Food-Drug Interactions

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Definition of Terms

- Drug-nutrient interaction: the result of the action between a drug and a nutrient that would not happen with the nutrient or the drug alone
- Food-drug interaction: a broad term that includes drug-nutrient interactions and the effect of a medication on nutritional status

Food-Drug Interaction

- For example, a drug that causes chronic nausea or mouth pain may result in poor intake and weight loss

Key Terms

- **Bioavailability:** degree to which a drug or other substance reaches the circulation and becomes available to the target organ or tissue
- **Half-life:** amount of time it takes for the blood concentration of a drug to decrease by one half of its steady state level
- **Side effect:** adverse effect/reaction or any undesirable effect of a drug

Other Terms

- Bioavailability: % free to function
- Absorption rate: % absorbed and time for absorption
- Transported: amount in blood (free or bound)
- Metabolized: altered by enzymes in tissues

Pharmacokinetics

Movement of drugs through the body by

- Absorption
- Distribution
- Metabolism
- Excretion

Absorption

- Movement of the drug from the site of administration to the bloodstream; depends on
  - The route of administration
  - The chemistry of the drug and its ability to cross membranes
  - The rate of gastric emptying (for oral drugs) and GI movement
  - The quality of the product formulation
- Food, food components and nutritional supplements can interfere with absorption, especially if the drug is taken orally

Distribution

When the drug leaves the systemic circulation and moves to various parts of the body

- Drugs in the bloodstream are often bound to plasma proteins; only unbound drugs can leave the blood and affect target organs
- Low serum albumin can increase availability of drugs and potentiate their effects

Metabolism (biotransformation)

- Primarily in the liver; cytochrome P-450 enzyme system facilitates drug metabolism; metabolism generally changes fat soluble compounds to water soluble compounds that can be excreted
- Foods or dietary supplements that increase or inhibit these enzyme systems can change the rate or extent of drug metabolism

Excretion

- Drugs are eliminated from the body as an unchanged drug or metabolite
  - Renal excretion the major route of elimination; affected by renal function and urinary pH
  - Some drugs eliminated in bile and other body fluids

Pharmacodynamics

- Physiologic and biochemical effects of a drug or combination of drugs
- The mechanism of action, e.g. how a drug works
- Often the drug molecule binds to a receptor, enzyme, or ion channel, producing a physiological response

Pharmacogenomics

- Genetically determined variations that are revealed solely by the effects of drugs
- Affect only a subset of people
- Examples include G6PD (glucose-6-phosphate dehydrogenase) enzyme deficiency, warfarin resistance, and slow inactivation of isoniazid (IHN) or phenelzine

G6PD (glucose-6-phosphate dehydrogenase) enzyme deficiency

- X-chromosome-linked
- Can lead to neonatal jaundice, hemolytic anemia or acute hemolysis
- Most common in African, Middle Eastern, and Southeast Asians
- Also called favism
- Fava beans or pollen, Vitamin K or Vitamin C can cause hemolysis

Benefits of Minimizing Food Drug Interactions

- Medications achieve their intended effects
- Improved compliance with medications
- Less need for additional medication or higher dosages
- Fewer caloric or nutrient supplements are required
- Adverse side effects are avoided

Benefits of Minimizing Food Drug Interactions

- Optimal nutritional status is preserved
- Accidents and injuries are avoided
- Disease complications are minimized
- The cost of health care services is reduced
- There is less professional liability
- Licensing agency requirements are met

Therapeutic Importance

Therapeutically important interactions are those that:

- Alter the intended response to the medication
- Cause drug toxicity
- Alter normal nutritional status

Patients at Risk for Food-Nutrient Interactions

- Patient with chronic disease
- Elderly
- Fetus
- Infant
- Pregnant woman
- Malnourished patient
- Allergies or intolerances

Food and Drug-Related Risk Factors

- Special diets
- Nutritional supplements
- Tube feeding
- Herbal or phytonutrient products
- Alcohol intake
- Polypharmacy
- Drugs of abuse
- Non-nutrients in foods
- Excipients in drugs or food

