ONE PILL CAN KILL: PEDIATRIC POISONINGS

LISA BOOZE, PHARM.D.
ONE PILL CAN KILL: PEDIATRIC POISONINGS

ACTIVITY DESCRIPTION
Each year, more than 1 million poisonings in small children are reported to poison centers in the United States. Most of these exposures result in little or no toxicity; however, there are a number of medications and household products that can produce serious effects and death when as little as one or two tablets or teaspoonfuls are ingested. Pharmacists should be aware of these low dose-high risk drugs and products and help educate parents to prevent serious poisonings with these common agents.

TARGET AUDIENCE
The target audience for this activity is pharmacists, nurses and pharmacy technicians in hospital, community, and retail pharmacy settings.

LEARNING OBJECTIVES
After completing this activity, the pharmacist and nurse will be able to:
- List the most common substances that can cause fatalities in pediatric patients as reported to poison centers
- Identify the medications and household products that can cause serious toxicity or death when ingested by toddler in small quantities
- Describe the clinical effects that are observed in pediatric patients who have ignored low dose-high risk drugs and products
- Identify strategies that pharmacists can take to help prevent pediatric poisonings

After completing this activity, the pharmacy technician will be able to:
- List household products that can cause death or serious toxicity when ingested by small children
- List medications that can cause death or serious toxicity when ingested by small children

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One Pill Can Kill: Pediatric Poisonings

Lisa Booze, PharmD, CSPR

Objectives

- List the most common substances that cause fatalities in pediatric patients as reported to poison centers
- Identify the medications and household products that can cause serious toxicity or death when ingested by toddlers in small quantities
- Describe the clinical effects that are observed in pediatric patients who have ingested low dose-high risk drugs and products
- Identify strategies that pharmacists can take to help prevent pediatric poisonings

Pediatric Poisonings

- >1 million poisonings in children ≤ 5 years old reported to U.S. poison centers each year
- >500,000 involved medicines
- In 2011, > 67,000 children treated in an ED for medicine poisoning
  - 1 child every 8 minutes!
  - ED visits in kids <5 years old Increased 30% since 2002

National Poison Data System
Safe Kids Worldwide, Washington DC, March 2013
Toddlers

- They are curious and explore
- Capable of finding and opening containers
- Imitate older children and adults
- Don’t know “right from wrong”
- Physiological differences
  - Higher mg/kg dose
  - Metabolism and distribution

86% of ER Visits Due to Adult Medicine

![Bar chart showing the percentage of ER visits due to adult medicine by relationship to the patient.](chart.png)

Whose Medicine?

- Grandparent: 38%
- Mother: 31%
- Sibling: 12%
- Father: 8%
- Aunt/Uncle: 5%
- Other: 6%

Safe Kids Worldwide, Washington DC, March 2013

Location, Location, Location

- 67% left within a child’s reach (table, counter, purse...)
  - 27% on the floor, under a sofa cushion...
  - 20% in a purse, bag or wallet
  - 20% on a counter, table or nightstand
- 15% in a pillbox or bag of pills
- 6% put away in a cabinet or drawer

Safe Kids Worldwide, Washington DC, March 2013

Top 10 Medications in Pediatric Poisonings Reported to Poison Centers

- Ibuprofen
- Diaper rash products
- Children’s acetaminophen
- Children’s vitamins without iron or fluoride
- Antihistamines (excluding cough and cold meds)
- Antibiotics
- Calcium supplements
- Diphenhydramine (alone)
- Laxatives
- Homeopathic agents
Pediatric Fatalities (< 5 years old)

- 25 fatalities reported to poison centers in 2011.
  - 48% of deaths reported to poison centers are due to medications (National Poison Data System)
- 64% of deaths were due to medications in 2010 compared to 40% in 2000 (CPSC; NEISS Estimates Query Builder)

Pediatric Drug Fatalities – Most Common Causes (U.S. Poison Centers)

- Opioids
  - Methadone, fentanyl
- Acetaminophen
- Stimulants and street drugs
  - Methamphetamine
- Tricyclic antidepressants
- Bupropion
- Aspirin/Salicylates
- Quetiapine
- Calcium Channel Blockers
- Cough and Cold Meds

*1990’s: Iron

“One Pill Can Kill”

- Opioids (e.g. methadone, oxycodone, fentanyl)
- Clonidine, guanfacine
- Topical imidazolines (like Visine)
- Oral Hypoglycemics (sulfonylureas)
- Calcium channel blockers
- Camphor
- Methyl salicylate (oil of wintergreen)

