Calcium Channel Blocker Overdose

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Case Study (Day 0)

• 57 year old 100 kg male
• PMHx: hypertension, high cholest., NIDDM, depression
• After a night of drinking came home and took ALL of his recently filled medications (3 month supply)
• Discovered by family vomiting...to hospital
Case Study

Meds ingested:

- Diltiazem HCL SR 240mg x 90 tabs
- Atorvastatin 900mg x 90 tabs
- Ramipril (ACE)900mg x 90 tabs
- Chlorthalidone (thiazide; undetermined amount)
- Metformin (undetermined amount)
Case Study

In ER

- Initially alert and oriented, vomiting +++ pills
- Gradual hypotension with decreased LOC/unresponsive
- Intubated for airway protection (CPAP10/10 40%)
- Vitals: HR 80-90 SR progressing to bradycardia 40-60, BP 70-90/30-40
- ABG: 7.04/41/93/11/-18/96
- 4 large bore peripheral IV’s inserted
Case Study

- Phenylephrine IV infusion, titrated up to 300mcg/min
- Intralipid 20% 150ml IVP/infusion started @.25ml/kg/min
- Calcium Gluconate 60mg/kg IVP over 5 minutes
- Glucagon 10mg IVP, infusion 2mg/hr
- Sodium bicarbonate 1 amp IVP
- Transported to ICU
Case Study

- in ICU decreased LOC but obeying commands, nodding
- Trilumen CVAD, introducer sheath inserted
- Rapid deterioration in vitals
- Progressively hypotensive, bradycardic
- Vitals: BP 60-105/35-40, HR 22-80 3\textsuperscript{rd} degree CHB
- ABG 6.98/41/79/10/-22/97
Case Study

Medications (rapid escalation):

- Phenylephrine, norepinephrine, dopamine, vasopressin, epinephrine infusions
- Intralipid infusion, glucagon infusion
- High dose insulin @150 units/hr with D50W infusion
- Methylene blue IVP, with an infusion
Case Study

• Midazolam infusion started for comfort
• Large bore nasogastric tube inserted; gastric lavage initiated followed by activated charcoal and Pegalyte 4L NG
• Patient having prolonged recurrent episodes of complete heart block with ventricular response in 20’s
Case Study

• Transcutaneous pacing initiated as a bridge to transvenous pacing
• Odd!..after a few minutes of tv pacing, reverted to SR 80-90
• Dual lumen CVAD inserted, CRRT initiated
Physiology/Pharmacology (sorry)
Overview

• Calcium channel blockers used to treat HTN, angina, arrythmias
• Wide clinical use, commonly prescribed
• Examples: amlodipine, diltiazem, verapamil
• Available in immediate and extended release
• Substantial toxicity, CCB account for ~40% of deaths in cardiovascular drug OD
Physiology/Pharmacology

- Calcium is critical for myocardial contractility and conduction
- Maintains tonic constriction in vascular smooth muscle; contraction of skeletal and cardiac muscle cells
- CCB block calcium channels causing vasodilation, depressed myocardial contractility or altering conduction and pacemaker cells
Physiology/Pharmacology

- CCB are chosen based on their primary target tissue or "selectivity" (myocardial vs. vascular)
- Selectivity is lost with overdose
- Negative inotropic and chronotropic effects, as well as "vasoplegia" (widespread vasodilation)
- At toxic levels will also inhibit insulin release from pancreas by blocking calcium channels in beta cells
Physiology/Pharmacology

Calcium channel blocker prevents release of internal calcium stores into cell cytosol.