Malnutrition Effect on Drugs

- Low albumin levels can make drugs more potent by increasing availability to tissues
  - Lower doses often recommended for persons with low albumin
  - Warfarin and phenytoin are highly protein bound in blood; ↓ albumin can result in poor seizure control (phenytoin) or hemorrhage (warfarin)
- Body composition: obese or elderly persons have a higher ratio of adipose tissue; fat soluble drugs may accumulate in the body ↑ risk of toxicity

Food/Nutrient Effects on Drugs

Absorption

- Presence of food and nutrients in intestinal tract may affect absorption of drug
- Antiosteoporosis drugs Fosamax or Actonel: absorption negligible if given with food; ↓ 60% with coffee or orange juice

Food/Nutrient Effects on Drugs

Absorption

- Absorption of iron from supplements ↓↓ 50% when taken with food
- Best absorbed when taken with 8 oz of water on empty stomach
- Food may ↓↓ GI upset
- If take with food, avoid bran, eggs, fiber supplements, tea, coffee, dairy products, calcium supplements

Food/Nutrient Effects on Drugs

Absorption

- Ciprofloxacin and Tetracycline form insoluble complexes with calcium in dairy products or fortified foods; also zinc, calcium, magnesium, zinc or iron supplements; aluminum in antacids
- Stop unnecessary supplements during drug therapy or give drug 2 hours before or 6 hours after the mineral

Food/Nutrient Effects on Drugs

- Absorption
  - Presence of food enhances the absorption of some medications
  - Bioavailability of Axetil (Ceftin), an antibiotic, is 52% after a meal vs 37% in the fasting state
  - Absorption of the antiretroviral drug saquinavir is increased twofold by food

Food/Nutrient Effects on Drugs

- Adsorption: adhesion to a food or food component
  - High fiber diet may decrease the absorption of tricyclic antidepressants such as amitriptyline (Elavil)
  - Digoxin (Lanoxin) should not be taken with high phytate foods such as wheat bran or oatmeal

Food/Nutrient Effects on Drugs

- GI pH can affect drug absorption
- Achlorhydria or hypochlorhydria can reduce absorption of ketoconozole and delavirdine
- Antacid medications can result in reduced acidity in the stomach
- Taking these meds with orange or cranberry juice can reduce stomach pH and increase absorption

Food/Nutrient Effects on Drugs

Metabolism

Changes in diet may alter drug action

- Theophylline: a high protein, low CHO diet can enhance clearance of this and other drugs
- Grapefruit/juice: inhibits the intestinal metabolism (cytochrome P-450 3A4 enzyme) of numerous drugs (calcium channel blockers, HMG CoA inhibitors, anti-anxiety agents) enhancing their effects and increasing risk of toxicity; may interfere with the absorption of other drugs

Grapefruit Inhibits Metabolism of Many Drugs

- Inactivates metabolizing intestinal enzyme resulting in enhanced activity and possible toxicity
- Effect persists for 72 hours so it is not helpful to separate the drug and the grapefruit
- Many hospitals and health care centers have taken grapefruit products off the menu entirely

Drugs known to interact with grapefruit juice

- Anti-hypertensives (filodipine, nifedipine, nimodipine, nicardipine, isradipine)
- Immunosuppressants (cyclosporine, tacrolimus)
- Antihistamines (astemizole)
- Protease inhibitors (saquinavir)
- Lipid-Lowering Drugs (atorvastatin, lovastatin, simvastatin)
- Anti-anxiety, anti-depressants (buspirone, diazepam, midazolam, triazolam, zaleplon, carbamazepine, clomipramine, trazodone

Food/Nutrient Effects on Drugs

- Excretion
  - —Patients on low sodium diets will reabsorb more lithium along with sodium; patients on high sodium diets will excrete more lithium and need higher doses
  - —Urinary pH: some diets, particularly extreme diets, may affect urinary pH, which affects resorption of acidic and basic medications

Food/Nutrient Effects on Drug Action: MAOIs

- Monoamine oxidase inhibitors (MAOI) interact with pressor agents in foods (tyramine, dopamine, histamine)
- Pressors are generally deaminated rapidly by MAO; MAOIs prevent the breakdown of tyramine and other pressors
- Significant intake of high-tyramine foods (aged cheeses, cured meats) by pts on MAOIs can precipitate hypertensive crisis

Food/Nutrient Effects on Drug Action: Caffeine

- Increases adverse effects of stimulants such as amphetamines, methylphenidate, theophylline, causing nervousness, tremor, insomnia
- Counters the antianxiety effect of tranquilizers