Opioid Overdose

- A 2 year old drank juice, then took a nap
- Was found cold, limp and barely breathing
- No response to naloxone, intubated
- Urine toxicology + methadone
- Juice contained methadone dose
- Died on day 7
Opioid Analgesics

- Methadone
- Oxycodone
- Fentanyl
- Hydrocodone
- Hydromorphone

Mu, kappa and delta opioid receptors

Opioid Toxicity

- Lethargy, coma
- Respiratory depression
- Constricted pupils
- Hypotension, bradycardia, hypothermia
- QT prolongation (methadone)
- Seizures (tramadol, meperidine)

Opioid Equivalent Doses

- 5 mg/kg codeine has caused respiratory depression

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Equivalent dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>100 mg</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>?</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>15 mg</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>3.75 mg</td>
</tr>
<tr>
<td>Methadone</td>
<td>10 mg</td>
</tr>
<tr>
<td>Morphine</td>
<td>30 mg</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>15 mg</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>3 mg</td>
</tr>
</tbody>
</table>

* 50 mg methadone = 500 mg codeine-equivalent
* 10 kg child: 500 mg/10 kg = 50 mg/kg codeine-equivalent

Treatment

- Supportive care
- Activated charcoal if soon after the ingestion
- **Naloxone**: Reverses CNS and respiratory depression
  - Child dose: 0.1-2.0 mg IV, IM, intranasal
    - IN: < 1 mL/nostril; ½ dose in each nostril
  - Short duration: 1.5 hours
    - Infusion for long-acting opioids
Clonidine

- Selective alpha-2 adrenergic receptor agonist
- Hypertension, ADHD, narcotic & alcohol withdrawal
- Since the late 1990's, most cases involve clonidine belonging to children
- Numerous case reports of 0.1-0.3 mg causing severe toxicity

Clonidine

- Clinical Effects – onset is ½ – 4 hrs
  - Mild hypertension initially and tachycardia followed by hypotension and bradycardia
  - CNS depression
  - Respiratory depression, apnea
  - Constricted pupils
  - Hypothermia
- Naloxone might reverse CNS and respiratory depression

Clonidine Patch

- 12 mo found unarouseable in crib. HR 72, BP 80/40, RR 22, miosis. Found a transdermal clonidine 2.5 mg patch stuck to hard palate.
- 2 yo with lethargy, gasping respirations, HR 75, BP 90/50, miosis. Had a discarded clonidine patch on her.

Guanfacine: A Clonidine-like Drug

- 4 yo taking Tenex for 7 months for ADHD.
- Switched to Intuniv 1mg x 7 days, then 2 mg
- After 2 days, dose was decreased to 1 mg due to excessive sleepiness
- 3 days later: falling asleep, staring. HR 50-66
- Naloxone reversed the CNS depression and bradycardia
- Required naloxone infusion x 24 hours

JAMA 1989;261:42.*

*Pediatr Emer Care 2012;28:1060-1*
**Imidazoline Decongestants**

- Tetrahydrozoline
- Oxymetazoline
- Naphazoline
- Xylometazoline

- Stimulate peripheral alpha 2 receptors
- In overdoses: also stimulate central alpha 2 receptors

**Toxic Effects**

**Mild toxicity**
- Tachycardia
- Hypertension
- Agitation
- Diaphoresis
- Cyanosis
- Ataxia

**Severe Toxicity**
- Lethargy
- Bradycardia
- Hypotension
- Respiratory depression
- Apnea
- Hypothermia

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**Oral Hypoglycemic Overdose**

- 2-year old girl ate one of her father’s Glucotrol XL 10 mg
- Pediatrician: “observe for changes in behavior”
- 4 hours later → lethargy → to emergency department
- Blood glucose concentration: 39 mg/dL
- 2 mL/kg D50W, food & juice
- 1 hour later → lethargy, 47 mg/dL
- Admission of 2 days

*J Emerg Med 2005, 28:305-10*

**Sulfonylureas**

- Chlorpropamide, tolazamide, tolbutamide
- Glipizide, glyburide, glimepiride
- Stimulate insulin secretion from the beta cells of the pancreas & enhance insulin action on target cells
- Prolonged hypoglycemia leads to depletion of glucose and glycogen stores. Amino acids and lipids are utilized instead resulting in irreversible CNS damage.
- Numerous case reports of 1 or 2 tablets causing severe and sometimes prolonged hypoglycemia in children
Hypoglycemia
(Glucose < 60 mg/dL)

