Why Should I Care About Drug Interactions?

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Objectives

- Describe the absorption, distribution, metabolism, and elimination of drugs in the body
- Review how drug interactions occur
- Highlight methods to minimize the risk for drug interactions
- Questions/Discussion
Medications in the Body

- All meds must undergo:
  - Absorption
  - Distribution
  - Metabolism
  - Excretion
Mechanisms for Drug Interactions

- The effect a drug has on a person may be different than expected because the drug may interact with:
  - Another drug the person is taking (drug-drug interactions)
  - Food, beverages, or supplements the person is consuming (drug-nutrient interactions)
  - Another disease the person has (drug-disease interaction)
  - Life style choices the person participates in (drug-life style interactions)
Drug-Drug Interactions

- Involves all types of medications:
  - Prescription
  - Over-the-Counter
  - Dietary/Herbal Supplements

- Types of interactions include:
  - Duplication
  - Antagonism
  - Alteration
DDI: Duplication

- When two drugs with the same or similar effect are taken together, the side effects may be intensified.

- Examples:
  - Prescription and over-the-counter pain meds (Vicodin, Percocet, or Tylenol #3 + acetaminophen = liver toxicity)
  - Statins and Fibrates (simvastatin + gemfibrozil = muscle pain)
  - Antiplatelet drugs (aspirin + Plavix = increased bleeding)
Examples:

- Nitrates and erectile dysfunction meds (SL nitroglycerin + Viagra = lowered BP)
- Beta-blockers and ACE inhibitors (metoprolol + lisinopril = lowered BP)
- ACE inhibitors and Aldosterone antagonists (lisinopril + spironolactone = high potassium levels)
DDI: Antagonism

- Two drugs with opposing actions can interact, thereby reducing the effectiveness of one or both drugs.

- Examples:
  - NSAIDs and BP meds (ibuprofen, naproxen + BP meds = decreased effectiveness of BP med)
  - NSAIDs and Diuretics (ibuprofen, naproxen + furosemide = decreased fluid elimination)
  - NSAIDs and Aspirin (ibuprofen + aspirin = decreased effectiveness of aspirin)
DDI: Alteration

- One drug may alter how the body absorbs, distributes, metabolizes, and excretes another drug.
Alteration: Absorption

Absorption of a drug may be reduced in the gastrointestinal (GI) tract by:

- A reduction in stomach pH
  - Example: antacids, H2 blockers, and proton pump inhibitors with some antibiotics, antifungals

- Changes in motility
  - Example: metoclopramide and digoxin
Alteration: Absorption

- Bind with another drug
  - Specific drugs susceptible to binding interactions:
    - Some antibiotics, thyroid hormone
  - Examples of drugs that bind with others:
    - Iron, calcium, magnesium, zinc
    - Antacids that contain magnesium, aluminum, or calcium
    - Cholestyramine, colestipol
  - To prevent binding interactions, take binding drug a minimum of 2 hours after other drugs
Alteration: Distribution

- Some drugs affect the distribution of another drug to its site of action in the body.
  - Example: NSAIDs and Diuretics
    - Ibuprofen and naproxen inhibit the delivery of hydrochlorothiazide and furosemide into the kidney which decreases the effectiveness of the diuretic at removing extra fluid
Many drugs are metabolized (or broken down and inactivated) by enzymes in the liver.

- Some drugs can increase or decrease the activity of liver enzymes to affect the metabolism of another drug.
- The extent of this interaction is dependent on a person’s age, ethnicity, and general health.
Alteration: Metabolism

- General Drug Metabolism Changes:
  - Increase activity of enzymes to enhance metabolism of another drug and decrease its effectiveness
  - Example: rifampin and warfarin
    - Rifampin increases the activity of liver enzymes to enhance the breakdown of warfarin. To maintain warfarin’s effectiveness, higher doses must be given.
Alteration: Metabolism

- General Drug Metabolism Changes:
  - **Decrease activity of enzymes** to reduce metabolism of another drug and increase its effectiveness
  - **Example:** amiodarone and warfarin
    - Amiodarone inhibits the activity of liver enzymes to decrease the breakdown of warfarin. To prevent side effects from warfarin therapy, lower doses must be given.
Alteration: Metabolism

Examples:

- Plavix + Prilosec = decreased effectiveness of Plavix
Drugs Most Susceptible to Alterations in Metabolism

- Warfarin (Coumadin)
- Digoxin (Lanoxin)
- Phenytoin
- Theophylline
Alteration: Elimination

- Some drugs affect the rate at which the kidneys excrete another drug
  - Example: high doses of vitamin C may affect the excretion of acidic drugs

- Some drugs affect kidney function which alters the elimination of other drugs
  - Example: furosemide may alter kidney function which may decrease the elimination of digoxin. A reduction in digoxin clearance increases blood concentration, enhances the drug’s activity, and increases the risk for side effects.
Drug-Nutrient Interactions

- Types of Drug-Nutrient Interactions:
  - Drug-food
  - Drug-beverage
  - Drug-supplement
Foods, like drugs, must be absorbed through the lining of the stomach or small intestine.

The presence of food in the GI tract may reduce the absorption of a drug.

Example: Bisphosphonates for bone health must be taken on an empty stomach (Fosamax, Actonel, Boniva)
The type and amount of food in a person’s diet may affect the beneficial activity of a drug.

