Food-Drug Interactions

Definition of Terms

- Drug-nutrient interaction:

  - The effect of drug on nutrient and vice versa.

- Food-drug interaction: is a broader term that includes:
  - ✓ Drug-nutrient interactions, and
  - ✓ The effect of a medication on nutritional status.

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

Key Terms

- Bioavailability of a drug:
  - % of a drug in blood that is free to function in the intended organ or tissue.

- Half-life of a drug:
  - ✓ Time period it takes blood concentration of a drug to decrease by one half.

- Side effect of a drug:
  - ✓ Adverse effect/reaction or any undesirable effect of a drug.

Other Terms

- Drug absorption rate: % absorbed and time for absorption.
- Transported drug: amount of drug in blood (free or bound).
- Metabolized drug: drug altered by enzymes in tissues.
  - ❖ Mixed-function oxidase system (MFOS): enzyme system that metabolizes many compounds such as drugs, carcinogens, compounds in foods, etc.

Pharmacokinetics

- Movement of drugs through the body by:
  - Absorption,
  - Metabolism,
  - Distribution,
  - Excretion.

Absorption

- Drug movement 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 drug.

- Food components and nutritional supplements:

  - ✓ Can interfere with absorption, especially in oral drugs.

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.

E.g.

- Low serum albumin can increase the availability & effect of drugs.

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 can:

  ➢ Increase or inhibit these enzyme systems,

  ✓ Can change the rate or extent of drug metabolism.

Excretion

Drugs are eliminated from the body as either an unchanged drug or its metabolite.

- Renal excretion is:
  - The major route of elimination,
  - Affected by renal function and urinary pH.

❖ Some drugs are eliminated in bile and other body fluids.

Pharmacodynamics

- The branch of pharmacology concerned with:
  - ✓ The effects of drugs, and
  - ✓ The mechanism of their action. (how drugs work).

  - ○ Often the drug molecule binds to a receptor, or enzyme, or ion channel, producing a physiological response.

Pharmacogenomics

- Pharmacogenomics is the study of how genes affect a person's response to drugs:

  - Genetic variations affect some people.

  Genetic variations can lead to:

  - Drug resistance: reduction in the effectiveness of medications such as:
    - Warfarin (anticoagulant),
    - Isoniazid (antibacterial to treat tuberculosis),
    - Phenelzine (antidepressant).

Therapeutic Importance of Interactions

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-Drug Interactions

- Patient with a chronic disease,
- Elderly,
- Fetuses,
- Infants,
- Pregnant women,
- Malnourished patients,
- Allergies or intolerances.

Food and Drug-Related Risk Factors for Interactions

- Special diets,
- Polypharmacy,
- Excipients (fillers) in drugs,
- Nutritional supplements,
- Tube feeding,
- Non-nutrients in foods such as:
  - Fiber,
  - Phytochemicals,
  - Herbs,
  - Preservatives,
  - Colorings,
  - Artificial sweeteners,
  - Etc.
- Alcohol intake,
- Drugs of abuse.

Malnutrition Effect on Drugs

- Low blood albumin levels can make drugs more potent by increasing availability to tissues:
  - ✓ Lower doses often recommended for persons with low albumin.

  e.g.
  - Warfarin (anticoagulant) and Phenytoin (anti-seizure):
    - Are highly protein bound in blood,
    - Low albumin can result in: hemorrhage or poor seizure control.

- Body composition:
  - ✓ Obese or Elderly persons have a higher ratio of adipose tissue
  - ➢ Fat soluble drugs may accumulate in the body and increase the risk of toxicity.

Food/Nutrient Effects on Drugs

Absorption:

- ✓ Presence of food and nutrients in the intestinal tract may affect absorption of drugs.

e.g.

- Anti-osteoporosis drugs “Fosamax” or “Actonel”:
  - ✓ Absorption is negligible if given with food and/or drinks:

    e.g. 60% decreased absorption when taken with coffee or orange juice.

Food/Nutrient Effects on Drugs Cont'd.

Absorption: Cont'd.

- ✓ Absorption of iron supplements is 50% decreased when taken with food.
- ✓ Best absorbed when taken with 8 oz. of water on empty stomach.

- ✓ Food may decrease GI upset:
  - ✓ If taken with food, avoid bran, fiber, tea, coffee, eggs, dairy products, and calcium supplements.

Food/Nutrient Effects on Drugs Cont'd.

Absorption: Cont'd.

- ✓ Ciprofloxacin and Tetracycline (antibiotics) form insoluble complexes with:
  - Calcium in dairy products or fortified foods,
  - Zinc, calcium, magnesium, 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 Cont'd. Absorption: Cont'd.

Orange or cranberry juice can:

- Increase stomach acidity, and
- Increase absorption of some drugs.

High fiber diet may:

- Decrease absorption of some drugs such as: digoxin (anti congestive hear failure):
  - ✓ Digoxin should not be taken with high phytate foods such as: wheat bran or oatmeal.