Heart muscle cell does not respond to calcium ion signal.
Physiology

Typical Symptoms of CCB toxicity

- Drowsiness/confusion (can be surprisingly lucid)
- Hypotension and bradycardia (prolonged PR, blocks)
- Pulmonary crackles, signs of failure
- Hyperglycemia
- Initially stable may deteriorate quickly
Toxicity

- Usual max single dose of sustained release 360mg
- Pt took 21,600mg (~22g)
- In addition to other antihypertensive meds
Treatment

Focus on 4 Elements

• STABILIZATION – ABC’s
• DECONTAMINATION
• ANTIDOTE(S)
• SUPPORTIVE THERAPY
Stabilization

• Correct immediate life threatening complications
• For CCB overdose most commonly hypotension and bradycardia
• Intubation (Atropine)
• IV access, fluids
GI Decontamination

Oro-gastric lavage
• Within 1-2 hours of ingestion

Activated Charcoal
• Within 1 hour of ingestion

Whole Bowel Lavage
• Pegalyte
Antidote Administration

Administration of calcium salts:
• Used to overcome CV effects of CCBs
• **Calcium chloride**: 3x bioavailable calcium than Ca-gluconate; nonacidotic patients
• **Calcium gluconate**: preferred in acidic patients; less bioavailable calcium
• Often ineffective because CCB produce a non-competitive block
Supportive Therapy

Vasopressors

- Following fluid resuscitation: dopamine, phenylephrine, norepinephrine, epinephrine
- Positive inotropy, chronotropy and vasoconstrictive effects of agents
Supportive Therapy

Glucagon

• Increases intracellular cyclic AMP which activates calcium channels
• Increases heart rate
• 5mg IV push (repeat at 10 minute intervals)
• infusion
Supportive Therapy

Insulin and Glucose

• Mechanism is not clear
• CCB block FFA metabolism and produce insulin resistance in myocardial cells (carbohydrate dependence)
• Overcomes insulin resistance in myocardium and replaces insulin blocked at pancreatic level by CCB
• Not all patients will need glucose because CCB may cause hyperglycemia
• At high doses insulin will actually act as an inotrope
• 120-150 units/hr...monitor glucose
Supportive Therapy

Lipid Emulsion Therapy

• Lipid surrounds CCB drug molecule
• Prevents it from binding to calcium channel
• Also proposed that lipid provides readily available energy source for myocardial cells
• Dosage 1.5 mg/kg IVP, infusion .25ml/kg/min
Supportive Therapy

Transvenous Pacing

• Assists with electrical conduction
• Does not correct negative inotropic effects of CCB or hypotension
Case Study (Day 1)

- Overnight patient aspirated pegalyte and charcoal (massive)
- By morning: PCV, rate 28, 12/28, Vt 490ml (was 700ml)
- Vasopressors all at maximum, with the addition of methylene blue infusion
Case Study

• BP 80/30 on pressors
• Tni risen from 10.7 to >40, lactate 17
• CK 4000
• WBC 28.6
• Gross mottling noted to extremities and torso
• Consult to CSICU cardiac anesthesia for possible ECMO
Case Study

- Transvenous pacer removed, PA catheter inserted (C.O. 5 l/min, C.I. 2.0, SVR 300)
- Prior to availability of ECMO, patient continued to deteriorate
- Idioventricular rhythm with sustained pauses
- Patient asystolic, no resuscitation attempted
- CTB almost exactly 24 hrs post ingestion
Other Therapies

ECMO/CP Bypass

• Some reports of favourable outcome for patients placed on prolonged ECMO/CPB
• Anecdotal only
Other Therapies

Methylene Blue?

• “hail Mary?”
• Has some efficacy in sepsis; not validated for CCB toxicity
• MB inhibits the nitric oxide cycle and vasodilation
• Improves SVR and MAP
Levosimendan (calcium “sensitizer”)  
- Used in severe CHF  
- Not recommended for use in CCB OD  
- Sensitizes calcium channels and promotes influx into cell; increases contractility  
- Theoretical benefit only  
- Conflicting animal studies
Other Therapies

Dialysis

• In this case CRRT initiated to assist with correction of acid/base imbalance
• CCBs are highly protein bound
• Ineffectively removed by dialysis
Compassionate People. World-Class Care.  
Des gens de compassion. Des soins de calibre mondial.