Introduction to Clinical Pharmacology

Chapter 33
Antihyperlipidemic Drugs

Lipoproteins

- Low-density lipoproteins (LDLs):
  - Transport cholesterol to the peripheral cells
  - Elevation of LDLs:
    - Atherosclerotic plaque formation
    - Increases the risk for heart disease
- High-density lipoproteins (HDLs):
  - Take cholesterol from the peripheral cells and transport it to the liver

Cholesterol Levels

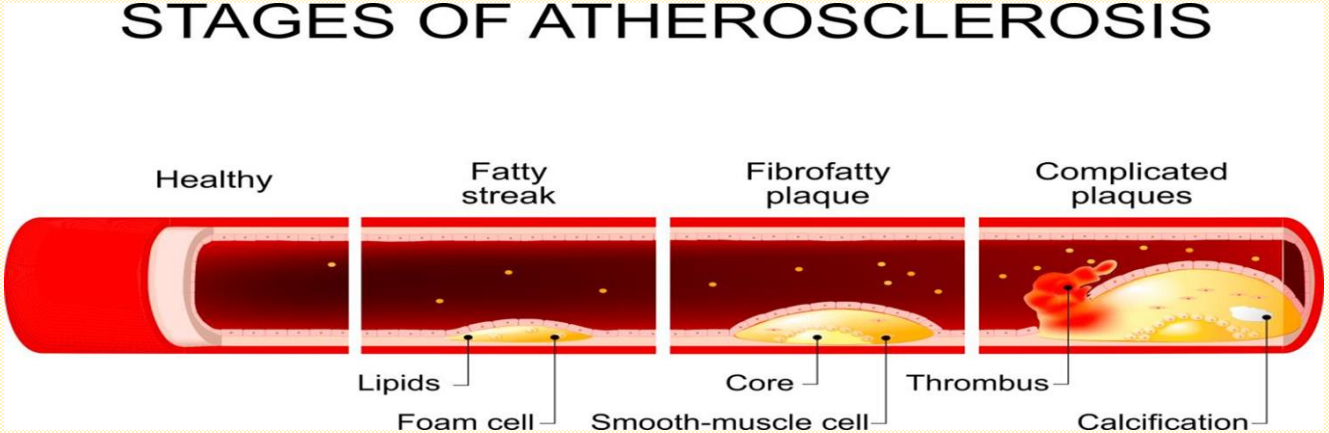
- HDL cholesterol: protects against heart disease
- The higher the LDL level, the greater the risk for heart disease
- Drugs used to treat hyperlipidemia:
  - Bile acid resins
  - HMG-CoA reductase inhibitors
  - Fibric acid derivatives
  - Niacin

HMG-CoA Reductase Inhibitors: Actions

- HMG-CoA reductase:
  - An enzyme that is a catalyst during the manufacture of cholesterol
- Inhibits the manufacture of cholesterol or promotes the breakdown of cholesterol
- Lowers the blood levels of cholesterol and serum triglycerides
- Increases blood levels of HDLs

HMG-CoA Reductase Inhibitors: Uses

- As adjunct to diet in the treatment of hyperlipidemia
- For primary prevention of coronary events
- For secondary prevention of cardiovascular events



HMG-CoA Reductase Inhibitors: Adverse Reactions

- Central nervous system reactions: headache, dizziness, insomnia, memory and cognitive impairment
- Gastrointestinal reactions: flatulence, abdominal pain, cramping, constipation, nausea, hyperglycemia in nondiabetic patients
- Other: elevated CPK level, rhabdomyolysis with possible renal failure

HMG-CoA Reductase Inhibitors: Contraindications and Precautions

- Contraindicated in patients: with hypersensitivity to the drugs, serious liver disorders
  - During pregnancy and lactation
- Used cautiously in patients with:
  - History of alcoholism, non-alcohol-related liver disease, acute infection, hypotension, trauma, endocrine disorders, visual disturbances, and myopathy

HMG-CoA Reductase Inhibitors: Interactions #1

Interactant drug	Effect of interaction
Macrolides, erythromycin, clarithromycin	Increased risk of severe myopathy or rhabdomyolysis
Amiodarone	Increased risk for myopathy and for severe myopathy or rhabdomyolysis
Niacin	Increased risk for severe myopathy or rhabdomyolysis

HMG-CoA Reductase Inhibitors: Interactions #2

Interactant drug	Effect of interaction
Protease inhibitors	Elevated plasma levels of HMG-CoA reductase inhibitors
Verapamil	Increased risk for myopathy
Warfarin	Increased anticoagulant effect

Bile Acid Resins: Actions and Uses

- Bile: manufactured, secreted by liver; stored in the gallbladder; emulsifies fat, lipids
- Increased loss of bile acids:
  - Liver uses cholesterol to manufacture more bile
- Used to treat hyperlipidemia; pruritus associated with partial biliary obstruction, gallstone dissolution

Bile Acid Resins: Adverse Reactions

- Constipation
- Aggravation of hemorrhoids
- Abdominal cramps
- Flatulence
- Nausea
- Increased bleeding tendencies related to vitamin K malabsorption, and vitamin A and D deficiencies

Bile Acid Resins: Contraindications and Precautions

- Contraindicated in patients:
  - With known hypersensitivity to the drugs
  - With complete biliary obstruction
- Used cautiously in patients:
  - With diabetes, liver disease, kidney disease, peptic ulcer
  - During pregnancy and lactation

Bile Acid Resins: Interactions #1

Interactant drug	Effect of interaction
Anticoagulants	Decreased effect of the anticoagulant (cholestyramine)
Thyroid hormone	Loss of efficacy of thyroid; also hypothyroidism (particularly with cholestyramine)
fat-soluble vitamins (A, D, E, K) and folic acid	Reduced absorption of vitamins

