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Case Report

Hypoglycemia After Ingestion of "Street Valium" Containing Glyburide, Alcohol, and Cocaine

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ABSTRACT

Background/Objective: Because of their similar appearance and inexpensive cost, sulfonylureas can cause hypoglycemia when substituted for benzodiazepines by the illicit drug market. We present a patient who developed hypoglycemia after ingestion of what she thought to be Valium; work-up revealed sulfonylurea exposure.
Case Report: A 33-year-old patient was brought to the hospital after being found unresponsive by paramedics with a reported venous blood glucose level of 18 mg/dL (reference range, 70-140 mg/dL). This prompted treatment with 12.5 g of dextrose administered intravenously. At the hospital, the venous blood glucose level was 15 mg/dL resulting in intravenous dextrose infusion initiation. Once stable, the patient endorsed a medical history of substance use disorder and anxiety. She reported ingesting 2 blue pills given to her by a friend as Valium for her anxiety. Laboratory values showed an elevated insulin level of 47.4 mIU/mL (2.6-24.9), an elevated C-peptide level of 5.4 ng/mL (1.1-4.4), and a glucose level of 44 mg/dL (>70 mg/dL). The patient underwent a 72-hour fasting test. Blood hypoglycemia agent screening showed positive results for glyburide (>5 ng/mL). The patient was discharged home in stable condition.
Discussion: There are approximately 2 to 5 case reports of hypoglycemia among persons taking illicit drugs containing sulfonylureas. Laboratory values consistent with the use of a hypoglycemic agent include elevated insulin and C-peptide levels, a low glucose level, and positive results for hypoglycemia agent screening.
Conclusion: Sulfonylurea-induced hypoglycemia may lead to clinical sedation, mimicking the effects of benzodiazepines. Sulfonylurea substitution or drug contamination should be suspected when severe hypoglycemia is diagnosed in unresponsive patients suspected of taking illicit drugs.

Introduction

Illicit drug abuse is a growing epidemic worldwide with benzodiazepines and other tranquilizers being the third most common misused prescription drug among U.S. adults.[1] Misuse of benzodiazepines has increased the availability of these drugs in the illicit market. Some of these illicit pills are highly potent due to being combined with fentanyl, whereas others are substituted with pharmaceuticals with little abuse potential but subsequent adverse effects.[2] Illicit drugs that are known to cause hypoglycemia include ecstasy, amphetamine, canabis,[3] and sulfonylureas marketed as benzodiazepines. Sulfonylureas increase the release of endogenous insulin, which can lead to hypoglycemia with overdose or ingestion by patients without diabetes. They can also reduce the clearance rate of insulin in the liver, reduce the secretion of glucagon, and enhance sensitivity to insulin in the peripheral tissues.[4] Alcohol is metabolized by the liver, resulting in decreased gluconeogenesis, which can lead to hypoglycemia. Cocaine is not known to cause hypoglycemia, but cocaine use and hypoglycemia can have a similar clinical presentation with agitation, tachycardia, increased perspiration, and variable neurologic signs and symptoms. Here, we present an interesting case of severe hypoglycemia with

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neuroglycopenic symptoms due to sulfonylureas ingested by a patient who believed she was taking diazepam.

Case Report

A 33-year-old patient was found unresponsive and diaphoretic by paramedics. In the field, point-of-care blood glucose was obtained and found to be 18 mg/dL (normal range >70). The patient received 12.5 g of dextrose (D50W) intravenously, with regain of consciousness and improvement in point-of-care blood glucose to 109 mg/dL. Upon arrival at the hospital, the patient was conscious. Vital signs were notable for blood pressure of 117/68 with a heart rate of 73/min oxygenating 98% on room air. Physical examination was notable for general appearance of mild distress with pupils' equal, round, and reactive to light, moist oral mucosa. Neurology examination was nonfocal with the patient being awake, alert, and oriented to person, place, and time. The patient's venous blood glucose level while in the emergency department was only 15 mg/dL. She received 2 additional treatments with D50W with improvement to her venous blood glucose level to 45 mg/dL. After a third injection of D50W, an intravenous D5W infusion was started with an improvement in the blood glucose level to 96 mg/dL.

