Refractory Hypoglycemia Due to Sulfonylurea Contamination of Illicit Opioid Medications

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ABSTRACT

Illicit drug supply adulteration can heighten the risk for adverse health outcomes. Sulfonylurea medications are widely used in the treatment of diabetes mellitus (DM). Unintentional or intentional overdose of sulfonylureas can cause refractory hypoglycemia. This case report describes a 62-year-old male patient who presented to the emergency department (ED) after being found on the ground with signs of mild trauma. He was noted to be persistently hypoglycemic despite boluses of intravenous dextrose, a dextrose infusion, and oral nutrition. The patient did report purchase and oral ingestion of pills sold as oxycodone and that the pill shape and color were different from his usual supply. The patient was empirically treated with octreotide resulting in normalization of his serum glucose. Testing demonstrated a serum glipizide concentration six times the reporting range. This case represents unintentional sulfonylurea exposure in the setting of non-prescribed oxycodone use, resulting in hypoglycemia refractory to intravenous dextrose and oral nutrition. Octreotide is an additional potential treatment for this condition. As in this case, ingestion of street drugs may present a potential source of sulfonylurea exposure. Opioid contamination with sulfonylureas has not been widely reported in the literature and knowledge about this potential exposure is important for the prompt recognition and treatment of these patients by emergency physicians.

KEYWORDS: sulfonylureas, substance-related disorders, hypoglycemia

BACKGROUND

Sulfonylurea medications were first developed in the 1950s as oral medications to treat diabetes mellitus (DM).[1] Second-generation sulfonylureas are widely used in the management of DM, as they are inexpensive and effective.[1] Sulfonylureas bind to and inhibit potassium channels on beta cells located in the pancreas; the subsequent resting potential shift leads to calcium influx into beta cells, which then releases insulin into the bloodstream.[1,2] For patients with DM, the increased insulin secretion works to decrease blood glucose concentrations and improve hyperglycemia.[1,2] Sulfonylurea-mediated insulin release occurs regardless of a patient's initial blood glucose levels and patients with normal blood glucose levels who are exposed to sulfonylurea medication may experience persistent hypoglycemia.[1,3-5] Here we present a unique case report of a patient presenting with refractory hypoglycemia after exposure to counterfeit oxycodone pills contaminated or substituted with glipizide, a sulfonylurea.

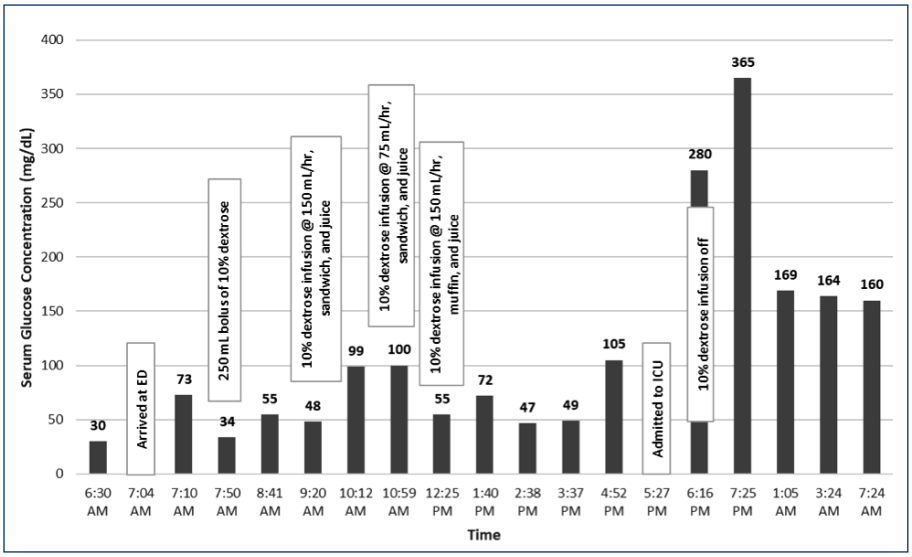
CASE REPORT

A 62-year-old male patient with a history of chronic back pain presented to the emergency department (ED) after being found on the ground outside his apartment. Emergency medical personnel noted abrasions to his face and extremities. The patient was initially lethargic and confused but was opening his eyes spontaneously and following commands. The patient's blood prehospital glucose was 30 mg/dL, and the patient was given 12.5 gm of dextrose 10% (D10). His mental status improved, and he was no longer confused upon arrival at the ED, although he was still amnestic to the preceding events. Trauma workup, including Computed Tomography (CT) of the brain, cervical spine, chest, abdomen, pelvis, and back, was negative for acute injury. The patient's history and medications were reviewed. He denied a history of diabetes, use of insulin, or known ingestion of any glucose-lowering medications.

The patient's glucose upon arrival at the ED was 73 mg/dL **(Figure 1)**. This was checked one hour later and was 34 mg/dL. An additional 25 gm bolus of D10 was administered with only a minimal increase in his blood glucose to 55 mg/dL. He was then started on a D10 infusion at 150 mL/hr. Once his trauma evaluation was complete, he was fed multiple calorie-rich meals. The patient's glucose rose to 100 mg/dL several hours after the D10 infusion was initiated, but the glucose rapidly dropped to 55 mg/dL after the rate of the D10 infusion was lowered to 75 mL/hr.

