Case Studies in Drug Interactions and Polypharmacy Issues

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Introduction

• The incidence of a clinical drug interactions 3-5% in pts taking 3 or fewer medication, but 20% in pts taking 10-20 drugs.
• 20% of hospital admissions result from an adverse drug event or a Drug-Drug Interaction
• 60-80% of computerized DDI alerts are overridden
• To prevent a SERIOUS drug interaction, you would have to review over 2,700 alerts
Introduction

• How drug interactions are studied by the pharmaceutical industry

• Case reporting

• Potential for a drug interaction vs. Actual occurrence
Case #1

A 65 yo F comes in for f/u

- She has a long hx of hypothyroidism and has been recently dx with osteopenia.
- Current Med list:
  - Centrum Silver 1 qday
  - Levothyroxine 88mcg 1 qday
  - Ca+D 600/400 1 bid
  - Alendronate 35mg 1 qweek

Recent labs

- 6/20/14: TSH 2 mIU/L FT4 1.4 ng/dL
- Today labs: TSH 9.5mIU/L and FT4 0.4 ng/dL
- She reports to be compliant with taking her medications and takes all of them in the morning 30 min before breakfast.
- What is the drug interaction?
Levothyroxine Drug interactions

- Levothyroxine should be taken on an empty stomach: 1 hour before or 2 hrs after a meal for best absorption
- Calcium and iron will reduce the absorption of levothyroxine
- Pt has 2 different sources of Calcium
- Pt should continue taking all of her medications, but Calcium should be administered 4hrs apart from Synthroid.
Case #2

• You are seeing your 70 yo pt for follow up
• Hx of HTN, DM type 2 and hyperlipidemia.
• His BP over the past several visits has been above goal at 150-160/90s
• Currently taking:
  – Metformin 1000mg bid
  – Glipizide 10mg bid
  – Losartan 100mg qday
  – Simvastatin 40mg qday
• You want to add another BP medication
• As you are entering Amlodipine 5mg in the EMR, a pop up for a severe drug interaction appears.
• What should you do next?
Simvastatin/Amlodipine Interaction

- Simvastatin is metabolized by CYP 450 3A4 pathway. Amlodipine inhibits 3A4 which could lead to myopathy.
- Dose related: 10 mg of amlodipine with 80 mg simvastatin resulted in a 77% increase in exposure to simvastatin compared to simvastatin alone.
- Close monitoring vs. going with a different class of anti-hypertensive.
Case #3

- A 85 yo Female with a hx of HTN, CHF and OA is taking the following meds:
  - Tylenol 500-1000mg BID prn
  - Meloxicam 7.5mg qday prn
  - Lisinopril 20 mg qday
  - Dyazide (HCTZ/Triamterene) 25/37.5mg 1 qday
  - Spironolactone 25mg 1 qday

- Her BPs appear to fluctuate from 120-130/70-80 to 150-160/90s.
- Her recent labs show a Cr of 1.3 and a K of 5.2
- Could there be DDI at play here?
NSAIDS and Antihypertensive Meds

- NSAIDs inhibit prostaglandin synthesis which results in inhibition of renal sodium excretion and can lead to increase in BP.
- Given this patient’s creatinine, Meloxicam may not be appropriate.
- Three different drugs on the list can increase K.
Case # 4

• 70yo F is here for follow up

• Hx of HTN, Anxiety, Insomnia and Chronic back pain

• Today her main complaint is insomnia. She has tried implementing some sleep hygeine tips w/o success

• Her current med list:
  – Lisinopril 20mg qday
  – HCTZ 12.5mg qday
  – Citalopram 10mg qday
  – Tramadol 50mg tid PRN pain
  – Ibuprofen 400mg tid

• You want to prescribe Trazodone 50mg qhs

• A drug interaction alert pops up
5HT Syndrome

- A syndrome of clinical findings ranging from benign to lethal. Observed in all age groups

