



Pediatric Toxic Hypoglycemia

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**Clinical Pharmacology and Medical Toxicology
Fellowship**

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Conflicts of Interests . . . None



THE
UNBRANDED
DOCTOR

Learning Needs . . .

- **By the end of this session, you should be able to**
 - Explain the risks factors for pediatric toxic ingestion
 - List various xenobiotics causing hypoglycemia
 - Demonstrate various management strategies in the management of toxic hypoglycemia
 - Determine the safety of octreotide in sulfonylurea induced hypoglycemia

Case Study . . .



Grand-Mother's Pill

- **24-months-old girl with likely ingestion of her grandmother's "pills"**
 - No other significant active complaints
 - Pill count was unreliable
 - The child was developmentally normal
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Grand-Mother's Pill

- **ED arrival ~ 90 minutes after ingestion**
 - HR 120 beats/min – RR 20 breaths/min
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 - Physical examination: unremarkable
- **Patient was admitted for continued observation**

Pediatric Poisoning (2014 NPDS-AAPCC)

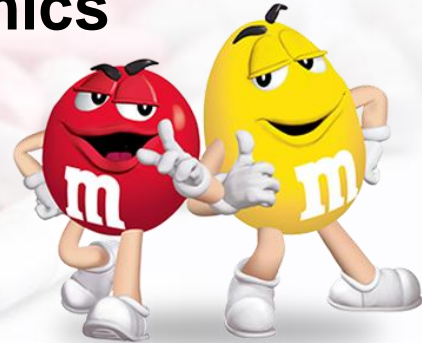


- **More than 1.2 million exposure to children younger than 20 years reported to poison control centers (AAPC 2014)**
- **More than 1 million involved children younger than 5 years**

Pediatric Poisoning (2014 NPDS-AAPCC)

- **Curious and are attracted to potentially toxic substances**
- **2% of all fatalities reported to the poison control centers are due to oral hypoglycemics**

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Pediatric Poisoning

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- Ingestion is usually unintentional
- Usually one xenobiotic is involved
- Usually nontoxic xenobiotic
- Present for evaluation early



Pediatric Poisoning

- **Ingestion occur at**
 - Own home (80%)
 - Relatives' home (grandparents)
- **Medications belongs to**
 - Child
 - Parents
 - Grandparents
- **Failure to safely store medications**

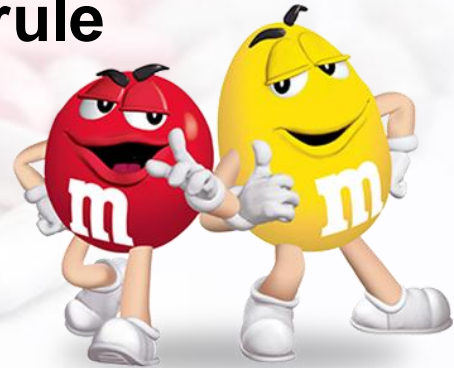
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“One Pill” rule

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- **Single adult therapeutic dose would not be expected to produce significant toxicity in a child**
- **Exception to the rule**



Common Drugs With Hypoglycemic Effects

- 
- **Insulin and its analogues**
 - **Sulfonylurea derivatives**
 - **Beta blockers**
 - **Salicylates**
 - **Tetracycline**
 - **Trimethoprim/ Sulfamethoxazole**
 - **Pentamidine**
 - **Ethanol**

Toxic Hypoglycemia – Insulin

- Regulates carbohydrate and fat metabolism

- Re

**None! Only Effective via Parenteral
route**

- Effect if ingested?