Bile Acid Resins : Interactions #2

Interactant drug	Effect of interaction
NSAIDS, penicillin G, tetracycline, glipizide, niacin, digitalis glycosides	Decreased serum level or decreased GI absorption
Furosemide, thiazide diuretics, hydrocortisone, methyldopa, propranolol	Decreased serum level or decreased GI absorption

Fibric Acid Derivatives: Actions #1

- Fenofibrate:
  - Reduces VLDLs
  - Stimulates catabolism of triglyceride-rich lipoproteins
  - Decreases plasma triglycerides, cholesterol

Fibric Acid Derivatives: Actions #2

- Gemfibrozil:
  - Increases excretion of cholesterol in the feces
  - Reduces the production of triglycerides by the liver
  - Lowers serum lipid levels

Fibric Acid Derivatives: Uses

- Gemfibrozil:
  - Used to treat individuals with very high serum triglyceride levels who are at risk for abdominal pain, pancreatitis
- Fenofibrate:
  - Used as adjunctive treatment for reducing LDLs, total cholesterol, triglycerides in patients with hyperlipidemia

Fibric Acid Derivatives

- Adverse reactions:
  - Nausea, vomiting, GI upset, diarrhea, cholelithiasis or cholecystitis
- Contraindicated in patients:
  - With hypersensitivity to the drugs and those with significant hepatic or renal dysfunction or primary biliary cirrhosis
- Used cautiously in patients:
  - With peptic ulcer disease, diabetes; during pregnancy and lactation

Fibric Acid Derivatives: Interactions #1

Interactant drug	Effect of interaction
Anticoagulants	Enhanced effects of the anticoagulants (particularly with gemfibrozil and fenofibrate)
Cyclosporine	Decreased effects of cyclosporine (particularly with gemfibrozil)

Fibric Acid Derivatives: Interactions #2

Interactant drug	Effect of interaction
HMG-CoA	Increased risk for rhabdomyolysis (particularly with gemfibrozil and fenofibrate)
Sulfonylureas	Increased hypoglycemic effects (particularly with gemfibrozil)

Miscellaneous Antihyperlipidemic Drugs: Niacin and Ezetimibe

- Action: lowers blood lipid levels
- Uses: adjunctive therapy for lowering very high serum triglyceride levels in patients who are at risk for pancreatitis
- Adverse reactions:
  - Gastrointestinal reactions: nausea, vomiting, abdominal pain, diarrhea
  - Other reactions: severe generalized flushing of the skin, sensation of warmth, severe itching or tingling

Miscellaneous Antihyperlipidemic Drugs: Contraindications and Precautions

- Contraindicated in patients:
  - With known hypersensitivity to niacin, active peptic ulcer, hepatic dysfunction, and arterial bleeding
- Used cautiously in patients with:
  - Renal dysfunction, high alcohol consumption, unstable angina, gout, pregnancy

Nursing Process: Assessment

- Preadministration assessment:
  - Take a dietary history; record vital signs and weight; inspect skin and eyelids for evidence of xanthomas
- Ongoing assessment:
  - Monitor liver function tests, such as serum transaminase levels
  - Frequently monitor blood cholesterol and triglyceride levels
  - Periodic lipid profiles

Nursing Process: Diagnoses

- **Constipation** related to antihyperlipidemic drugs
- **Risk for Imbalanced Nutrition: Less Than Body Requirements** related to malabsorption of vitamins
- **Risk for Impaired Skin Integrity** related to rash and flushing
- **Nausea** related to antihyperlipidemic drugs
- **Risk for Injury** related to dizziness

Nursing Process: Planning

- Expected outcome:
  - Optimal response to therapy
  - Management of common adverse drug reactions
  - Understanding of the dietary measures necessary to reduce lipid and lipoprotein levels

Nursing Process: Implementation #1

- Promoting an optimal response to therapy:
  - Explain drug regimen and possible adverse reactions
  - Emphasize the importance of following printed dietary guidelines

Nursing Process: Implementation #2

- Monitoring and managing patient needs:
  - Constipation: increase fluid intake, eat foods high in dietary fiber, exercise daily
  - Risk for imbalanced nutrition: less than body requirements
    - Bile acid resins used for long-term therapy: administer vitamins A, D in water-soluble form or parenterally

Nursing Process: Implementation #3

- Monitoring and managing patient needs (cont.)
  - Risk for impaired skin integrity: contact health care provider
  - Nausea: take drug with meal; provide patient with several small meals rather than three large meals
  - Risk for injury: place the call light within easy reach

Nursing Process: Implementation #4

- Monitoring and managing patient needs (cont.)
  - Potential complication:
    - Vitamin K deficiency: include foods high in vitamin K in the patient's diet
    - Rhabdomyolysis: be alert for unexplained muscle pain, muscle tenderness, or weakness, especially if accompanied by malaise or fever

Nursing Process: Implementation #5

- Educating the patient and family:
  - Provide and review the recommended diet with the patient and family
  - Explain the importance of taking the drug at prescribed time intervals and as directed
  - Explain the necessity of contacting the primary health care provider immediately if symptoms occur

Nursing Process: Evaluation #1

- Therapeutic effect is achieved; serum lipid levels are decreased
- Adverse reactions are identified, reported, and managed successfully
- Improved bowel movements
- Nutritional vitamin needs will be met

Nursing Process: Evaluation #2

- Skin will remain intact
- Nausea is controlled
- The patient reports no injury related to dizziness or falls
- The patient and family demonstrate understanding of the treatment regimen