Over-the-Counter Drug Overdoses

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Program Overview:
Over-the-counter drugs are presumed to be safe, but are they when more than the usual dose is taken? Overdoses of OTC drugs are a common occurrence in children and adults and can result in serious effects. Regulatory actions have been recommended and some have been implemented in response to the increasing number of overdoses. It’s important for pharmacists and pharmacy technicians to be aware of the toxicities associated with OTC drugs and how we can help to prevent overdoses from occurring.

Objectives:
• Describe reasons why overdoses of OTC drugs occur.
• Explain the clinical effects and treatment of overdoses of OTC drugs.
• Identify regulatory actions that have been considered and/or implemented to decrease the incidence of OTC drug overdoses.
• Outline what pharmacists can do to help prevent overdoses of OTC drugs.

Speaker:
Dr. Lisa Booze is the Clinical Coordinator and a Certified Specialist in Poison Information at the Maryland Poison Center, a division of the University Of Maryland School Of Pharmacy. She is responsible for developing and implementing toxicology continuing education programs for health professionals in Maryland. She is a co-coordinator of the Poison Center Surveillance for Chemical and Bioterrorism and Public Health Program, supported by the Maryland Department of Health and Mental Hygiene. Dr. Booze is a member of the American Association of Poison Control Centers, the American Academy of Clinical Toxicology, and the Expert Consensus Panel that develops Out-of-Hospital Management Guidelines for U.S. poison centers.

Speaker Disclosure:
Dr. Booze has no actual or potential conflicts of interest in relation to this program.

OTC Fast Facts
• > 100,000 OTC products
• > 1,000 active ingredients
• 33% of all OTC’s are consumed by adults > 65 years old
• 61% are not concerned about adverse effects
• 8% don’t read anything on the label
• 17% of adults take 3 or more pills of the same OTC medicine at a single time

CHPA, APHA
Reasons for OTC Misuse & Overdoses

- Assumed to be safe in any amount
- Therapeutic errors – dosing, measuring...
- Drug interactions
- Not aware of ingredients
- Drug name confusion
- Accessible to small children – unintentional overdoses
- Accessible to adults – intentional OD's

Medication Mix-Ups: Triaminic®, for example

- Fever Reducer Pain Reliever
- Day Time Cold & Cough
- Night Time Cold & Cough
- Multi-Symptom Cold
- Chest & Nasal Congestion
- Long-Acting Cough Cold & Allergy
- Triaminic-D Multi-Symptom

Medication Mix-Ups: Maalox Total Relief®

- Liquid; Contains bismuth subsalicylate
- FDA, February 2010: Confusion with other Maalox products could leading to overdoses and adverse effects

Acetaminophen Overdoses

- A 2 year old is found with an open & empty 4 ounce bottle of liquid Children’s Pain Reliever.
- A 62 year old man with a history of alcoholism has been taking 8-10 Vicodin + 12-16 Tylenol per day for a few weeks for back pain.
- A 16 year old girl tells her parents that she took 50 ES Tylenol 6 hours ago after breaking up with her boyfriend.
Acetaminophen

- In 2005, U.S. consumers purchased more than 28 billion doses of products containing acetaminophen (FDA)
- Estimated 56,000 emergency room visits, 26,000 hospitalizations, and 458 deaths related to acetaminophen-associated overdoses per year, 1990-1998 (Nourjah, Pharmacoepidemiol Drug Safety 2006;15:6)

Acetaminophen Liver Failure Cases On The Rise

- 662 acute liver failure patients at 22 centers from 1998-2003; 42% due to acetaminophen
  - 1998: 28% due to APAP
  - 2003: 51% due to APAP
- 48% of APAP cases were unintentional OD’s,
  - 63% of unintentional OD’s: APAP/narcotic combinations
  - 38% took > 2 APAP products

FDA Advisory Committee Recommendations - June 2009

- Single dose should be 650 mg maximum
- 500 mg tablets moved to Rx only
- Decrease maximum daily dose from 4000 mg
- Rx combination products should be eliminated or black box warning
- Limit OTC liquids to only 1 concentration
- Do not use “APAP” on labels