Toxic Hypoglycemia – Beta Blockers

- **Beta-2 receptors**
 - Glycogenolysis in liver and skeletal muscles
- **Beta Blockers**
 - Inhibit hepatic gluconeogenesis → Hypoglycemia
 - Enhance the release of counter-regulatory hormones → Hyperglycemia
- **Suppress neuroglycopenic response to hypoglycemia**

Toxic Hypoglycemia – ACE-Inhibitors

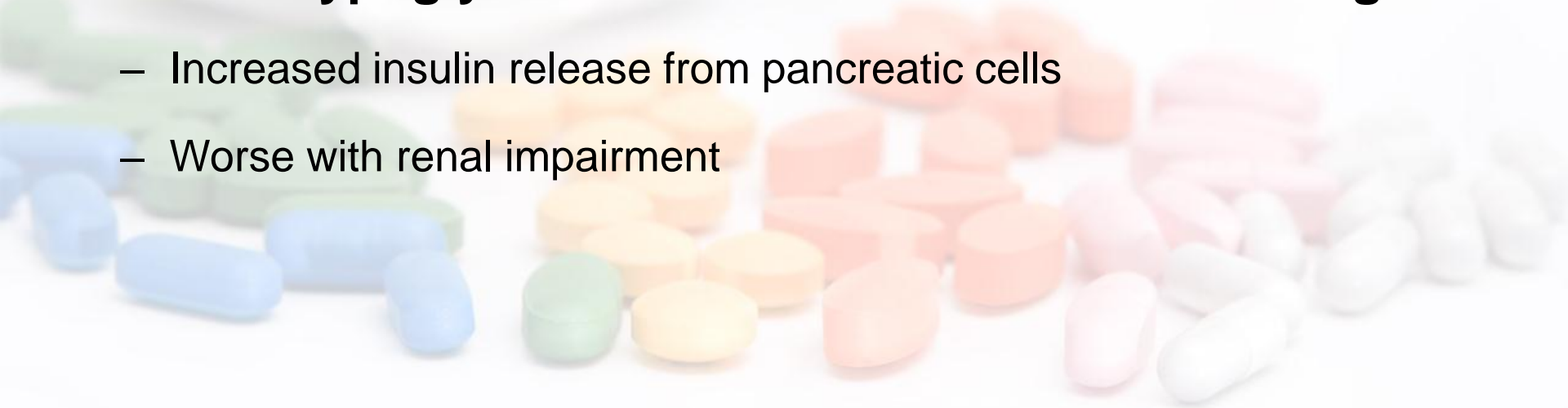
- **Potentiates hypoglycemic effects of other drugs**
- **Increases peripheral insulin sensitivity**



Toxic Hypoglycemia – Antibiotics

Trimethoprim/ Sulfamethoxazole

- **Severe hypoglycemia when combined with other agents**
 - Increased insulin release from pancreatic cells
 - Worse with renal impairment



Toxic Hypoglycemia – Antibiotics

Ciprofloxacin

- **Unknown exact mechanism**
- **Severe hypoglycemia when combined with other agents**
 - Increased insulin release from pancreatic cells
 - Worse with renal impairment

Toxic Hypoglycemia – Antibiotics

Tetracycline

- **Unknown exact mechanism**
- **Severe hypoglycemia when combined with other agents**
 - Increased peripheral insulin sensitivity
 - Decreased renal clearance

Toxic Hypoglycemia – Quinine and Quinidine

- **Unknown exact mechanism**
- **Severe hypoglycemia when combined with other agents**
 - Increased peripheral insulin sensitivity
 - Decreased renal clearance (Renal Impairment)
- **Antiarrhythmic Effect**

Toxic Hypoglycemia – Pentamidine

- **Pneumocystis Carinii prophylaxis**
- **Severe hypoglycemia when combined with other agents**
 - Increased pancreatic insulin release
 - Worse in HIV – Immunocompromised patients



Toxic Hypoglycemia – Ethanol

- **More with chronic use (6 – 36 hours post ingestion)**
 - Decreased glycogen stores
 - Suppression of counter-regulatory hormones