- Example: Vitamin K containing foods may decrease the effectiveness of warfarin (Coumadin) and increase the risk for a blood clot to form.
- Example: Calcium in dairy products may bind to a drug and reduce the absorption.
DNI: Grapefruit Juice

- GFJ may enhance the activity of many drugs by inhibiting metabolism
  - Grapefruit contains naringin, bergamottin, and dihydroxybergamottin which inhibit one set of enzymes in the liver
  - Inhibiting the metabolism of drugs leads to increased efficacy and risk for side effects
    - Examples: statins (simvastatin, atorvastatin, lovastatin), calcium channel blockers (nicardipine, felodipine, verapamil), amiodarone, carvedilol, losartan, erectile dysfunction meds, some prescription pain meds and antidepressants
DNI: Caffeine
DNI: Caffeine

- Caffeine may increase the benefit of some drugs:
  - Example: diuretics

- Increase the risk for side effects:
  - Example: beta-agonists for asthma/COPD, stimulant drugs for ADHD

- Decrease the benefit of drugs by:
  - Increasing blood pressure
  - Increasing heart rate
  - Increasing alertness
  - Decreasing oral absorption
DNI: Alcohol

“Don’t worry darling, you didn’t burn the beer!”
DNI: Alcohol

- Although not considered a nutrient, alcohol affects body processes and interacts with many drugs
  - Increase risk for side effects:
    - Sedation with pain meds
    - Nausea, vomiting, headache, and heart palpitations with some antibiotics and MAOI antidepressants
  - Inhibit metabolism and increase efficacy:
    - warfarin, acetaminophen
DNI: Dietary Supplements

- Dietary supplements are products that contain a vitamin, mineral, herb, or amino acid intended to supplement a normal diet.
- However they may interact with prescription and over-the-counter drugs.
DNI: Dietary Supplements

Potential interactions in patients with CV disease:

- Increase bleeding risk: alfalfa, angelica (dong quai), bilberry, fenugreek, garlic, ginger, gingko
- Increases blood pressure: ginseng, licorice, ephedra (ma-huang), yohimbine
- Increases heart rate: ephedra, yohimbine

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Potential interactions in patients with CV disease continued:

- Enhance activity of BP meds: fumitory, irish moss, kelp, lilly of the valley, night-blooming cereus,
- Inhibit activity of BP meds: butcher’s broom
- Enhance activity of digoxin: fumitory, hawthorn, night-blooming cereus, St Johns wort, storphanthus

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Potential interactions in patients with CV disease continued:

- Cause low potassium levels and increase risk for toxicity with digoxin and diuretics: aloe vera, gossypot, licorice
- Cause high potassium levels: oleander
- Cause low blood sugar: fenugreek, ginseng,
- Inhibit activity of warfarin: ginseng, green tea

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Drug-Disease Interactions

- Drugs that are helpful in one disease may be harmful in another disorder:
  - Example: some beta-blockers used for heart disease may make asthma/COPD symptoms worse (carvedilol, propranolol)
  - Example: acetaminophen may worsen liver function in patients with liver disease
  - Example: NSAIDs like ibuprofen may worsen kidney function in patients with chronic kidney disease
  - Example: pseudoephedrine may increase blood pressure and make blood pressure lowering drugs less effective
Drug-Lifestyle Interactions

- Diet:
  - May affect the effectiveness of medications:
    - Example: diets high in salt will decrease effectiveness of high blood pressure meds or diuretics used in heart failure
    - Example: diets low in cholesterol will improve the effectiveness of lipid lowering drugs
Drug-Lifestyle Interactions

- Tobacco:
  - May inhibit enzyme activity in the liver and enhance the activity of some drugs
    - Example: theophylline, propoxyphene
  - May inhibit the benefits of drugs by increasing the risk for damage to the body
    - Increases blood pressure
    - Worsens lung function
    - Increases cholesterol levels
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- Questions/Discussion
How to Reduce the Risk of Drug Interactions

- Consult your doctor or pharmacist before taking any new drug, including over-the-counter and dietary supplements.
How to Reduce the Risk of Drug Interactions

- Select a pharmacy that provides comprehensive services that includes checking for possible interactions.
How to Reduce the Risk of Drug Interactions

- Take drugs as instructed.
How to Reduce the Risk of Drug Interactions

- Learn about the purpose and actions of drugs prescribed.
- Learn how to take the drugs, what time of day they should be taken, and whether they can be taken during the same time period as other drugs or food.
  - Avoid dairy products or grapefruit juice?
  - If a drug should be taken on an empty stomach, take 1 hour before or 2 hours after a meal.
How to Reduce the Risk of Drug Interactions

- Review the use of over-the-counter drugs and dietary supplements with the pharmacist. Discuss any disorders present and any prescription drugs being taken.

- Avoid taking combination over-the-counter and dietary supplements. Use only the drug needed for the disorder and read product labels carefully.
How to Reduce the Risk of Drug Interactions

- Learn about the possible side effects of the drug and what to do if they occur.
- Report to the doctor or pharmacist any symptoms that might be related to the use of a drug.
- Keep all appointments for lab work to monitor a potential drug-drug interaction.
How to Reduce the Risk of Drug Interactions

- Keep a list of all drugs being taken. Periodically discuss this list with the doctor and pharmacist.
- Include all disorders in the list as well. Periodically discuss this list with all doctors and pharmacist.
- If seeing more than one doctor, make sure each doctor knows all the drugs being taken.
Questions/Discussion
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