Food/Nutrient Effects on Drugs Cont'd. Grapefruit Inhibits Metabolism of Many Drugs

- Inactivates:
  - ✓ Metabolizing intestinal enzyme (CYP3A) resulting in:
    - ➢ Increase the bioavailability of oral medications,
    - ➢ 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-hypertensive drugs,
- Immuno-suppressants lower the body's ability to reject a transplanted organ,
- Antihistamines for allergies,
- Protease inhibitors: antiviral drugs that are widely used to treat HIV/AIDS and hepatitis C,
- Lipid-Lowering Drugs
- Anti-anxiety, anti-depressants.

Food/Nutrient Effects on Drugs Cont'd.

Excretion

Urinary pH:

- Some diets, particularly extreme diets,
  - May affect urinary pH,
  - Which affects resorption of acidic and basic medications.

- If urine is acidic then weak acid medications are reabsorbed back to blood from renal tubules.

- When urine is basic then weak basic drugs are reabsorbed.

Food/Nutrient Effects on Drug Action
Tyramine & MAOIs

Tyramine:

- ✓ Is a monoamine compound:
  - ➢ Found in food,
  - ➢ In the body, it is derived from the amino acid tyrosine,
- ✓ Stimulates the release of neurotransmitters such as: norepinephrine and epinephrine which increase blood pressure.

- Monoamine Oxidase Enzyme in the body is an enzyme that inactivates (metabolizes) tyramine.

MAOI Effect in the Body

- Monoamine oxidase inhibitors (MAOIs):
  - ✓ Are prescribed to treat severe depression:
    - ➢ Inhibit monoamine oxidase enzyme,
    - ➢ Block inactivation (metabolism) of tyramine.

- Increased tyramine in the body which leads to:
  - ➢ An increase in blood pressure.
    - ❖ If blood pressure rises high enough, it can be fatal!

Tyramine in Food

- Tyramine is produced in foods due to:
  - Aging,
  - Curing,
  - Fermentation, and
  - Spoilage of produce, dairy products, and meats.

- Patients on MAOIs:

  ✓ Must restrict some “High Tyramine Foods” to prevent possible fatal rise in blood pressure.

Foods Restricted on a Tyramine Controlled Diet

- Wine (red or white), beer (alcoholic & alcohol free).
- Aged cheeses, such as: aged cheddar and Swiss, blue cheeses such as: Stilton and Gorgonzola, and Camembert and cheese containing dishes.
- Cured meats, which are treated with salt & nitrate or nitrite, such as: sausages, mortadella, salami etc.
- Meat extracts such as bouillon, beef broth.
- Smoked or pickled fish.

Blue Cheese

Stilton Cheese

Gorgonzola

Camembert

Foods Restricted on a Tyramine Controlled Diet Cont'd.

- Soy sauce, fish sauce and shrimp sauce.
- Yeast-extract spreads, such as Marmite.
- Broad beans, such as: fava beans: contain dopa which is converted to dopamine (a neurotransmitter) which can raise raise blood pressure.
- Other foods, cheese filled breads, crackers & deserts; salad dressings containing cheese.
- Fermented cabbage, such as: sauerkraut.
- Pickles and olives.
- Improperly stored foods or spoiled foods.

Cheeses & Other Foods Containing Less Tyramine

- Cheeses made from pasteurized milk are less likely to contain high levels of tyramine, including:
  - American cheese,
  - Cottage cheese,
  - Ricotta,
  - Farm cheese,
  - Cream cheese,

- Other Foods
  - Fresh milk,
  - Soy milk,
  - Yogurt,
  - Sour cream,
  - Ice cream,

All fresh produce and meats are allowed, all legumes except fava beans (broad beans).

Food/Nutrient Effects on Drug Action Cont'd.

Warfarin & Vitamin K

- ✓ Warfarin is an anticoagulant.
- ✓ Ingestion of vitamin K (coagulant) makes the drug less effective.
- ✓ Pts must achieve a balance or steady state between dose of drug and consumption of vitamin K.
- ✓ Recommendation: steady intake of foods containing vitamin K.
- ✓ Food sources of vitamin K are Dark green leafy vegetables.

Food/Nutrient Effects on Drug Action

Warfarin & Other Foods Cont'd.

- Foods with anti-clotting qualities are:
  - Garlic,
  - Onions,
  - Vitamin E in large amounts,
  - Ginseng: traditionally used to help boost the immune system and lower blood sugar level.

Ginseng

- May make the drug more potent, thus increasing the effect of anticoagulant medication.

Food/Nutrient Effects on Drug Action Cont'd.

Caffeine:

- Increased effects of CNS stimulants which are used to treat ADHD [attention deficit hyperactivity disorder],
- Decreased effect of tranquilizers [anti-anxiety drug].

