Case Studies in Drug Interactions and Polypharmacy Issues

Tatyana Gurvich, Pharm.D. CGP
USC School of Pharmacy
UCI Medical Center Senior Health Center
Glendale Adventist FPRP

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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

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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?

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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.

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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?

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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

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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?

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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

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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??

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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

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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?

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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

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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.

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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: Metfromin: 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

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Case #6: Continued

Selected Vitals/Labs

- Vitals: BP 14
- 150/80; 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

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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

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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

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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

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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

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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

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Case #8 Continued

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

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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

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Recommendations

- Pt's diabetic regiment 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

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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

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