Medical history was expanded due to persistent, undifferentiated hypoglycemia. No infectious signs or symptoms were reported. While the patient did consume alcohol frequently, he did not have laboratory evidence of hepatic dysfunction and a review of his dietary habits did not yield any concern for glycogen deficiency. Upon directed questioning,

Figure 1. Serum glucose monitoring and medications administered during the hospital course in a patient with counterfeit oxycodone exposure with contamination with glipizide.



*EMS = Emergency Medical Services; ED = Emergency Department; ICU = Intensive Care Unit

the patient finally admitted to illicit purchase of presumed oxycodone from a street vendor to treat chronic low back pain. He noted that the pill shape was different than his usual supply. The patient consumed several of these pills the night prior to his ED presentation. A urine drug screen tested positive only for oxycodone. A serum sulfonylurea detection assay was ordered, and the patient was empirically treated with octreotide 100 mg subcutaneously with resolution of his hypoglycemia shortly thereafter. The patient was admitted to the intensive care unit with eventual discontinuation of his D10 infusion after a total of 12 hours. His testing returned with a serum glipizide concentration of 240 ng/mL.

DISCUSSION

This case represents an inadvertent ingestion of glipizide, a type of sulfonylurea, resulting in hypoglycemia refractory to intravenous dextrose and oral nutrition. Contamination of prescription or illicit pharmaceuticals sold on the street with sulfonylurea compounds has been documented previously; this often presents as refractory hypoglycemia after exposure to these drugs.[6-9] Review of poison control data from 2001-2015 demonstrated that 63% of medication-mediated hypoglycemia cases involved sulfonylurea ingestion.[1] Hypoglycemia usually occurs within several hours of sulfonylurea ingestion but may persist for days and become refractory to intravenous dextrose.[4] Effects can last anywhere from six to 72 hours, depending on each individual drug's duration of action.[1] In addition to dextrose and oral nutrition, patients presenting with sulfonylurea-induced hypoglycemia should be treated with octreotide (50 to 100 mcg, subcutaneously, every six hours), which decreases insulin release from pancreatic beta cells. Several laboratories allow for testing for presence of sulfonylurea drugs in the serum or plasma, but results often take several days to come back, limiting usefulness in the immediate recognition and treatment of sulfonylurea toxicity.[10] Emergency physicians should take a thorough medication history, including both prescribed and illicit drugs, when caring for patients with undifferentiated hypoglycemia and should consider empiric octreotide if there is concern for sulfonylurea ingestion.

Limitations

This case was limited by the inability to test the composition of the offending pills, which could have confirmed whether the patient ingested glipizide pills that were substituted for oxycodone, or whether the oxycodone itself was contaminated with glipizide.

CONCLUSIONS

Refractory hypoglycemia may be due to inadvertent or intentional consumption of sulfonylurea medications. Ingestion of street drugs may present a potential source of sulfonylurea exposure and should be considered when treating patients with hypoglycemia.

References

1. Bosse GM. Chapter 47: Antidiabetics and Hypoglycemics/Antiglycemics. In: Nelson LS, Howland MA, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS, *Goldfrank's Toxicology Emergencies*. 11th ed. McGraw Hill. 2019;694-706.
2. Wexler DJ, Nathan DM, Rubinow K. Sulfonylureas and meglitinides in the treatment of type 2 diabetes mellitus. In: *UpToDate*, Post TW (Ed), UpToDate, Waltham, MA. (Accessed: 15 Apr 2023).
3. McLaughlin SA, Crandall CS, McKinney PE. Octreotide: an antidote for sulfonylurea-induced hypoglycemia. Ann Emerg Med. 2000 Aug;36(2):133-138.
4. Klein-Schwartz W, Stassinos GL, Isbister GK. Treatment of sulfonylurea and insulin overdose. Br J Clin Pharmacol. 2016 Mar;81(3):496-504.
5. Chu J, Stolback A, Burns MM, Hendrickson RG, Ganetsky M. Sulfonylurea agent poisoning. In: *UpToDate*, Post TW (Ed), UpToDate, Waltham, MA. Accessed: 15 Apr 2023.
6. Peng FB, Li S. Drug Abuse Manifesting as Persistent Hypoglycemia: A Case Report of Hidden Sulfonylurea Poisoning. Presented at *Thomas Jefferson University Department of Medicine Posters* 2018, Philadelphia, PA. P12.
7. Ross JA, Downs JW, Bazydlo LA, Bordwine PH, Gineste CE, Kopatic MC, Rege SV, Saady DM, Utah OF, Wyatt SA, Wills BK,

Rose SR, Holstege C. Outbreak of Severe Hypoglycemia After Ingestion of a Male Enhancement Supplement - Virginia, August-November 2019. MMWR Morb Mortal Wkly Rep. 2020 Jun 19;69(24):740-743.

8. Narayanaswamy AKP, Williams N, Agarwal N, Okosieme O. 2012. Hypoglycaemia outbreak: a new danger on the streets? Presented at Society for Endocrinology BES 2012, Harrogate, UK. *Endocrine Abstracts*. 28, P70.
9. Chin RL. Oral hypoglycemics sold as Valium on the streets: a case report. Ann Emerg Med. 2004 Nov;44(5):552.
10. Hypoglycemia panel (sulfonylureas), serum or plasma (no date). ARUP Laboratories Test Directory. Available at: https://ltd.aruplab.com/Tests/Pub/3005636 Accessed: 15 Apr 2023.

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