- Anxiety, agitation restlessness, diaphoresis, tachycardia, HTN, hyperthermia, tremor, muscle rigidity

- Symptoms present w/in 6-24hrs or change in dose or initiation of a new drug

- This pt is taking Celexa and Tramadol already

- Trazodone is added

- What can you do??
Case # 5

• 89 yo F coming in for new onset illness
• Hx of Afib, HTN, Hyperlipidemia, depression, chronic pain
• Presents today with new onset productive cough, Temp 100.5, fatigue
• Last INR was 2 weeks ago at 2.8

• Medications:
  – Lexapro 20 mg qday
  – Warfarin 1mg UD per coumadin clinic
  – Percocet 10/325 1 tab tid prn pain
  – Metoprolol 25mg 1 bid
  – Lovastatin 40mg qhs
  – Diltiazem 240mg/24hr 1 qday
Coumadin drug interactions

- Based on your physical exam you suspect pneumonia and treat with Zpack (Azithromycin) for 5 day and Tylenol 500mg for fever as needed
- A DDI alert pops as as you are entering new orders into the EMR
- What DDIs are at play here?
- Pt on multiple chronic medications which can increase her INR
- Order in which drugs are started is important.
- How would you handle starting the additional drugs?
Drug Induced QT interval

- Torsades de pointes is rare but more likely in:
  - Females
  - Geriatrics
  - Renal insufficiency
  - More than 1 QT prolonging drug
  - Dose related

- Medications which could induce a long QT:
  - Lexapro 20mg
  - Percocet 10/325mg tid prn
  - Z-pack
Case # 6

• An 81 yo Female brought in by her son for a medication evaluation.
• Her Medical Hx includes the following:
  – HTN, DM #2, HA, Urinary incontinence, GERD, OA, OP, Dementia, neuropathic pain
• Recently diagnosed with Dementia. She has been taking Ditropan (oxybutynin) for 6 months. She is supposed to take ASA for prophylaxis, but she decided to take it for pain. She has been taking Alendronate for the past 6 yrs. No fractures.

• Today her main complaints include increased agitation, urination, loose stools, nausea, and muscle pain especially in the legs which she attributes to old age.
Case # 6: Her Medication list

- Docusate 100mg bid
- Amitriptyline 10mg qhs
- Losartan 25mg qday
- Oxybutinin 5mg tid
- Gabapentin 300mg qhs
- Donepezil 10mg qday
- Pravastatin 40mg qhs
- Tramadol 50mg TID prn Pain
- Pantoprazole 40mg qhs

- ALLERGIES: Metformin: diarrhea

- Alendronate 70mg qweek
- Lantus 25 U qhs
- Vitamin D 2000IU 1 qday
- Novolog per sliding scale
- ASA 325 mg 2-4 tabs qday for pain
- B complex 1 qday
- Januvia (sitagliptin) 100mg qday
- Compazine (prochlorperazine) 10mg 1 tab prn nausea
Case #6: Continued

Selected Vitals/Labs

- Vitals: BP 141/50/80; HR 56; Ht 5’6’’; Wt 150lbs
- Labs:
  - Cr 1.0; K 4.0; Glu 150; B12 250; A1C 7.0
  - Lipid panel: Chol: 140; TG 190; HDL 38; LDL 90,

Issues to consider

- Symptoms could be drug side effects
- Lots of drug cascades
- Complex Drug regimens
- Antagonism-type of Drug-Drug interactions
Case #7: Polypharmacy

87 yo M referred for a pharmacy consult by PCP

- Chronic pain/peripheral neuropathy x7yrs. Achiness all over
- Excessive fatigue
- Constipation and diarrhea
- Herpes of the cornea
- Hyponatremia
- Memory impairment dx recently
- Adrenal insufficiency

