

EM CASE OF THE WEEK

BROWARD HEALTH MEDICAL CENTER DEPARTMENT OF EMERGENCY MEDICINE

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Sulfonylurea Poisoning

A 68-year-old female presents to the Emergency Department via EMS from an assisted living facility with altered mental status and a blood glucose level of 22 mg/dL. 1 amp of D50 was given upon arrival and she became arousable with a Glasgow coma scale score of 14. History reveals she is on glipizide for type-2 DM. She has continued to take her medication although she states she has not been eating the last three days due to abdominal pain and nausea. Vital signs are stable. Thirty minutes later she becomes altered and unarousable again. A fingerstick blood glucose level is obtained and is 43 mg/dL. In addition to repeating 1 amp of D50, the most appropriate next step in management involves scheduled glucose monitoring and:

- Glucagon (IM).
- Octreotide.
- Activated charcoal.
- Dextrose drip alone.



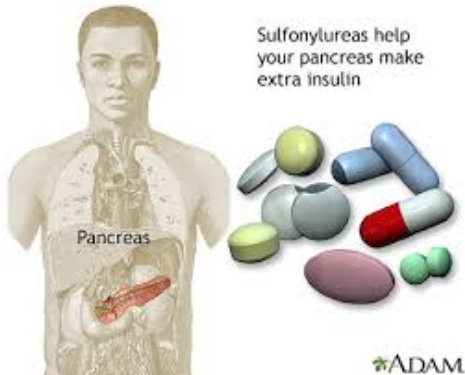
Sulfonylurea poisoning may produce sustained hypoglycemia refractory to IV dextrose. This month we will look at the role of octreotide in the management of intentional and unintentional sulfonylurea overdose.

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EM Case of the Week is a weekly “pop quiz” for ED staff. The goal is to educate all ED personnel by sharing common pearls and pitfalls involving the care of ED patients. We intend on providing better patient care through better education for our nurses and staff.



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Take Home Points

- Risk Factors for hypoglycemia from therapeutic sulfonylurea use:
 - > 65 years old
 - Multiple medications
 - Frequent hospitalizations
 - Use of agents with longer durations of action (Chlorpropamide and Glyburide)
 - Renal or hepatic dysfunction
 - Renal insufficiency
- Octreotide, a somatostatin analog, is useful in treating sulfonylurea poisoning.
- The duration of action for sulfonylureas ranges from 12-24 hours.
- Octreotide's half-life is 88-100 min.

Hypoglycemia: Sulfonylurea Poisoning

The correct answer is B.

The patient presents with hypoglycemia secondary to sulfonylurea use. The effects of sulfonylureas can last between 12-24 hours and can cause repeat episodes of hypoglycemia.

Octreotide, a somatostatin analog that inhibits insulin release from pancreatic beta-islet cells, is used in conjunction with dextrose at a dose between 50-150 mcg every 6 hours for the first 24 hours. If the patient develops repeat episodes of hypoglycemia during this time, the Octreotide should be continued for another 24 hours.

Glucagon (IM) raises serum glucose levels slightly and may be used as a temporizing measure while IV access is obtained, but it is not a substitute for dextrose.

Activated charcoal should be used within two hours after a sulfonylurea poisoning.

A dextrose drip alone is not recommended because elevation of the blood sugar will cause increased insulin release, which would worsen the patient's symptoms.

Discussion:

Sulfonylureas are commonly used to treat diabetes mellitus type 2. They were discovered during World War II and were first used to treat typhoid fever. First-generation sulfonylureas include chlorpropamide and tolbutamide, but these are rarely used now due to their increased side effects when compared to second-generation sulfonylureas. Second-generation sulfonylureas were introduced in the 1970's and they include glyburide, glipizide, glimepiride, and gliclazide. The second-generation sulfonylureas have a shorter half-life than the first-generation ones. Sulfonylurea medications decrease blood glucose by increasing the release of endogenous insulin from the pancreatic beta islet cells.

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and click on the "Conference" link. All are welcome to attend!

