The One Pill That Can Kill!!

Tony Pizon, M.D.
UPMC Presbyterian
Pittsburgh Poison Center
Children's Hospital of Pittsburgh
Division of Medical Toxicology

Topics for Today

Largely Pediatric Discussions of . . .

- Select Antidepressants
- Oral Hypoglycemics
- Opioids
- Beta Blockers
- Ca^{++} Channel Blockers

Case 1

2 yo boy ingests an "antidepressant" 20 minutes ago. Mom is concerned but child is playful.
HR 140, RR 20, BP 122/82, Sat 97% on RA
Neuro: Very active
HEENT: Dilated pupils
Resp: Clear
GI: Soft abdomen
CV: Tachy

Case 1

- What next . . .

Selective Serotonin Reuptake inhibitors (SSRI's)

- Fluoxetine (Prozac)
- Sertraline (Zoloft)
- Paroxetine (Paxil)
- Fluvoxamine (Luvox)
- Citalopram (Celexa)
- Escitalopram (Lexapro)

SSRI's

- In general, benign in overdose
  - Most likely class to produce serotonin syndrome
    - Sertraline is most likely to do so alone

SSRI's

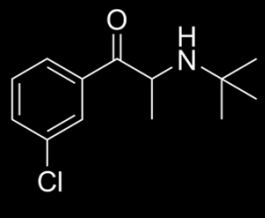
- Citalopram/Escitalopram
  - The only SSRIs with significant toxicity w/ large ingestion
  - **Seizures**
  - QRS prolongation
  - QT prolongation
  - Hypotension
  - Tachycardia

SSRI Treatment

- In general, very benign
- For Citalopram/Escitalopram
  - Accidental ingestion in asymptomatic child can be watched at home
  - Adults with ≥5 pills, observe in ED for 4-6 hours for signs of toxicity
  - Treat supportively = Benzo's for seizures

Bupropion

- AKA (Wellbutrin™ or Zyban ™)
- Reuptake inhibitor of. . .
  - Norepi
  - Serotonin
  - Dopamine



Bupropion

- Tachycardia
- Lethargy/confusion
- Tremor
- Seizures
- Vomiting
- QRS prolongation

BupropionTreatment

- All SR ingestions >10mg/kg should be admitted
  - Delayed symptoms have been reported
  - May be delayed for >10hrs post ingestion
  - Symptoms likely due to hydroxybupropion

BupropionTreatment

- Pediatric weights (approx)
  - 1 yo = 10 kg
  - 2 yo = 12 kg
  - 3 yo = 15 kg
- Bupropion
  - Wellbutrin SR/XL 100, 150, 200, or 300 mg doses
  - Zyban 150 mg doses

Case 1 - Continued

2 yo boy ingests an "antidepressant" 20 minutes ago. Mom is concerned but child is playful.
HR 140, RR 20, BP 122/82, Sat 97% on RA
Neuro: Very active
HEENT: Dilated pupils
Resp: Clear
GI: Soft abdomen
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Case 1 - Continued

During transport. . .
- IV started
- On monitor, HR 160
- He vomits and becomes restless and tremulous. A few minutes later, he has a seizure self-terminating after 20 sec.

BupropionTreatment

- Patient is showing signs of toxicity
  - Tachy
  - Hypertensive
  - Dilated pupils

  =At risk for seizure
- Treatment
  - IV with fluids
  - Oxygen
  - Benzo's for seizure prophylaxis
    - 0.05-0.1 mg/kg of Ativan

Case 2

2 yo boy ingests unknown diabetic med shortly before EMS arrival. He is lethargic and vomited once.
HR 120, RR 20, BP 90/40, Sat 97% on RA
Neuro: Obtunded, limp
HEENT: Normal pupils
Resp: Clear
GI: Soft abdomen
CV: RRR

Case 2

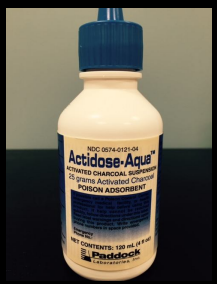
- O2 administered
- Monitor demonstrates sinus rhythm
- IV established
- What next . . .

Case 2

Blood glucose 22 mg/dL

Case 2

Should we give activated charcoal?



GI Decontamination Techniques

Ipecac Syrup

Gastric Lavage

Activated Charcoal

Cathartics

Whole Bowel Irrigation

Endoscopy

GID - Risk: Benefit Analysis

Benefits	Risks
Limit Systemic Absorption (Biological Plausible)	Aspiration
Changed Patient Management (minimal evidence)	Prolonged Emesis
Improve Patient Outcome (minimal data)	Diarrhea
Punitive Measures (NEVER Proven)	GI Perforation
	Patient Agitation
	Mechanical Trauma
	Hypoxia
	Wasted Time

Bottom Line for Ipecac, Lavage and Cathartics

Limited, time dependent effect

Never shown to change outcome

Potentially harmful

Not indicated in routine management

Bottom Line for Activated Charcoal

Best if given within 60 minutes of ingestion

Endeavor to give orally

Benefits *may not* outweigh Risks
particularly when given via NG tube and when clinical toxicity already present

Case 2

After 4 ml/kg of 25% dextrose, patient is awake and alert.