Once stabilized, awake, and alert, she recounted events leading up to hospitalization. On the day preceding hospital admission, the patient reported that she was given 2 light blue pills by a friend for anxiety. The patient reported the pills were presented to her as Valium and she ingested them around 5 PM. She voiced that she had felt "bad all night" with bouts of nausea and diaphoresis. Upon awakening for work at 4 AM the next morning, she felt shaky and weak. Around 11 AM, the patient consumed a large meal for lunch and felt much better. In the afternoon, she proceeded to use cocaine and had 3 beers before a planned dinner out with her parents at 7 PM, where she lost consciousness and paramedics were called to the scene.

The patient reported a personal history of substance use disorder and anxiety. She denied a personal and family history of diabetes, had no family or friends on insulin therapy, and denied taking any medications for diabetes. She denied any previous occurrence of symptoms, bariatric surgery, or acute medical illness. Current medications included methadone (120 mg daily). The patient denied any known allergies. Social history was notable for daily tobacco use and alcohol use consisting of a "couple" of beers a few times a week.

The patient was continued on D5W infusion, which progressively improved her blood glucose values >20 hours. Urine toxicology screening showed positive results for detectable benzodiazepines (>75 ng/mL), ethyl alcohol (>0.020 g/dL), and cocaine (>50 ng/mL). Laboratory values were notable for elevated insulin of 47.4 mIU/mL (2.6-24.9 mIU/mL), elevated C-peptide of 5.4 ng/mL (1.1-4.4 ng/mL), and a glucose level of 44 mg/dL. Additional laboratory studies included morning cortisol of 14.8 mcg/dL (5-25 mcg/dL), thyroid stimulating hormone of 0.88 mIU/L (0.3-4.2 mIU/L), and free thyroxine of 0.9 ng/dL (0.9-1.7 ng/dL); serum insulin antibodies were undetectable (≤0.02 nmol/L).

Serum glucose stabilized with values >70 mg/dL off the D5W and the infusion was discontinued. The patient underwent a 72-hour fast. Results at the conclusion of the 72 hours fast showed C-peptide of 0.8 ng/mL (1.1-4.4 ng/mL), proinsulin of 3.4 pmol/L (3.6-22 pmol/L), serum insulin of 6.9 mIU/mL (2.6-24.9 mIU/mL), venous blood glucose of 67 mg/dL, and β-hydroxybutyrate of 1.8 mmol/L (<0.4 mmol/L). Hypoglycemia agent screening on admission showed the presence of glyburide (>5 ng/mL). Levels were not quantified. The patient was diagnosed with severe hypoglycemia induced by accidental ingestion of oral hypoglycemic medications, and she was discharged home in stable condition with recommendations to abstain from using illicit substances and information about available community resources for substance dependency.

Highlights

- Sulfonylureas can be substituted for illicit benzodiazepines
- Sulfonylurea-induced hypoglycemia may mimic benzodiazepine effects
- Physicians should consider sulfonylurea abuse when evaluating hypoglycemia

Clinical Relevance

Sulfonylurea-induced hypoglycemia leads to clinical sedation, mimicking benzodiazepine effects. Sulfonylureas are being sold by the illicit drug market, mislabelled as benzodiazepines, increasing the potential for misuse. Physicians should be aware of this possibility and consider intentional or unintentional sulfonylurea abuse, with or without other drugs, when evaluating patients with hypoglycemia.

Discussion

The major presenting clinical feature of the patient was unresponsiveness. The differential diagnosis for unresponsiveness is broad including central nervous system events, toxic ingestion, cardiovascular events such as myocardial infarction, and endocrine dysfunctions such as hypoglycemia.[5] Hypoglycemia has been associated with diaphoresis and loss of consciousness. We believe that the major cause of unresponsiveness in the patient presented here was marked hypoglycemia, given the demonstration of Whipple's triad with loss of consciousness with a blood glucose level of 18 mg/dL and resolution of symptoms when treated with dextrose.[6]

In this case, laboratory values were consistent with endogenous hyperinsulinism demonstrated by elevated insulin and C-peptide levels and a low-blood glucose level. The patient eventually showed positive results for hypoglycemia agent screening for glyburide. Hypoglycemia agent screening is a specialized test performed in an external laboratory, with a processing time of 2 to 8 days. While awaiting these results, the 72-hour fasting test was performed to assess for other causes of hyperinsulinemia (namely insulinoma) and it showed negative results.[6]