Mild Hypoglycemia
- Tremor
- Diaphoresis
- Tachycardia
- Nausea
- Drowsy

Severe Hypoglycemia
- Delirium
- Coma
- Seizures
- Dysrhythmias

Sulfonylureas – Treatment

- Fingersticks every 1-2 hours; observe 12-24 hours
- Activated charcoal if within 1 hour of ingestion
- Free access to food & drink
- Dextrose 1 g/kg bolus if sx or <60 mg/dL
  - Follow with dextrose infusion prn
- Octreotide
  - Somatostatin analog
  - Inhibits insulin release
  - Child dose: 2 mcg/kg SC q6-12 h prn

Calcium Channel Blocker Overdose

- 2 year old (25 lbs) is found lethargic by her grandmother.
- Open bottle of Grandma’s heart medicine (Isoptin SR® 180 mg) and scattered pills on the floor of her room. Pill count reveals 1 or 2 tablets missing.
- RR 20 minute and shallow, lungs clear, P not detectable, BP 30 systolic, grayish skin color
- ECG: third degree block, with intermittent P waves. Narrow QRS

Calcium Channel Blockers

- Verapamil
- Diltiazem
- Nifedipine
- Amlodipine
- Felodipine
- Nimodipine
- Nicardipine
- Isradipine
- Nisoldipine

Mechanism
- Bind to and antagonizes L-type calcium channels
- Results in relaxation of vascular smooth muscle and arterial vasodilation, decreased force of cardiac contraction, and decreased heart rate and conduction
Clinical Effects

- Lethargy, slurred speech, confusion, seizures, coma, vomiting
- Hypotension, bradycardia, AV block, asystole
  - Reflex tachycardia with dihydropyridines (e.g. nifedipine)
- Hyperglycemia
- Ileus, bowel ischemia

Treatment

- Admit for 12-24 hours even if no sx(s)
- Supportive care
- Activated charcoal (recent ingestion)
- Whole bowel irrigation (for SR products)
- IV fluids, vasopressors
- Atropine
- Calcium
- Glucagon
- Hyperinsulinemia euglycemia
- Intravenous fat emulsion
- ECMO (ExtraCorporeal Membrane Oxygenation)

Camphor

- Available in topical products, liniments/rubs, vapor products, mothballs (rare)
- 1982: 20% camphorated oil (camphor oil, camphor liniment) was taken off the market due to toxicity
- FDA set a limit of 11% camphor in consumer products

Camphor

- Nausea and vomiting with 10 mg/kg camphor
- Serious toxicity at > 30 mg/kg (some sources name 500 mg as a toxic dose in children)
- 1 gram has resulted in death in a small child
  - = 10 mL Campho-phenique (10.8%)
  - = 16 mL Vicks Vapo-steams (6.2%)
  - = 20 mL Vicks Vapo-rub (4.8%)
**Camphor**
- Rapid absorption and onset of symptoms (5-60 minutes)
- Vomiting, confusion, agitation, tachycardia, hyperreflexia, cyanosis
- Seizures begin abruptly and may precede other symptoms
- Treatment
  - Supportive care
  - Activated charcoal within 1 hour of ingestion
  - Benzodiazepines

**Methyl Salicylate**
- Used as a flavoring agent, topical liniments, counter-irritant; Chinese patent medicines
- Oil of wintergreen (98%)
- Very rapidly absorbed orally
- 1 tsp oil of wintergreen contains ~7 grams salicylate
  - Equals 22 aspirin tablets!
- 30% methyl salicylate in many products

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**Methyl Salicylate Toxicity**
- 4 mL oil of wintergreen has been lethal
- GI: Nausea, vomiting
- CNS: Lethargy, confusion, tinnitus, hyperventilation, seizures, coma, hyperthermia, cerebral edema
- CV: Tachycardia, hypotension, dysrhythmias
- Acid-base: Respiratory alkalosis, anion gap metabolic acidosis

**Treatment**
- Supportive care
- Activated charcoal
- Labs (ABG’s, Salicylate, BMP)
- IV’s, Sodium bicarbonate (ion trapping)
- Hemodialysis
  - Indications: severe sxs unresponsive to standard therapy; salicylate ≥ 90-100 mg/dL
- Avoid the urge to intubate
Other Low Dose High Risk Pharmaceutical Products