Food/Nutrient Effects on Drug Action: Warfarin

- Warfarin (anticoagulant) acts by preventing the conversion of vitamin K to a usable form
- Ingestion of vitamin K in usable form will allow production of more clotting factors, making the drug less effective
- Pts must achieve a balance or steady state between dose of drug and consumption of vitamin K; recommend steady intake of K
- Other foods with anticlotting qualities may also have an effect (garlic, onions, vitamin E in large amounts, and ginseng)

Food/Nutrient Effects on Drug Action: Alcohol

- In combination with some drugs will produce additive toxicity
- With CNS-suppressant drugs may produce excessive drowsiness, incoordination
- Acts as gastric irritant; in combination with other irritants such as NSAIDs may increase chance of GI bleed

Food/Nutrient Effects on Drug Action: Alcohol

- Should not be combined with other hepatotoxic drugs such as acetominophen, amiodarone, methotrexate
- Can inhibit gluconeogenesis when consumed in a fasting state; can prolong hypoglycemic episode caused by insulin or other diabetes meds

Food/Nutrient Effects on Drug Action: Alcohol

- Can produce life-threatening reaction when combined with disulfiram (Antabuse) which prevents the catabolism of ethanol by the liver
  - Causes nausea, headache, flushing, increased blood pressure
- Metronidazole, Cefoperazone, chlorpropamide (Diabenese) and procarbacine cause similar symptoms

Drug Effects on Nutrition: Metabolism

- Phenobarbital and phenytoin increase metabolism of vitamin D, vitamin K, and folic acid
  - Patients on chronic tx may need supplements
- Carbamazepine may affect metabolism of biotin, vitamin D, and folic acid, leading to possible depletion

Drug Effects on Nutrition: Metabolism

- INH (anti-tuberculosis) blocks conversion of pyridoxine to active form
  - Patients with low intake at higher risk
  - May cause deficiency and peripheral neuropathy
  - Pts on long term tx may need supplements
- Hydralazine, penacillamine, levodopa and cycloserine are also pyridoxine antagonists

Drug Effects on Nutrition: Metabolism

- Methotrexate (cancer and rheumatoid arthritis) and pyrimethamine (malaria, toxoplasmosis) are folic acid antagonists
  - May treat with folinic acid (reduced form of folic acid, does not need conversion to active form) or folic acid supplements

Drug Effects on Nutrition: Excretion

- Loop diuretics (furosemide, bumetanice) increase excretion of potassium, magnesium, sodium, chloride, calcium
  - Patients may need supplements with long term use, high dosages, poor diets
  - Electrolytes should be monitored

Drug Effects on Nutrition: Excretion

- Thiazide diuretics (hydrochlorthiazide) increase the excretion of potassium and magnesium, but reduce excretion of calcium
  - High doses plus calcium supplementation may result in hypercalcemia
- Potassium-sparing diuretics (spironolactone) increase excretion of sodium, chloride, calcium
  - Potassium levels can rise to dangerous levels if pt takes K+ supplements or has renal insufficiency

Drug Effects on Nutrition: Excretion

- Corticosteroids (prednisone) decrease sodium excretion, resulting in sodium and water retention; increase excretion of potassium and calcium
  - Low sodium, high potassium diet is recommended
  - Calcium and vitamin D supplements are recommended with long term steroid use (lupus, RA) to prevent osteoporosis

Drug Effects on Nutrition: Excretion

- Phenothiazine antipsychotic drugs (chlorpromazine) increase excretion of riboflavin
  - Can lead to riboflavin deficiency in those with poor intakes
- Cisplatin causes nephrotoxicity and renal magnesium wasting resulting in acute hypomagnesemia in 90% of patients (also hypocalcemia, hypokalemia, hypophosphatemia)
  - May require intravenous mg supplementation or post-treatment hydration and oral mg supplementation
  - May persist for months or years after therapy is finished

Drug Effects on Nutrition: Absorption

- Drug-nutrient complexes: example, ciprofloxacin and tetracycline will complex with calcium, supplemental magnesium, iron, or zinc
  - Take minerals 2 to 6 hours apart from the drug
- Decreased transit time: cathartic agents, laxatives, drugs containing sorbitol, drugs that increase peristalsis

