

Management of Pediatric Sulfonylurea Ingestions

Case: 3 year-old female with no PMHx is rushed in by her parents for acting abnormal and having difficulty breathing. Upon arrival to the ED, the patient is noted to be seizing. The patient is connected to the monitors, IV access is obtained, and a point-of-care (POC) glucose is performed. It results at 14 mg/dl. A bolus of D25 is pushed IV, along with IV Ativan and the child subsequently stops seizing. Shortly thereafter, the patient wakes up and begins acting like her normal self. The glucose is re-checked 5 minutes later and results at 87 mg/dl. At the 30 minute glucose re-check, the child is acting more lethargic and the POC glucose again results very low at 24 mg/dl. Another IV bolus of D25 is pushed with normalization of patient's glucose and behavior. Over the next hour, this happens 2 more times. Upon further questioning of the family, we learned that the patient was at home being watched by her **grandmother**, who also lives in the home. The grandmother was contacted by telephone and it was learned that she takes several medications and that they were all in reach of the 3 year-old – including **glimepiride**, a long-acting sulfonylurea. The patient was then placed on a D5 with 1/2NS continuous infusion and an octreotide drip with frequent POC glucose checks. The patient was admitted and after an observation period of 24 hours, the patient's glucoses had stabilized within normal limits, the drips were stopped, and after 48 hours the patient was discharged home.

Background: Sulfonylureas are commonly prescribed medications to treat type 2 diabetes mellitus. Their mechanism of action is to **inhibit an ATP-dependent K⁺ channel that results in increased insulin secretion from pancreatic beta-islet cells**. Sulfonylureas **also potentiate the action of the released insulin and inhibit gluconeogenesis in the liver by decreasing hepatic insulin clearance**. As a drug class, they are very effective medications for diabetes; however, it has been well documented that pediatric ingestions of **even a single sulfonylurea tablet can lead to profound hypoglycemia** and significant morbidity and mortality if unrecognized and untreated (Koren article). Further complicating these ingestions is that these medications are long-acting, with elimination half-lives exceeding 10 hours and duration of actions of up to 24 hours. The American Association of Poison Control Centers' most recent annual report for all cases called to poison centers across the United States in 2013 showed that 3,950 sulfonylurea ingestions were reported that year, with 828 cases occurring in children under the age of 12. Several studies have shown that **hypoglycemia from single tablet ingestions will occur in 30-58% of patients**.

Management: Given the potential consequences of hypoglycemia, it is generally recommended that all known and suspected sulfonylurea ingestions are **observed for a minimum of 8-16 hours** with hourly glucose checks. For asymptomatic patients, **oral glucose sources** should be made readily available to the child during this time. However, the patient should note be prophylactically given concentrated glucose or dextrose solution unless symptomatic. If the patient becomes hypoglycemic, a **bolus of concentrated dextrose** should be given. For children over 2 years of age, a 1-2 mL/kg bolus of D50 or D25 should be given and for children under 2 years old, a 5 mL/kg bolus of D10 is preferred. Depending on the degree of hypoglycemia, **continuous fluids containing dextrose** can be started and titrated as needed. However, some cases will be refractory to IV dextrose therapy, given the low concentration that can be safely

infused via a peripheral IV. In these cases of recurrent or refractory hypoglycemia, **octreotide** given IV, subcutaneous (SC), or in a continuous infusion should be started early. Octreotide will inhibit the release of insulin, as it is an analogue to endogenous somatostatin. Recommended SC or IV dosing is 1-2 micrograms/kg up to a max of 50-100 micrograms every 6-12 hours. Several retrospective studies and a prospective RCT have demonstrated the benefit of octreotide in patients with refractory hypoglycemia after sulfonylurea ingestion. Patients given octreotide had a significant decrease in hypoglycemic episodes after the octreotide was initiated.

Less frequently used and with limited availability in the US is IV diazoxide. It also works to inhibit insulin release from pancreatic beta-islet cells. However, diazoxide is also a potent vasodilator and therefore has a worse side effect profile, including hypotension and tachycardia. Rarely, IM glucagon is used for patients without IV access and unable to take oral glucose; however, this is generally avoided as it does not inhibit insulin release and therefore could actually increase insulin secretion and potentiate the hypoglycemia. Glucagon requires adequate glycogen stores in order to work, so in patients with malnutrition, liver disease, or with prolonged fasting, it will not work in restoring normal glucose levels.

References/Further Reading:

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