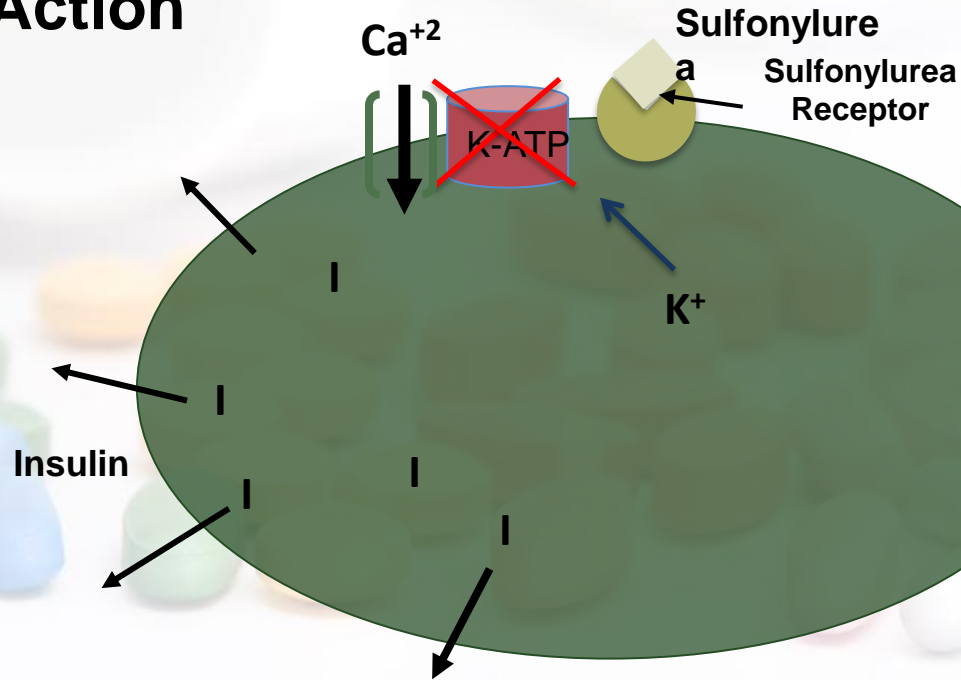
Toxic Hypoglycemia – Sulfonylurea

Mechanism Of Action



Toxic Hypoglycemia – Sulfonylurea

Mechanism Of Action



Toxic Hypoglycemia – Sulfonylurea

- **2014 National Poison Data System report of the American Association of Poison Control Centers (Sulfonylurea)**
 - 778 exposures to sulfonylurea in children less than 6 years of age
 - 84 of which were treated with octreotide



Toxic Hypoglycemia – Sulfonylurea

- **Management**
 - **Glucose?!**
 - Enteral glucose “Free access to food”
 - Parenteral dextrose
 - 0.2 – 0.5 g/kg
 - Lowest dose to reverse hypoglycemia symptoms

Toxic Hypoglycemia – Sulfonylurea

- **Glucose**

- **Problems?!**

- Volume overload with renal insufficiency or heart failure
 - Phlebitis → complications from central venous access insertion
 - Rebound hypoglycemia
 - Acute glucose load → hyperinsulinemia → rebound hypoglycemia
→ glucose administration → hypoglycemia

Toxic Hypoglycemia – Sulfonylurea

- **Octreotide**
 - **Binds to somatostatin receptors → inhibit insulin release**
 - **Used for the treatment of sulfonylurea induced hypoglycemia**
 - Reduces incidence of recurrent hypoglycemic episodes
 - Maintains higher blood glucose levels

