POISON PEARLS

Toxicology Topics for the Healthcare Team of a Poisoned Patient

Sulfonylurea Toxicity

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Background

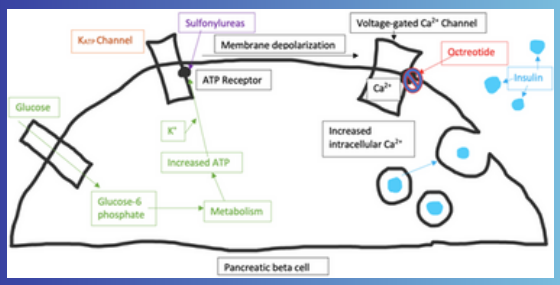
Sulfonylureas are insulin secretagogues used in the management of Type 2 diabetes mellitus. The first generation (acetohexamide, chlorpropamide, tolazamide, and tolbutamide) are no longer widely used and have largely been replaced by the second generation sulfonylureas (glimepiride, glipizide, and glyburide). Second generation sulfonylureas are more potent and can be administered in lower doses once daily **(Costello et al, 2023)**. Some sulfonylureas are formulated with metformin or the thiazolidinediones.

Mechanism of Toxicity

Sulfonylureas bind to the pancreatic beta cell and cause a closure of the K+ channels. Inhibition of potassium efflux mimics the effect of naturally elevated intracellular ATP and causes membrane depolarization. The subsequent rise in intracellular potential opens the voltage gated calcium channels, which increases the intracellular calcium concentration. The increase in calcium results in the release of insulin and subsequently hypoglycemia **(Bosse GM, 2019)**.

Clinical Presentation

All sulfonylureas in overdose cause hypoglycemia and associated neuroglycopenia. The risk for hypoglycemia is greater in drug naïve patients, especially young children. The onset of hypoglycemia varies depending on multiple factors (e.g. timing of the last meal or available glycogen stores) and can be significantly delayed **(Bosse GM, 2019)**.



Key Points:

- Sulfonylurea overdose causes hypoglycemia
- This class remains on the list of “one pill can kill”
- The treatment consists of achieving euglycemia with dextrose and then halting further release of insulin from the pancreatic beta cells with the use of octreotide
- Avoid the use of prophylatic dextrose supplementation in asymptomatic patients

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Treatment

Decontamination with activated charcoal can be considered for appropriate patients.
The primary treatments for sulfonylurea toxicity are dextrose and octreotide. Dextrose can correct hypoglycemia. Octreotide is a somatostatin analog used to treat severe diarrhea, manage symptoms associated with certain intestinal tumors, reduce growth hormone levels in acromegaly, control gastroesophageal variceal hemorrhages, and manage sulfonylurea overdoses. It has no effect on the existing blood glucose, but halts the release of insulin by closing the calcium channel on the pancreatic beta cell which minimizes the risk for recurrent hypoglycemia. Managing hypoglycemic sulfonylurea overdose patients with dextrose alone can prolong toxicity because dextrose will serve as a cell signal to release more insulin, causing a cycle of recurrent hypoglycemia. Octreotide use in a given patient will be dependent on their clinical status and blood glucose values. The patient should be monitored for recurrent hypoglycemia for 8-16 hours depending on their last dose of dextrose or octreotide **(Dougherty & Klein-Schwartz, 2010)**. Hemodialysis has no role in managing sulfonylurea overdoses given the high protein binding of these drugs.

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