Drug Effects on Nutrition; Absorption

- Change GI environment
  - Proton pump inhibitors, H2 receptor antagonists inhibit gastric acid secretion, raise gastric pH; cimetidine reduces intrinsic factor secretion; this impairs B12 absorption; ↑ pH may impair absorption of calcium, iron, zinc, folic acid, and B-carotene

Drug Effects on Nutrition: Absorption

Damage GI Mucosa

- Chemotherapeutic agents, NSAIDs, antibiotic therapy
- Alters ability to absorb minerals, especially iron and calcium

Affect Intestinal Transport

- Cochicine (gout) paraaminosalicylic acid (TB) sulfasalazine (ulcerative colitis) trimethoprim (antibiotic) and pyrimethamine (antiprotozoal)
  - Impair absorption of B12 or folate

Drug Effects on Nutrition: Adsorption

- Cholestyramine (antihyperlipidemic bile acid sequestrant) also adsorbs fat-soluble vitamins A, D, E, K, possibly folic acid; may need supplements for long term therapy, especially if dosed several times a day
- Mineral oil: (>2 tbsp/day) ↓ absorption of fat soluble vitamins
  - take vitamins at least 2 hours after mineral oil

Drug Side Effects that Affect Nutritional Status

- Appetite changes
- Oral taste and smell
- Nausea
- Dry mouth
- Gastrointestinal effects
- Organ system toxicity
- Glucose levels

Examples of Drug Categories That May Decrease Appetite

- Antiinfectives
- Antineoplastics
- Bronchodilators
- Cardiovascular drugs
- Stimulants

Drugs That May Increase Appetite

- Anticonvulsants
- Hormones
- Psychotropic drugs
  - —Antipsychotics
  - —Antidepressants, tricyclics, MAOIs

Drugs Affecting Oral Cavity, Taste and Smell

- Taste changes: cisplatin, captopril (anti-hypertensive) amprenavir (antiviral) phenytoin (anti-convulsive), clarithromycin (antibiotic)
- Mucositis: antineoplastic drugs such as interleukin-2, paclitaxel, carboplatin
- Dry mouth: Anticholinergic drugs (tricyclic antidepressants such as amytriptyline, antihistamines such as diphenhydramine, antispasmodics such as oxybutynin

Drugs that Affect the GI Tract

- Alendronate (Fosamax) anti-osteoporosis drug—patients must sit upright 30 minutes after taking it to avoid esophagitis
- Aspirin or other NASAIDs –can cause GI bleeding, gastritis
- Orlistat – blocks fat absorption, can cause oily spotting, fecal urgency, incontinence
- Narcotic agents cause constipation

Examples of Drug Classes That Cause Diarrhea

- Laxatives
- Antiretrovirals
- Antibiotics
- Antineoplastics
- + liquid medications in elixirs containing sugar alcohols

Drugs That May Lower Glucose Levels

- Antidiabetic drugs (acarbose, glimepiride, glipizide, glyburide, insulin, metformin, miglitol, neteglinide, pioglitizone, repaglinide, roiglitizone
- Drugs that can cause hypoglycemia: ethanol, quinine, disopyramide (antiarrhythmic) and pentamidine isethionate (antiprotozoal)

Drugs That Raise Blood Glucose

- Antiretrovirals, protease inhibitors (amprenavir, nelfinavir, ritonavir, saquinavir)
- Diuretics, antihypertensives (furosemide, hydrochlorothiazide, indapamide)
- Hormones (corticosteroids, danazol, estrogen or estrogen/progesterone replacement therapy, megestrol acetate, oral contraceptives)
- Niacin (antihyperlipidemic) baclofen, caffeine, olanzapine, cyclosporine, interferon alfa-2a

Nutrition Implications of Excipients in Drugs

- Excipients: are inactive ingredients added to drugs as fillers, buffers, binders, disintegrant, flavoring, dye, preservative, suspending agent, coating
- Approved by FDA for use in pharmaceuticals
- Vary widely from brand to brand and formulation strengths of the same drug

Nutrition Implications of Excipients in Drugs

- Excipients may cause allergic or health reactions in persons with celiac disease, dye sensitivity, other allergies, inborn errors of metabolism
- Examples of excipients that might cause reactions are albumin, wheat products, alcohol, aspartame, lactose, sugar alcohols, starch, sulfites, tartrazine, vegetable oil
- Some meds may contain sufficient CHO or protein to put a patient on a ketogenic diet out of ketosis

