One Pill CAN Kill
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Objectives

- Name common substances that in small doses are lethal to children
- Understand the pathophysiology of these substances
- Discuss the clinical presentations of each
- Describe the management of overdoses of these substances

Pediatric Issues
Which is Candy?
Sweet tarts or Ecstasy

- These drugs are responsible for over 40% of fatalities from pediatric poisonings.
- Over 1 million exposures to toxic substances per year for kids <3 years old.
- Hand-mouth behavior about 10 times per hour
- Iron is #1 medicinal killer in children
  - Multiple pills are needed to cause toxicity
Case

- 2 year old male brought in to the ED for altered mental status. Mother states she thinks he got into some of her pills.
- PE
  - Lethargic
  - VS bp 60/38, P 170 RR 34 O2 sat 95%

Case

- Neuro exam
  - Pupils 7mm sluggish
  - Poor gag reflex
  - Withdrawal from painful stimulus
- EKG
  - Wide QRS

Chemical structures of Aminazine, Imipramine, Chlorpromazine, and Trimipramine.
Tricyclic Antidepressants

- Leading cause of poisoning fatalities in the USA until 1993.
- Amitriptyline
- Desipramine
- Imipramine
- Nortriptyline
- Doxepin

TCA Pharmacology

- Biogenic Amine Reuptake Inhibition
- Causes its therapeutic effects
- Blocks reuptake of serotonin, dopamine, and norepinephrine
- Alpha adrenergic effects
- Hypotension
- GABA-Chloride channel Blockade
- Seizures

TCA Pharmacology

- Myocardial Sodium Channel Blockade
- Wide QRS
  - Decreased inotropy, dysrhythmias
- Anticholinergic
  - Increases HR, pupil dilatation, urinary retention
TCA Treatment

- Activated charcoal
- Benzodiazepines for seizures
- Sodium Bicarb
  - If QRS >100ms
  - Serum alkalization reduces binding of drug to Sodium Channel
  - Sodium competes with TCA for Sodium Channel
  - 1-2 mEq/kg bolus, then place on a drip if needed

TCA Treatment

- IV fluids for hypotension
- Dialysis not effective as TCAs are highly protein bound
- IV fluids for hypotension
Lomotil

- Antidiarrheal agent containing both diphenoxylate and atropine.
- Both are absorbed well by the GI tract
- Absorption delayed in overdose due to inhibitory effects on smooth muscle motility
- Diphenoxylate is an opioid that is metabolized to difenoxin
  - 5 times more potent than the parent compound
  - Half life 12-14 hours

- Patients manifest signs and symptoms of opioid toxicity
- Respond well to naloxone and supportive care
- Admit for minimum 24 hours

Antimalarials

- These include chloroquine, hydroxychloroquine, quinine and their relatives.
- They work by both sodium channel blockade as well as blockade of the potassium channel.
- These lead to QRS widening as well as QT prolongation.
- Torsades is a known complication of overdose.
Antimalarials

Cinchonism

- Tachycardia, cardiac arrhythmias, nausea, vomiting, hearing loss, tinnitus, headache, vertigo, dystonia, and diarrhea.
- Patients have a flushed appearance.

Antimalarials

Treatment

- These patients require aggressive management of electrolytes.
- Sodium bicarb
  - For wide QRS
- Magnesium should be used for Torsades.
- If ventricular arrhythmias occur despite optimal management, lidocaine is the treatment of choice.
- Avoid Class 1a and 1c because they can make it worse.
Camphor

- Found in large evergreen and other trees in Asia
- Dried rosemary leaves
- Synthetically produced from oil of turpentine
- Used for its scent in cooking, as an embalming fluid, for medicinal purposes, and in religious ceremonies

Camphor - Epidemiology

- 10,000 annual ingestion exposures to camphor containing products
- Over-the-counter products cannot have >11% camphor since 1983
- Imported ethnic remedies may contain more

Camphor

- Skin exposure
  - Wash skin
  - No clinical significance if asymptomatic
- Toxic ingestion
  - 30mg/kg
Camphor Toxicity

- Mechanism unknown
- Patients become symptomatic within 20 minutes
- Throat burning
- Nausea and vomiting, abdominal pain
- CNS depression
  - Headache, confusion
  - Dizziness, agitation, anxiety, hallucinations, myoclonus, hyperreflexia
- Seizures
- Death
  - Respiratory Failure, Convulsions