In the mean time, mom discovers the pill is Glipizide.

Sulfonylureas

- Acetohexamide
- Chlorpropamide
- Tolazamide
- Tolbutamide
- Glimeripide
- Glipizide
- Glyburide

Sulfonylurea Mechanism

- Stimulate pancreatic β cells to release insulin
- Bind sulfonylurea receptor on the β cell
  - Inhibit the K_{ATP} channel in the β cell membrane → depolarization, calcium influx, and release of stored insulin from secretory granules within the cell
- Tend to be long acting

Sulfonylureas

Agent	Onset (h)	Peak (h)	Duration (h)
Acetohexamide	2	4	12-24
Chlorpropamide	1	5	24-72
Glimepride		2.5	24
Glipizide	0.5	1	< 24
Glyburide	0.5	4	24
Tolazamide	1	5	18
Tolbutamide	1	6	6-12

Sulfonylurea Treatment

- Single tablet may produce hypoglycemia
- 5 year retrospective review (ClinTox 34(3)1996)
  - 93 cases, 25 patients (27%) developed hypoglycemia
  - 79% onset within 4 hours
  - Remainder up to 16 hours
    - IV D_5 infusion during this time

Sulfonylurea Treatment

- 10 yr retrospective review (Ped Emerg Care 27(9)2011)
  - 93 total patients, average age 1.8 yo
  - 41/93 (44%) patients developed hypoglycemia
    - Glyburide
    - Glipizide
    - Glimepiride
  - Median time to hypoglycemia 4-5 hrs
  - 4 patients had hypoglycemia >8 hrs post ingestion

Sulfonylurea Treatment

- Other reviews suggest that hypoglycemia should be evident within 4 hours of ingestion
- In cases where it was delayed it was likely masked by administration of glucose

Sulfonylurea Treatment

- Admit
- If euglycemic
  - Do not administer dextrose
  - Feed
  - Check blood sugar hourly while asleep, every 2 hours while awake
  - Must tolerate overnight fast before discharge

Sulfonylurea Treatment

- Initial control
  - IV dextrose, bolus
    - Adult initially 1g/kg of $D_{50}W$
    - Children .5 to 1 g/kg $D_{25}W$
    - Neonates .5 to 1 g/kg $D_{10}W$
- Followed by continuous infusion

Sulfonylurea Treatment

- Glucagon
  - Recruits hepatic glycogen stores and induces gluconeogenesis
  - Partially dependent on the adequacy of glycogen stores
  - Stimulates insulin release – may lead to prolonged hypoglycemia
  - Reserve for temporizing treatment in patients in whom IV access cannot be rapidly established

Non-Sulfonylureas

- "Meglitinides"
  - Prandin™ (Repaglinide) (FDA approved 1997)
    - Duration of action = 4 hrs
  - Starlix™ (Nateglinide) (FDA approved 2000)
    - Duration of action = 6 hrs

Cause hypoglycemia but much shorter acting

Case 3

2 yo boy ingests unknown med shortly before arrival. He is lethargic and vomited once.
HR 89, RR 8, BP 90/40, Sat 89% on RA
Neuro: Obtunded, limp
HEENT: Miotic pupils
Resp: Clear
GI: Decreased bowel sounds
CV: RRR

Case 3

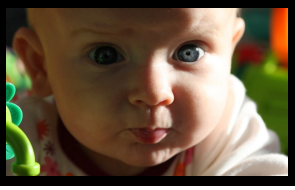
- O2 administered
- Monitor demonstrates sinus rhythm
- IV established
- What next . . .

Case 3

Naloxone

Opioid toxicity

- Clinical Triad
  - Miosis
  - Respiratory Depression
  - Altered mental status



Opioid Toxicity

- Long-acting opioids
  - Lomotil (Diphenoxylate)
  - Methadone
  - Oxycontin
  - Buprenorphine

These often require admission

Lomotil

- Diphenoxylate and Atropine combined
  - Diphenoxylate
    - Opioid analogue of meperidine
    - Metabolized to long-acting active metabolite
    - Decrease gut motility
    - Erratic absorption in children
  - Atropine
    - Decrease gut motility

Opioid Toxicity Treatment

- Naloxone
  - 0.1 mg/kg (may repeat as necessary until breathing)
  - Half-Life:
    - Approx 1 hour
    - In neonates, as long as 4 hours

Must observe 4-6 hrs after last dose

Case 4

2 yo boy ingests unknown med shortly before arrival. He is lethargic and vomited once.
HR 40, RR 8, BP 190/80, Sat 89% on RA
Neuro: Obtunded, limp
HEENT: Miotic pupils
Resp: Clear
GI: Decreased bowel sounds
CV: RRR

Case 4

Hint. . .This is NOT an opioid ingestion
What could it be?