- Bupropion
  - Tachycardia, QTc prolongation, seizures
- Chloroquine, hydroxychloroquine
  - Hypotension, QRS/QTc prolongation, dyspnea, drowsiness, hypokalemia, apnea, seizures
- Diphenoxylate and atropine – Lomotil
  - Coma, respiratory depression, anticholinergic toxicity
- Tricyclic Antidepressants?
  - Deaths with > 15 mg/kg: dysrhythmias, conduction delays, hypotension

Preventing Poisonings

- Raise awareness of “one pill killers” when dispensing Rx’s
- Keep medicines, vitamins and household products out of sight and reach—locked is better than high
- Keep medicines in their original, labeled containers

Other Low Dose High Risk Pharmaceutical Products

- Atypical antipsychotics? (olanzapine, aripiprazole, clozapine)
  - CNS depression, EPS
- Quinidine, procainamide, disopyramide
  - Vomiting, visual disturbances, dysrhythmias, seizures
- Benzocaine, lidocaine (teething gels, EMLA)
  - Confusion, seizures, tachycardia, QRS prolongation, hypotension

Child Resistant Containers

- The Poison Prevention Packaging Act of 1970 (PPPA)
  - Requires child protective packaging
  - Substances: medicines, solvents, and oils
  - Pediatric fatalities dropped from >200/year to 20-35/year

  They’re NOT CHILD-PROOF!
Preventing Poisonings

- Teach children to never touch or put anything in their mouth unless they ask an adult
- Be aware of look-alikes

Preventing Poisonings

- Never take medicine in front of children and never call medicine candy
- Get rid of old or expired medicines
- Read and follow directions on all medicines
ACTIVITY TEST

1. Most children who are treated in an emergency department for an ingestion of a pharmaceutical have taken medicine belonging to whom?
   A. Mother
   B. Father
   C. Grandparent
   D. Aunt

2. The Poison Prevention Packaging Act of 1970 mandated child resistant caps on products harmful to children if ingested. Which of the following is TRUE?
   A. The caps are child-proof
   B. Pediatric fatalities increased after the act was implemented
   C. Many poisonings are due to the caps being improperly secured or products that do not have child resistant caps
   D. Child resistant caps are to be used on prescriptions only if the patient asks for them

3. All of the following can cause serious poisoning in a small child with just one tablet EXCEPT:
   A. Ibuprofen
   B. Clonidine
   C. Methadone
   D. Verapamil

4. All of the following are likely to occur after a 2 year old ingests one methadone 10 mg tablet EXCEPT:
   A. Hypoglycemia
   B. Lethargy
   C. Respiratory depression
   D. Constricted pupils

5. A 4 year old is very lethargic and is “barely breathing” according to his parent. When EMS arrives and examines the boy, they find a clonidine patch adhered to his back. What antidote should be given in an attempt to reverse the toxic effects?
   A. Calcium chloride
   B. Acetylcysteine
   C. Octreotide
   D. Naloxone
6. A 12 month old girl swallowed 1 Glucotrol (glipizide) XL 10 mg tablet 1 hour ago and is sleepy. Which of the following is TRUE?

A. The baby can be watched at home since toxicity is unlikely to occur with this dose.
B. Fingersticks (glucose) should be checked every 1-2 hours for at least 24 hours.
C. The child should not be given anything to eat and drink for 24 hours.
D. If the child becomes hypoglycemic, octreotide should be given instead of dextrose.

7. All of the following drugs might be administered to a toddler who ingested one extended release diltiazem 240 mg and presents to the ED with a heart rate of 40 bpm and a blood pressure of 80/36, EXCEPT:

A. Calcium
B. Atropine
C. Insulin
D. Nifedipine

8. An 18 month old girl is found with an open bottle of oil of wintergreen. Approximately 1 ounce is missing. Which of the following is TRUE?

A. 1 ounce of oil of wintergreen is equivalent to 1 adult-strength (325 mg) aspirin.
B. Oil of wintergreen is another name for salicylic acid.
C. The toxic effects are expected to be similar to that of an aspirin overdose.
D. Alkalinization with sodium bicarbonate is not effective for oil of wintergreen poisoning.

9. A child who swallows 1 tablespoonful of liniment containing 11% camphor is at risk for which of the following life-threatening symptom?

A. Bradycardia
B. Liver failure
C. Seizures
D. Gastrointestinal bleeding

10. All of the following may help to prevent pediatric poisonings and fatalities EXCEPT:

A. Call a poison control center as soon as a poisoning is suspected.
B. Take medicine in front of small children so they’ll know what medicines are in the home.
C. Raise awareness of which medicines are “one pill killers”.
D. Keep medicines in their original containers.

Please submit your final responses on freeCE.com. Thank you.