Acetaminophen

- Acute toxic dose
  - children >200 mg/kg
  - adults ≥ 7.5 - 10g
- Toxicity with chronic use
  - ≥ 4-10 g/day in adults
  - > 150-200 mg/kg/day in children
- Hepatotoxicity results from the formation of a metabolite that is normally detoxified by glutathione
Clinical Presentation

- Only mild GI sx in first 24 hours
- Delayed signs and symptoms
  - RUQ pain
  - Jaundice
  - Elevated AST & ALT, increased INR
  - Encephalopathy
  - Metabolic acidosis
  - Renal failure
  - Death

Assessment & Treatment

- Plasma levels
  - > 4 hours post acute ingestion
  - Universal testing
- Activated Charcoal (acute OD’s)
- Acetylcysteine
- Liver Transplant

Acetylcysteine

- EARLY
  - glutathione precursor
  - glutathione substitute
- LATE
  - improves microcirculatory blood flow
  - scavenges oxygen free radicals
- Oral or IV administration

Oral N-Acetylcysteine

- 140 mg/kg po load; 70 mg/kg po q4h X 17 doses (72 hours total, 1330 mg/kg)
- Early presenting patients may be treated successfully with a shorter course of oral NAC
- side effects: nausea, vomiting!
  - dilute, chill, give antiemetics
**Intravenous Acetylcysteine (Acetadote®)**

- 300 mg/kg over 21 hours
  - 150 mg/kg IV over 1 hour, 50 mg/kg IV over 4 hrs, 100 mg/kg IV over 16 hrs
- Longer infusion sometimes necessary!
- Many errors in administration!
- Adverse effects: flushing, urticaria, angioedema, bronchospasm

**Question #1**

**Aspirin Case**

- A woman brings her 75 year old mother to the ED with confusion and shortness of breath that has progressed over 3 weeks
- Medical history: HTN, arthritis. Pain from arthritis had been worse for the last 2 months
- Daughter finds 2 empty bottles of aspirin products
Aspirin

- Toxic dose
  - Acute: > 150 mg/kg
  - Chronic: > 100 mg/kg/day
- Delayed absorption

Toxic Effects

- Gastrointestinal:
  - nausea, vomiting, abdominal pain
- Central Nervous System
  - dizziness, lethargy, delirium, tinnitus, hyperventilation, seizures, coma, cerebral edema
- Acid-Base abnormalities
  - Respiratory alkalosis, metabolic acidosis, increased anion gap

Toxic Metabolic Effects

- Fever
- Dehydration
- Hypokalemia
- Non-cardiogenic pulmonary edema
- Cardiac arrhythmias, tachycardia, hypotension
- Hypoglycemia
- Coagulation abnormalities

Treatment

- Activated charcoal
- Ion trapping with sodium bicarbonate
  - increases plasma salicylate & decreases intracellular (brain) salicylate
  - Goal – pH 7.45-7.55
- Hemodialysis
Antihistamines
- Antihistamines are H₁ receptor antagonists.
- Examples: chlorpheniramine, brompheniramine, diphenhydramine, doxylamine, loratadine...
- Older antihistamines bind to peripheral and central H₁ receptors, and cholinergic, α- and β-adrenergic receptor sites.
- 2nd generation are peripherally selective.

Cough & Cold Meds

Antihistamines - Anticholinergic Toxidrome
“Mad as a hatter, hot as a hare, dry as a bone, red as a beet, blind as a bat”
- Confusion, hallucinations, coma
- Hyperthermia
- Dry, flushed, warm skin
- Dilated pupils
- Hypertension, tachycardia
- Urinary retention
ALSO: Sodium channel blockade (conduction delays)

Decongestants: Toxic Effects
- Sympathomimetics
- α - adrenergic receptor agonists
- CNS stimulation
- Headache
- Hypertension (4-5 x recommended dose)
- Tachycardia or reflex bradycardia
- Seizures, MI, stroke, dysrhythmias
Pediatric Cough & Cold Med Controversy

- 64,658 exposures to cough & cold products in children <2 years old reported to poison centers in 2005
  - 28 had a major effect or died
- 7,000 children <11 years old go to ED’s yearly; 2/3 are unintentional ingestions (CDC estimate)
- >120 pediatric deaths from 1969-2006 (FDA)
- No data that they are effective in children