Camphor- Treatment

- Supportive care
- Benzodiazepines for seizures
- Activate Charcoal is not recommended
- Admit symptomatic
- May discharge home if asymptomatic after 4 hours

Salicylates

- 10,000 tons of aspirin are consumed each year
- One teaspoon of methyl salicylate (oil of wintergreen) contains 7,000 mg of salicylate. This is the same as 86 baby aspirins
Salicylates-Pathophysiology

- Local gastric irritation
- Stimulation of the chemoreceptor zone
- Stimulation of the medullary respiratory center
- Stimulation of the skeletal muscle metabolism
- Uncoupling of oxidative phosphorylation
- Enhancement of lipolysis

Salicylates-Pathophysiology

- Inhibition of Krebs cycle
- Increased vascular permeability
- Mobilization of glycogen stores
- Inhibition of gluconeogenesis
- Reversible ototoxicity
- Antiplatelet activity
**Salicylates - Clinical Features**

- Onset of symptoms within a few hours of ingestion
- Children <4 - metabolic acidosis and acidemia
- Older children - mixed disorder
  - Respiratory alkalosis
  - Increased anion gap metabolic acidosis
  - Alkalemia

**Salicylates - Diagnosis**

- Use of Done monogram not recommended
- 150mg/kg or 150mg/dL result on blood test
- Enteric coated relies on gastric emptying time
  - Peak levels may be delayed up to 60 hours
- Serial testing for suspected ingestion

**Salicylates - Treatment**

- No specific antidote
- Gastric lavage
- Activated charcoal
- Whole bowel irrigation
- Supportive care
- Urine alkalinization
Salicylates - Treatment

- Maintain urine output 1-2mL/kg/hour
- Bicarb Drip
  - 2-3mL/kg/hour to maintain urine pH > 7.5
- Watch out for hypoglycemia
- Monitor potassium
  - Acidemia and hypokalemia
  - Distal tubule excretes protons for sodium
- With moderate and severe toxicity - check electrolytes and salicylate levels every 1-2 hours

Salicylates - Hemodialysis

- If patients require ventilatory support
- Lack of improvement or worsening with standard treatments
- Lack of success with urine alkalinization
- Renal insufficiency
- Renal failure
- Severe acid-base disturbance
- Altered mental status
- Pulmonary edema
- Salicylate level >100mg/dL
- Continue until salicylate level <20mg/dL

Salicylates - Disposition

- Observe enteric coated or delayed-release for at least 24 hours
- Discharge if exposure can be determined to be nontoxic
Case

- Grandmother brings in a 2yo male with increased drowsiness for 2 hours.
- He was acting normal 2 hours ago.
- Grandmother states that he was running around earlier when she was washing the dishes.

Case

- PMH: Neg
- PSH: Neg
- All: NKDA
- Soc hx: IMM UTD
- ROS: Drowsy, otherwise negative

Case

- VS
  - BP 60/38, P 65, RR 10, 97% on RA; Temp 36.0 rectally, Glucose 100
  - PE
    - HEENT: Constricted pupils
    - ABD: hypoactive bowel sounds
    - Skin: warm, dry
    - Neuro: Withdrawals from painful stimuli, lethargic
Clonidine

- 9,000 calls per year to poison control center
- 60% of patients presented with symptoms
- 20% had moderate to severe symptoms

Clonidine

- Central alpha-adrenoreceptor agonist that causes inhibition of sympathetic outflow
- Significant functional overlap with the opiate receptor
- Symptoms within 30-60 minutes
- Common symptoms
  - Neurologic depression, hypothermia, bradycardia, miosis, and respiratory depression
- 1-2 pills is sufficient to cause serious toxicity

Clonidine-Treatment

- Supportive care
- Naloxone
  - Reverses neurological, cardiovascular, and respiratory effects in about 50% of patients
  - Mechanism unknown
- Activated charcoal if given early
Case

- 3 year old female brought to the ED after consuming 2 glyburide pills 30 minutes prior to arrival.
- Medical history is unremarkable
- VSS
- FSBS 90mg/dL

Sulfonylureas

- First available in 1954
- Increase intracellular ATP, triggering the release of insulin from secretory granules, and increases insulin receptor sensitivity
- Usually symptomatic within 8 hours

Sulfonylureas-symptoms

- Altered mental status
- Fatigue
- Diaphoresis
- Lightheadedness
- Dizziness
- Agitation
- Confusion
- Tachycardia
- Status epilepticus
- Cardiovascular collapse
Sulfonylureas-Treatment