Nutrition Implications of Excipients in Drugs

- Some drugs at usual dosages may contain enough excipients to be nutritionally significant
  - Agenerase: 1744 IU vitamin E
  - Accupril: 50-200 mg magnesium
  - Fibercon/Fiberlax: 600 mg ca+ in 6 tabs
  - Propofol (Diprivan) contains 10% soybean emulsion; may provide 1663 kcals/day for 70 kg person

Food/Nutrient Effects on Drugs – Enteral Feedings

- Most medications should not be mixed with enteral feedings; physical incompatibilities can occur including granulation, gel formation, separation of the feeding leading to clogged tubes
- Enteral feedings interfere with phenytoin absorption; window the feeding around drug dose (2 hours before and after)

Enteral Nutrition and Drugs

- Drugs put in feeding tubes may cause:
  - Diarrhea
  - Drug-nutrient binding
  - Blocked tube
- If patient does not receive total volume of enteral feeding, he/she will not receive the full dose of the drug

Enteral Nutrition and Drugs

- Avoid adding drug to formula
- When drugs must be given through tube:
  - Stop feeding, flush tube, give drug, flush
  - Use liquid form of drug (but be aware of effects of elixirs on bowel function)
  - Avoid crushing tablets

Enteral Nutrition and Drugs

- Be aware of potential interactions between enteral feedings and drugs
  - Phenytoin
  - Ciprofloxacin

MNT for Food-Drug Interactions

- Prospective: MNT offered when the patient first starts a drug
- Retrospective: evaluation of symptoms to determine if medical problems might be the result of food-drug interactions

TJC 2006 Standards Re Education on Medications

Standard PC.6.10 Elements of Performance

- As appropriate to the patient's condition and assessed needs and the hospital's scope of services, the patient is educated about the following:
  - The safe and effective use of medications
  - Nutrition interventions, modified diets, or oral health

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Avoiding Food-Drug Interactions: Prospective

- When medications are initiated, patients should be provided with complete written and verbal drug education at an appropriate reading level including food-drug interaction information
- Patients should be encouraged to ask specific questions about their medications and whether they might interact with each other or with foods
- Patients should read the drug label and accompanying materials provided by the pharmacist

Avoiding Food-Drug Interactions: Prospective

- In acute-care settings, patients receiving high risk medications should be identified and evaluated
- Nurses should have information regarding drug-food interactions and drug administration guidelines available at the bedside
- Med pass times should be evaluated in light of potential food-drug interactions

Avoiding Food-Drug Interactions: Prospective

- Systems should be established so that pharmacists can communicate with food and nutrition staff regarding high risk patients

Avoiding Food-Drug Interactions: Retrospective

- Clinicians including dietitians should obtain a full drug and diet history including the use of OTC and dietary supplements and review potential drug-food interactions
- A plan should be developed for dealing with potential drug-food interactions for short and long term drug therapy
- When therapeutic goals are not met, clinicians should ask questions about how and when drugs are being taken in relation to foods and nutritional supplements

Avoiding Food-Drug Interactions: Retrospective

- Clinicians should evaluate whether medical problems could be the result of drug-food interactions
- Often it may be the dietitian who is most aware of these issues

Avoiding Food-Drug Interactions: Example

- A 20-year-old disabled patient who was a long term resident of a nursing home was admitted to an acute care hospital for a workup to determine the cause of chronic diarrhea
- The enteral feeding had been changed numerous times in an effort to normalize the patient's bowel function
- The patient was currently receiving a defined formula feeding at a slow rate

Avoiding Food-Drug Interactions: Example

- The workup revealed no apparent medical reason for the impaired bowel function
- After reviewing the pts medications, the dietitian suggested that the patient's medications (given in liquid elixir forms containing sugar alcohols) might be causing the diarrhea
- The patient's medications were changed, and the diarrhea resolved
- The patient returned to the nursing home on a standard enteral feeding formula

Summary

- Most drugs have nutritional status side effects.
- Always look for therapeutically significant interactions between food and drugs
- Identify and monitor high risk patients, those on multiple medications and marginal diets