition or treatments.

Image 2. Detail of outer coating of the partially digested pill fragments.

Conclusion

With ever-changing pharmacology and new methods of drug delivery, the potential for refractory toxidromes is high. Our patient's clinical course clearly demonstrated the utility of EGD and pill removal for the management of his refractory toxidrome and resulted in less time on the ventilator and a shorter hospitalization. An EGD has the unique potential of being both a diagnostic and therapeutic procedure in prolonged and severe toxicities, particularly if there is poor response to conventional therapies, concern for extended-release formulations, or suspicion of parachuting. In addition, it may improve both morbidity and mortality if utilized sooner in a patient's clinical course. Given the literature to support the phenomena of protracted cases benefiting from more advanced management strategies, endoscopic evaluation should be considered early in poisoned patients' refractory to standard medical therapy.

Authors' Note

Previous presentations of information contained in this article: Hollon H, Allen K, Marvin W. Esophagogastroduodenoscopy as an Adjunctive Therapy in Drug Overdose. 49th Critical Care Conference. February 2020.

Declaration of Conflicting Interests

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series. The basics of our case were reviewed with Medical University of South Carolina's (MUSC) institutional review board (IRB) staff. Per our institution's policy, the information presented in this case report does not qualify as human research, and therefore IRB approval is not needed.

Informed Consent

Informed consent for patient information to be published in this article was not obtained because the patient has not had a repeat contact with our health care system in the more than 3 years since the encounter took place. We, therefore, have been unable to contact the patient and/or family members to discuss the consent process requested for this form of publication.

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