2006: FDA is petitioned to take action
2007: FDA advisory committee recommends not giving OTC cough & cold products to children <6 years old
- Voluntary withdraw of products labeled for children <2 yo
2008: Drug makers not to be used in children <4 years old; FDA agrees

After the Voluntary Withdrawal

- Concerns that excessive doses of other products would be given to small children
- 54% decrease in rate of therapeutic errors with cough & cold meds in children <2 yo
  - No decrease in rates in 2-5 yo’s
- No decrease in rates of unintentional poisonings from cough & cold meds in <2 yo

Klein-Schwartz W. Pharmacoepidemiol Drug Saf 2010;19:819-824

After the Voluntary Withdrawal

- CDC: sampled 63 ED’s for visits for cough & cold med-related adverse effects in children <12
  - 14 months pre-withdrawal, 14 months post-withdrawal
- ED visits post-withdrawal for <2 year olds was < ½ those pre-withdrawal

Shehab N. Pediatrics 2010;126:1100-1107
**Cough Medicine Abuse**
- A 16 year old girl was found sleeping on the lawn outside of her home when her parents came home from work. When awakened, she was confused and hallucinating. She admitted to ingesting 20 "Triple C" tablets after school to get high.
- HR 150, BP 170/100, RR 18, pupils are 5 mm & reactive with horizontal nystagmus.

**Dextromethorphan**
- DXM, dex, C-C-C, Robo, Red Devils, Triple C
- Abused dose = \( > 200-400 \text{ mg} \)
- Produces hallucinations, CNS depression, opioid effects, seizures
- Hypertension, tachycardia, agitation, ataxia often seen

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**Question #2**

**Iron Overdose**
- A 23 year old woman took 30 of her iron supplement tablets containing 325 mg iron (as ferrous sulfate) per tablet.
- In ED 2 hours later with vomiting, abdominal pain and diarrhea; VSS.
Pediatric Vitamin Overdoses

- Pediatric vitamins look and taste like candy
- Iron: leading cause of poisoning deaths in children 1983-1990 (30% of deaths)

FDA & Industry Actions, 1997

- FDA:
  - Label warnings
  - Child-resistant package if >250 mg Fe/package
  - Unit-dose if >30 mg/dosage unit; overruled by court in 2003
- Industry:
  - Withdraw of non-CRC packages
  - Products less appealing to children

Iron Poisoning Deaths, Children < 6

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<th>Year</th>
<th>Number of Deaths</th>
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<td>1987-1997</td>
<td>30</td>
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<td>1997-2002</td>
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Toxic Doses

- Ferrous sulfate (20% Fe), ferrous fumarate (33% Fe), ferrous gluconate (12% Fe)
- > 40 mg/kg elemental Fe of high-dose or liquid iron products
- Children’s products...unlikely to produce toxicity except for GI upset
- Carbonyl Iron – low toxicity
Toxic Effects

- 30 min – 2 hrs: vomiting, diarrhea
- Period of apparent recovery
- 4-12 hrs: hypotension, shock, metabolic acidosis, lethargy
- 2-4 days: liver & kidney failure, coma, acidosis, abnormal coagulation, death
- 2-8 weeks: pyloric scarring & stenosis

Assessment & Treatment

- serum iron levels
- X-ray
- activated charcoal - NOT EFFECTIVE
- whole bowel irrigation
- deferoxamine

Deferoxamine (Desferal®)

- Complexes iron to form ferrioxamine which is renally excreted
- Red urine color change = free iron being complexed

What Can We Do?

- Advise when to self-treat and when not to self-treat
- Choose appropriate products for illness with fewest ingredients possible
- Be careful of confusing product names
- Remind patients to always read & follow instructions on label
- Look for duplicate ingredients
What Can We Do?

- Only give children medications specifically made for their age and weight
- Properly measure liquids
- Do not take for longer than what’s recommended on the label
- Use non-drug alternatives if possible
- Keep out of the reach of children
- Give drug disposal guidelines

Resources

  [www.bemedwise.org](http://www.bemedwise.org)
- Medicines In My Home (FDA):
  [www.fda.gov](http://www.fda.gov)
- Consumer Healthcare Products Association:
  [www.OTCSafety.org](http://www.OTCSafety.org)
- United Health Foundation (AAP):
  [www.unitedhealthfoundation.org](http://www.unitedhealthfoundation.org)