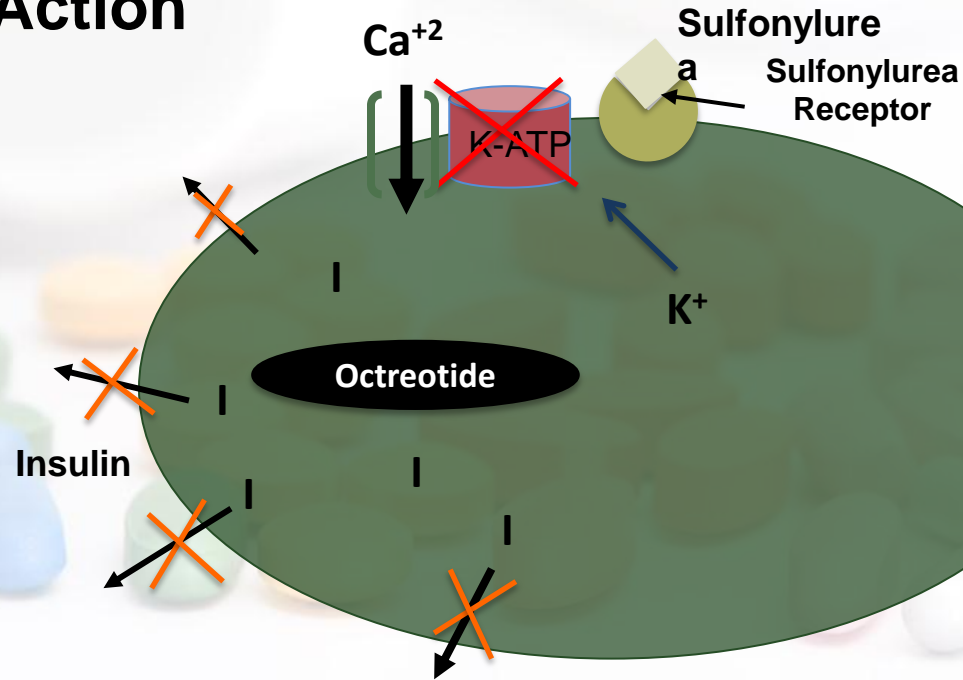
Toxic Hypoglycemia – Octreotide

Mechanism Of Action



Toxic Hypoglycemia – Octreotide

Mechanism Of Action



Octreotide

TOXICOLOGY/ORIGINAL RESEARCH

Comparison of Octreotide and Standard Therapy Versus Standard Therapy Alone for the Treatment of Sulfonylurea-Induced Hypoglycemia

Charles J. Fasano, DO

Gerald O'Malley, DO

Paul Dominici, MD

Elizabeth Aguilera, MD

Daniel R. Latta, BS

From the Department of Emergency Medicine, Albert Einstein Medical Center, Philadelphia, PA.

Comparison of octreotide and standard therapy versus standard therapy alone for the treatment of sulfonylurea-induced hypoglycemia

- **Prospective double blind placebo-controlled trial**
- **Octreotide 75 mcg SC plus standard therapy VS. standard therapy alone**
- **Outcome:**
 - Blood glucose concentration
 - Frequency of post treatment hypoglycemic episodes

Comparison of octreotide and standard therapy versus standard therapy alone for the treatment of sulfonylurea-induced hypoglycemia

• Results

- **Blood glucose levels were lower in the octreotide group in the initial 4 – 8 hours after treatment**
- **10 out of 22 patients – octreotide group**
 - Single hypoglycemic episode
- **6 out of 18 patients – standard therapy group**
 - Multiple hypoglycemic events (2 to 4)