Current Medications

- Intrathecal pump: Dilaudid 20mg/ml/Clonidine 66.7mcg/ml/20cc q3mo
- Synthroid 50mcg qday
- Prednisone 20mg qday
- Lexapro 20mg qday
- Folic Acid 1mg qday
- Modafinil 100mg qday
- Vitamin B 1 100mg qday
- NaCl 1gm bid
- Imipramine 10mg qday for diarrhea
- Gabapentin 400mg tid
- Donepezil 10mg qday
- Valtrex 1gm bid
- Colace 100mg PRN
- Pepcid Complete PRN
- Zofran 4mg prn N/V
Case # 7: Additional information

Vitals/labs

• BP 95/53
• HR 53
• Na129
• CrCl calculated 28.5ml/min
• TFT’s WNL

Interview

• Pt and wife don’t know what to do about meds
• A new neurologist recommended reducing gabapentin, changing an antidepressant and reducing Aricept. Prescribing neurologist disagrees.
• Self titrated Modafinil from 200mg daily due to cost
• Recent ER visit due to dry heaves nausea
Things to Consider

- Pt getting 4.4mg of Dilaudid and 0.1mg of Clonidine daily
- Several medications can cause fatigue, memory impairment, GI symptoms
- Modafinil does not appear to be effective

- Clcr below 30ml/min: Renally cleared drugs need to be adjusted
- SSRI induced hyponatremia is possible
- Pain not adequately managed
- Bowel/GI regimen not effective
Recommendations

- Stop Dilaudid/clonidine
- Adjuvant analgesics are more appropriate
- Stop Pepcid Complete and start a PPI
- Stop Lexapro and start Effexor or Cymbalta
- Stop Midafinil
- Once high dose SSRI is stopped NaCl may not be necessary

- Stop Imipramine
- Reduce dose of Gabapentin to reflect renal fx
- Reduce or stop Aricept
- Reduce the dose of Valtrex to reflect renal fx
- Colace prn not effective
Case # 8: Polypharmacy Case

87 yo F here for a HAPS assessment

- HTN
- DM
- Urinary Incontinence
- Hypothyroidism
- Hyperlipidemia
- GERD
- Afib

Primary concern

- Daughter feels mom is overmedicated.
- Would like to present recommendations to her PCP so that changes can be made
Medications

- Valsartan 80mg bid
- KCL liquid 20 meq bid
- Senna Plus 1 tab qday
- Synthroid 50mcg qday
- Myrbetriq ER 25mg qday
- Imdur 30mg qday
- Digoxin 0.125mg qday
- Atorvastatin 40mg qday
- Carvedilol 6.25mg bid
- Pantoprazole 40mg qday

- Xarelto 15mg qday
- Furosemide 40mg qday
- Docusate 100mg bid
- Amlodipine 2.5mg qday
- Vitamin D 1000 iu bid
- Lantus 8 u bid
- Humalog 2 u tid and per sliding scale
Case #8 Continued: Interview

- Pt manages her own medications
- Multiple hypoglycemic episodes in the past 2 weeks. Dose of insulin being adjusted down. PO meds never tried. Last AIC 6; Cr 0.8 GFR > 60
- Hx of falling
- Feels like Myrbetriq not working. Has urgency during the day. No issues at night
- Multiple cardiac medications. Today’s vitals: BP 117/67 P 50
- Pt has bilateral ankle edema
Pt’s diabetic regimen is too aggressive. Simplify. PO meds are appropriate.

Re-assess need for Lasix and KCl.

KCl liquid tastes very metallic and can contribute to esophageal irritation.

Myrbetriq can increase BP and may not be necessary once Lasix is stopped.

Re-assess need for digoxin. Pulse is already low.

Simplify HTN regimen.

Amlodipine may be causing edema and GERD symptoms.
Tips to avoid drug interactions and polypharmacy

- VERY careful prescribing
- Choose a drug within a class which is less likely to cause a DDI
- DDI risk is often theoretical not actual
- Close monitoring is necessary to avoid problems
- Drug list must be rational: Drug choice and dose
- Drug cascades MUST be avoided
- Patient education improves compliance