Alcohol: Avoid with most of the medications:

- Increases drowsiness caused by CNS-suppressant,
- Increases the chance of stomach bleeding with NSAIDs such as: Ibuprofen which cause stomach irritation,
- Increases the toxicity with hepatotoxic drugs such as drugs to treat cancers,
- Inhibits gluconeogenesis when consumed in a fasting state,
- Prolongs hypoglycemic episode caused by insulin or other diabetes medications.

Drug Effects on Nutrient Excretion

- Diuretics used to treat edema and congestive heart failure:

  - ➢ Increase excretion of potassium, magnesium, sodium, chloride, calcium.

  - ✓ Patients with long term use, high dosages, + poor diets may need supplements.

  - ✓ Electrolytes should be monitored.

Drug Effects on Nutrient Excretion

- Other diuretics increase the excretion of potassium & magnesium, but reduce excretion of calcium:
  - High doses + calcium supplementation may result in hypercalcemia.
- Potassium-sparing diuretics increase excretion of sodium, chloride, calcium, but not K^+:
  - Potassium levels can rise to dangerous levels if patient takes K^+ supplements or has renal insufficiency.

Drug Effects on Nutrient Excretion

Corticosteroids such as prednisone are steroid hormones used to treat conditions like rashes, asthma, & many other conditions:

- Low sodium excretion,
- Sodium and water retention,
- High excretion of potassium & calcium.

Recommendations:

- ✓ Diet: Low sodium, high potassium,
- ✓ Supplements: Calcium & vitamin D with long term use of steroids to prevent osteoporosis.

Drug Effects on Nutrition Excretion

- Phenothiazine (antipsychotic drug) for mental disorders:
  - Increase excretion of riboflavin,
  - Can lead to riboflavin deficiency in those with poor intake.

- Cisplatin (cancer chemotherapy drug):
  - Causes nephrotoxicity and renal magnesium wasting,
  - Resulting in acute hypomagnesemia in 90% of patients (also hypocalcemia, hypokalemia, hypophosphatemia).

    - May require supplementation.

Drug Effects on Nutrition Absorption

- Drug-nutrient complexes: e.g. ciprofloxacin & tetracycline (antibiotics):

  - Form complex with calcium in dairy and fortified foods, & from supplements of calcium, magnesium, iron, or zinc.

  - Take minerals 2 to 6 hours apart from the drug.

Drug Effects on Nutrition Absorption

- Decreased transit time which leads to decreased nutrient absorption.

  ✓ Cathartic agents which accelerate defecation:
  - Laxatives,
  - Drugs containing sorbitol,
  - Drugs that increase peristalsis,
  - Mineral oil: (>2 Tbsp./day) : Laxative
    - decreased absorption of fat soluble vitamins.
    - Take vitamins at least 2 hours after mineral oil.

Drug Effects on Nutrition Absorption

- Some drugs change GI environment.

✓ Drugs used to treat excess acid in stomach such as:

1. Proton pump inhibitors decrease gastric acid secretion.

2. H2 receptor antagonists, commonly known H2 blockers, e.g.
   - ✓ Cimetidine, an H2 blocker reduces gastric pH & intrinsic factor secretion and this impairs B12 absorption.

- When pH is high (= low acidity): may impair absorption of many nutrients such as: calcium, iron, zinc, folic acid, and B-carotene.

Drug Effects on Nutrition Absorption

Damage GI Mucosa:

- Chemotherapeutic agents, NSAIDs, and antibiotics:
  - Alter ability to absorb minerals, especially iron and calcium.
- Anti gout, anti ulcerative colitis, antibiotics, antiprotozoal (e.g. to treat Malaria or Amoeba) drugs:
  - Impair absorption of B12 and folate.

Drug Effects on Nutrition Absorption

Cholestyramine :

- Is a bile acid sequestrant [binds certain components in bile],
- Helps lower cholesterol in blood (anti-hyperlipidimic),
- Adsorbs (binds) fat-soluble vitamins A, D, E, K,
- May need supplements for long term therapy, especially if dosed several times a day.

Drug Side Effects that Affect Nutritional Status

- Appetite changes,
- Oral taste and smell,
- Dry mouth,
- Nausea,
- Gastrointestinal effects,
- Glucose levels.

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, aspartame, lactose.

- Some medications may contain sufficient CHO or protein to put a patient on a ketogenic diet out of ketosis.

Enteral Nutrition and Drugs

- Drugs put in feeding tubes may cause:
  - Diarrhea,
  - Drug-nutrient binding,
  - Blocked tube:
    - Because of granulation, gel formation, separation of the feeding which thing leads to clogged tubes.

- 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 Cont'd.

- ✓ Avoid adding drug to formula.

- ❖ When drugs must be given through tube:

  - ✓ Stop feeding, flush tube, give drug, flush tube.
  - ✓ Use liquid form of drug (but be aware of effects of elixirs on bowel function).
  - ✓ Avoid crushing tablets.

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.