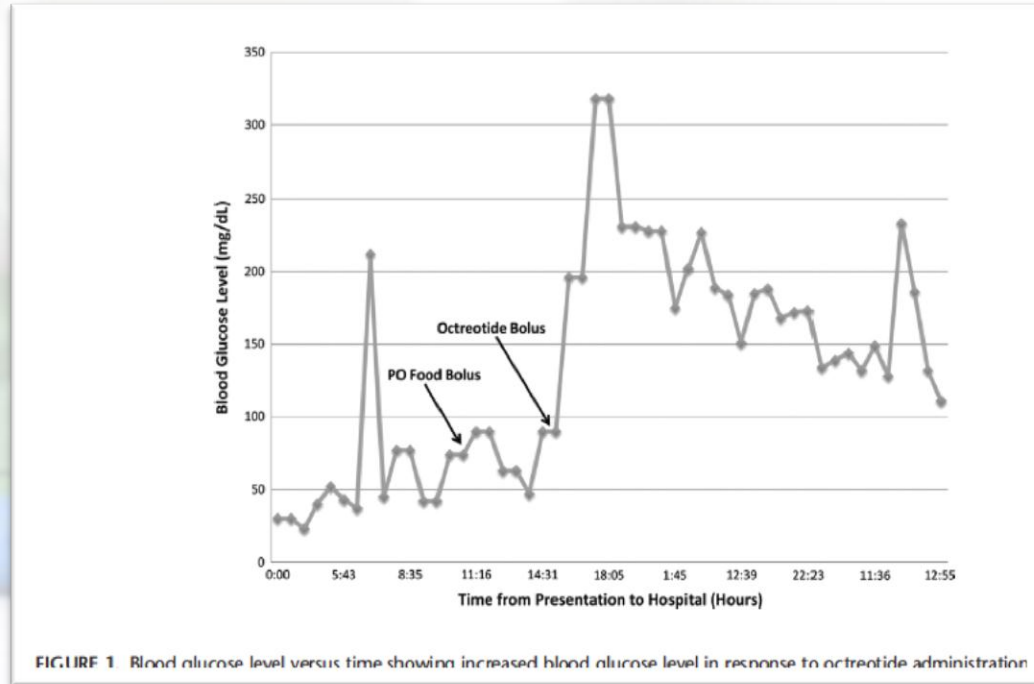
Octreotide: A novel therapy for refractory sulfonylurea induced hypoglycemia

- **Case report of successful treatment with octreotide for refractory hypoglycemia due to intentional sulfonylurea ingestion**
 - **51 years old F presented to the ED with psychosis and blood glucose level of 23 mg/dl**
 - **Treatment received**
 - Parenteral dextrose boluses
 - Oral glucose
 - Dextrose infusion

Octreotide: A novel therapy for refractory sulfonylurea induced hypoglycemia

- **Case report of successful treatment with octreotide for refractory hypoglycemia due to intentional sulfonylurea ingestion**
 - Multiple hypoglycemic episodes
 - Octreotide 50 mcg every 4 hrs. for 48 hrs
 - Blood glucose level remained above 100 mg/dl

Octreotide: A novel therapy for refractory sulfonylurea induced hypoglycemia



Barkin JA, et al. Octreotide: a novel therapy for refractory sulfonylurea-induced hypoglycemia. *Pancreas*. 2013;42(4):722-3

What is the dose of octreotide for sulfonylurea induced hypoglycemia?

- **No consensus about the dose for sulfonylurea induced hypoglycemia**
- **Commonly used dosages**
 - **Bolus**
 - 0.51 – 2.5 mcg/kg IV or SC every 6 hrs.
 - 40 – 100 mcg SC every 6 – 12 hrs.
 - **Infusion**
 - 1-2 mcg/kg/hr.
 - 125 mcg/hr IV for 9 hrs.

Is octreotide safe?

- **Adverse effects of octreotide**

- Nausea
- Abdominal pain
- Vomiting
- Bradycardia
- Hypotension
- Metabolic acidosis



Is octreotide safe?

- **Adverse effects of octreotide**
 - Seen with doses used for hyperinsulinemia
 - 5-25 mcg/kg/dose
 - Relatively safe when used for sulfonylurea induced hypoglycemia

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Back To . . . Grand-Mother's Pill

- **6-hours post ingestion**

- The child became lethargic
- Blood glucose 55 mg/dl (3 mmol/L)
- Dextrose boluses followed by infusion
- Blood glucose continued to fluctuate
- Octreotide 1.5 mcg/kg SC
- Dextrose infusion was weaned off and discontinued 11 hours after octreotide dose

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Questions !!!



Thank You !!!