In this case, hypoglycemia was likely induced by both sulfonylureas compounded by alcohol ingestion. The patient reported unknowingly ingesting a sulfonylurea believing that it was Valium to treat her anxiety. Benzodiazepine intermixed with sulfonylureas, or "street Valium," has previously been reported in the literature (Table).[2,7-9] According to Substance Misuse Resources, "street Valium" is a benzodiazepine-type tablet that may be known by many terms including blues, vallies, and diazepam.[10] It has become a collective term used to describe real, fake, and novel benzodiazepines obtained without a legitimate prescription. Unlike benzodiazepines, sulfonylureas are not a controlled substance, making them easier and cheaper to obtain. The physical appearance and sedating effects of sulfonylureas (due to hypoglycemia) are similar to those of benzodiazepine, making them an easy substitute. This allows illicit drug marketers to easily mislabel sulfonylureas as benzodiazepines to increase profit. In this case, the patient reported ingesting 2 blue pills that she was given under the guise of Valium to treat her anxiety. In a different case, the patient identified a

Table
Case Reports Related to Hypoglycemia Due to Sulfonylurea Ingestion Intended for Drug of Abuse

Author, y	Patient age (y)	Intended drug of abuse	Sulfonylurea detected	Lowest glucose level reported (mg/dL)
Chin, 2004[7]	47	Diazepam	Glyburide[a]	30
Lung et al, 2012[2]	57	Benzodiazepine	Glyburide	47
	48	Diazepam	Glyburide	40
Peng and Li, 2018[8]	45	Alprazolam	Glipizide	27
Gothong and Whitlatch, 2022[9]	61	Cocaine	Glipizide	26

[a] Screening of hypoglycemic agents was not performed, but they were visually identified.

picture of glyburide as the "Valium" she had bought from the illicit drug market.[7]

Sulfonylureas inhibit pancreatic β-cell potassium channels, which causes depolarization and insulin secretion from these cells.[4,11] In an overdose situation, the mechanism of action remains the same but the duration of the secretory effect can be prolonged resulting in extended hypoglycemia.[12]

This patient did report cocaine use hours prior to hospital presentation, which was confirmed by a urine drug screening test. Cocaine is not known to cause hypoglycemia. However, Gothong and Whitlatch[9] described a 61-year-old man with a history of cocaine abuse and documented hyperinsulinemic hypoglycemia due to cocaine-laced sulfonylurea, which was thought to increase the drug volume. Therefore, physicians must maintain awareness of illicit drug use when evaluating patients.

As illustrated in this case, sulfonylurea-induced hypoglycemia is typically treated with intravenous dextrose to rapidly correct glucose levels.[12-14] Octreotide can be initiated to further treat hypoglycemia; as a somatostatin analog, it inhibits insulin release from pancreatic β-cells. Lung et al[2] reported 2 cases of persistent hypoglycemia due to supratherapeutic levels of glyburide, making octreotide a useful drug for treatment. This is concerning because it suggests that ingestion of high doses of sulfonylureas carries the potential for more severe and prolonged adverse effects. Glyburide levels were not obtained for the patient, but fortunately, hypoglycemia was not persistent.

To our knowledge, there are a few reported cases of sulfonylurea poisoning by ingestion of "street Valium." This lack of reported cases may be a result of the particular patient population involved; the cost, timing, and availability of hypoglycemic agent screening; and limited recognition of possible poisoning by clinicians.

Conclusion

Sulfonylurea-induced hypoglycemia leads to clinical sedation, mimicking the effects of benzodiazepines and opioids. Sulfonylureas can be sold by the illicit drug market, purposely mislabelled as benzodiazepines, or mixed with opioids, increasing the potential for misuse of these medications. Alcohol consumption can potentiate hypoglycemia and encephalopathy. When all these substances are taken in combination, severe hypoglycemia can result. Physicians should be aware of this possibility when evaluating unresponsive patients suspected of illicit drug use; if hypoglycemia is confirmed, one should consider intentional or unintentional sulfonylurea ingestion, alone or potentiated by other drugs. Depending on the sulfonylurea dose ingested, repeated and prolonged intravenous dextrose administration may be needed to reverse potentially life-threatening neuroglycopenia.

Disclosure

The authors have no conflicts of interest to disclose.

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