Case 4

Clonidine!!

Clonidine

- Alpha$_2$ agonist
  - Peripheral effects early
    - Vasoconstriction = hypertension
    - Reflex bradycardia
  - Central effects late
    - "Sympatholytic"
    - Bradycardia, hypotension
    - Pin-point pupils
    - Sedation

Other Alpha$_2$ Agonists

- Guanabenz (Wytensin™)
- Guanfacine (Tenex ™)
- Oxymetazoline (Afrin ™)
- Tetrahydrozoline (Visine ™ products)

Clonidine

Should atropine be given?

"HR 40, RR 8, BP 190/80, Sat 89% on RA"

Clonidine - Treatment

- Hypertension is short-lived
  - If necessary, use short acting meds (i.e. NTG)
- IV, O_2, Monitor
- For hypotension
  - Usually only need IV fluids
  - Can use dopamine

Any other treatments available?

Clonidine - Treatment

Naloxone!!

Case 4

During transport. . .
- IV fluids started
- HR 60, BP 90/45, Sat 100% on NC
- Miotic pupils
- Sleepy but arouses to deep pain

Case 5

2 yo girl accidentally ingests 1 (240mg tab) verapamil SR tablet that Grandma left on the bed. It has been 8 hours since ingestion and the child has normal exam and normal vitals. What do you do?

Case 5

What do you do?
a. Reassure family and leave.
b. Transport to hospital, no EMS treatment needed.
c. Give IV calcium and transport to hospital.
d. Give charcoal and transport to hospital.

Verapamil SR

- Easy disposition – Transport/Admit
- All pediatric Ca Channel Blocker SR preparations should be admitted even if they look great
- Verapamil is most likely to cause delayed toxicity
- If asymptomatic for >6 hrs after ingestion of reg release Ca Channel okay to send home

Case 6

2 yo girl accidentally ingests 1 (100mg tab) metoprolol XL tablet that Grandma left on the bed. It has been 8 hours since ingestion and the child has normal exam and normal vitals. What do you do?

Case 6

What do you do?

a. Reassure family and leave.
b. Transport to hospital, no EMS treatment needed.
c. Give IV calcium and transport to hospital.
d. Give charcoal and transport to hospital.

Lopressor XL

- Okay to send home after 8hr obs period
- The same concerns with SR Ca Channel Blockers doesn't apply to Beta Blockers
- Except Sotalol which should be watched for 12hrs

- ONLY APPLIES TO KNOWN SINGLE PILL INGESTIONS!

β-blocker/CCB Treatment

- Treatment
  - Vasopressors
  - Glucagon
  - Atropine
  - Insulin
  - Phosphodiesterase Inhibitors
  - Calcium
  - Pacer
  - Balloon Pump

β-blocker/CCB Treatment

- Vasopressors – dopamine, epi, norepi, isoproterenol
  - Good first choice
  - Very high doses may be required
- Atropine
  - Should help, but is only short-lived

β-blocker/CCB Treatment

- Dopamine
  - 2-20 mcg/kg/min
- Epi
  - 0.01 mg/kg (max 1 mg/dose)
- Atropine
  - 0.02 mg/kg (max 1 mg/dose)

β-blocker/CCB Treatment

- Glucagon (Specifically for β-blockers)
  - Some suggest as first-line treatment
  - Dose
    - 2-5mg every few minutes till effect
    - Effective dose started as hourly drip
  - At inotropic doses, pts will vomit

β-blocker/CCB Treatment

- Insulin
  - Can be given as continuous infusion
  - Must follow blood sugar
  - Demonstrated benefit in dogs
  - Anecdotal evidence support use
  - Theorized to:
    - Increase myocardial glucose uptake
    - Increase myocardial calcium uptake
  - Still don't recommend it's use (unless very sick)

β-blocker/CCB Treatment

- Calcium
  - Increases intra-cellular Ca
  - May be able to counteract effects of CCB toxicity
  - Ca chloride can be very irritating to veins
  - Dose – exact dose is unclear
    - Calcium chloride (10%) 20 mg/kg

β-blocker/CCB Treatment

- Last resort!!!
  - Pacer – good idea but often doesn't help

Medical Toxicology Call Us Anytime

Poison Center at 800-222-1222
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