Sulfonylureas are rapidly absorbed with peak plasma concentrations within 2-4 hours after therapeutic doses. The liver extensively metabolizes them, and to a lesser extent weakly active metabolites are excreted renally. The duration of action is 12-24 hours, and can be significantly increased in an overdose. Hypoglycemia may last up to 72 hours. Sulfonylurea poisoning may be intentional or unintentional. Unintentional overdose, like the patient discussed, can be caused by continuing to take the sulfonylurea while not consuming calories. Other risk factors include patients who are over 65 years old, take multiple medications, and have hepatic insufficiency, renal insufficiency, or frequent hospitalizations.

Differential:

Excess use of insulin, liver failure, renal failure, acute alcohol intoxication, sepsis, hypopituitarism, adrenal insufficiency, myxedema, insulinoma, postprandial hypoglycemia, drugs (Quinine, Bactrim), extrapancreatic tumors.

Signs and Symptoms:

Patients will present with hypoglycemic symptoms including neuroglycopenia symptoms such as confusion, difficulty speaking, dizziness, hemiparesis, seizures, or coma. They may also present with autonomic symptoms including anxiety, nausea, sweating, and palpitations. It is important to obtain a history from the patient if possible as to the timing of ingestion, reason for ingestion, and whether or not there were any coingestions (i.e. acetaminophen or salicylates).

Diagnosis:

The diagnosis of sulfonylurea poisoning is made clinically based on the history of unintentional or intentional overdose and presentation of the patient.

Management:

Symptomatic Intentional Overdose:

In a patient with AMS who is unable to take anything by mouth, the initial treatment is generally 25g (50ml) of 50 percent dextrose (D50W) solution to raise the blood glucose level, followed by octreotide, a dextrose drip, and periodic serum glucose monitoring.

Octreotide is a synthetic long-acting octapeptide analog of somatostatin. It inhibits the release of insulin from pancreatic beta-islet cells. The dose of octreotide is 50 to 150 mcg administered IM, every 6 hours, due to its short-half life (88-100 minutes). It may be given as an IV bolus or by continuous IV infusion, but in almost all cases intermittent IM dosing is sufficient to maintain euglycemia. Octreotide should be given for 24 hours with the IV dextrose infusion gradually tapered off. The patient's glucose level should be monitored for an additional 24 hours after cessation.

Unintentional Single-Episode Hypoglycemia:

A patient who presents with a single episode of hypoglycemia from therapeutic sulfonylurea use should have their symptomatic hypoglycemia corrected with an amp of D50 or a calorie rich meal if able to eat and have their glucose monitored. The sulfonylurea should be stopped and they should be observed for 24 hours. If a second episode of hypoglycemia occurs, then octreotide should be administered and treated as stated earlier.

Drugs that potentiate the action of sulfonylureas

Inhibition of membrane transporters
Clarithromycin, fluoroquinolones (eg, levofloxacin), verapamil
Decreased hepatic CYP2C metabolism
Antiinfectives: Clarithromycin, fluconazole, metronidazole, isoniazid, miconazole (oral), trimethoprim-sulfamethoxazole (and other sulfonamide antibiotics), voriconazole
Other: Amiodarone, capecitabine, cimetidine, fluorouracil, fluvastatin, gemfibrozil (and other fibric acid derivatives), losartan, MAO inhibitors [¶] , mifepristone, nicardipine, omeprazole, ticagrelor, warfarin
Intrinsic hypoglycemic activity
Alcohol, androgens (anabolic steroids), beta-blockers (variable effects), fluoroquinolones, MAO inhibitors [¶] , pentamidine, quinine, salicylates*, other antihyperglycemic drugs
Decreased renal excretion
Allopurinol, probenecid, salicylates*
Masks autonomic signs of hypoglycemia
Beta-blockers

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ABOUT THE AUTHOR:
This month's case was written by Christopher Scholten. Christopher is a 4th year medical student from NSU-COM. He did his emergency medicine rotation at BHMC in December 2015. Christopher plans on pursuing a career in Emergency Medicine after graduation.