- Activated charcoal
- Monitor for 24 hours
- Feed
- Dextrose as needed
- Octreotide
  - Suppresses the release of insulin by binding to a somatostatin receptor that blocks a calcium channel
  - The dose is 1-2 mcg/Kg bolus IV or SC.
  - Continuous infusion versus every 8 hour dosing regimen

Case

- 4 year old brought by father for lethargy.
- Father states they are in the process of moving and hasn’t been watching him.
- No previous illness
- VS BP 54/30, P 52, RR 15, Temp 36.8, 96%
- Regular release ingestions are symptomatic within 4-6 hours
- Sustained-release ingestions can be asymptomatic for 14 or more hours

Calcium Channel Blockers

- Affect the slow voltage-gated Calcium channels
  - blood vessels, SA, and AV nodes
- May have reflex tachycardia
- Hyperglycemia associated with hypotension and bradycardia strongly suggests CCB OD
## Calcium Channel Blockers

- Supportive care
- IV fluids
- Activated charcoal
- Whole bowel irrigation
- Atropine
- Calcium
- Vasopressors

- Glucagon
  - stimulates adenylate cyclase activity
  - increases cAMP

- Insulin
  - Positive inotropic effect

## Opioids

- Multiple combinations and forms
- Always consider acetaminophen poisoning

50% of children exposed to >1mg/kg of codeine will develop toxicity within one hour

2.5 mg of hydrocodone is lethal to infants

Symptoms generally occur within 1 hour
Opioids
Pharmacology
- Analogous to 3 families of endogenous opioid peptides
  - enkephalins, endorphins, and dynorphin
- Modulate the release of neurotransmitters in the central and peripheral nervous system
- Wide variation in serum half-life

Opioids
Clinical presentation
- Decreased level of consciousness
- Decreased respiratory rate
- Decreased tidal volume
- Decreased bowel sounds
- Miotic pupils
  - Normal pupils do not exclude ingestion

Opioids
Clinical Features
- The best indicator of opioid poisoning is a respiratory rate <12
- Mild hypotension
  - Histamine release
- Seizures
  - Tramadol, propoxyphene, or meperidine
  - Hypoxia
Opioid Management

- Naloxone 0.1mg/kg up to 2mg every 3-5 minutes as needed to max dose of 10mg
- Onset within 2 minutes
- Duration 20-90 minutes
- If a drip is needed, calculate how much was given in the first hour and use 2/3 of that as the dose of the drip per hour.
- If asymptomatic patients may be discharged after 6 hours

Case

- 3 year old female was found by parents with an empty bottle of acetaminophen. She is asymptomatic.
Acetaminophen

- Conjugated in the liver by glucuronidation and sulfation
- Excreted unchanged in the urine
- 5-15% oxidized by cytochrome P450 to N-acetyl-p-benzoquinoneimine (NAPQI)
  - Binds to cells and induces oxidation of enzymes
  - Results in cell death

Acetaminophen Overdose

- Metabolism through glucuronidation and sulfating is saturated and a larger proportion of acetaminophen is metabolized to NAPQI
  - NAPQI causes hepatic necrosis

Acetaminophen Stage 1

- Anorexia
- Nausea and vomiting
- Malaise
Acetaminophen Stage 2

- Days 2-3
  - Improvement in anorexia, nausea, and vomiting
  - Abdominal pain
  - Hepatic tenderness
  - Elevated Transaminases
  - Elevated bilirubin and PT time if severe

Acetaminophen Stage 3

- Days 3-4
  - Recurrence of anorexia, nausea, and vomiting
  - Encephalopathy
  - Anuria
  - Jaundice
  - Hepatic failure
  - Metabolic acidosis
  - Coagulopathy
  - Renal failure
  - Pancreatitis

Acetaminophen Stage 4

- Clinical improvement and recovery
  - Days 7-8
  - Deterioration to multi-organ failure and death
Acetaminophen Diagnosis

- Rumack-Matthew nomogram
- >150mcg/mL at 4 hours
- >10 grams as single ingestion or over 24 hours
- >6 grams or 150mg/kg per 24 hour period for 2 consecutive days

Acetaminophen Treatment

- Acetylcysteine
- Supportive care
Bar-Oz, Benjamin. Medications that can be fatal for a toddler with one Tablet or Teaspoonful. Pediatric Drugs. 2004:6 (2): 123-126

