PHARMACOLOGY II KRNMHP

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HEMATOLOGIC DRUGS – ANTI COAGULANTS

- Anti coagulant refers to any substance which inhibits normal blood clotting, lowers coagulability of blood.
- The anti coagulant interfere with normal coagulation process by interfering with the clotting cascade and thrombin formation.
- These agents are used to inhibit clot formation but they do not dissolve existing clots.

Classification of anticoagulants

- **Parenteral anticoagulants:**

Heparin

- **Low molecular weight heparin;** enoxaparin, dalteparine, nadroparin, arteparin.
- Semisynthetic heparinoid; heparin sulphate, dextran sulphate, ancrod, danaparoid.
- Others; lepirudin, bivalirudin, argatroban

- **Oral anticoagulant;** warfarin, acenocoumarin, dicoumarol

HEPARIN

mechanism of action: heparin acts prophylactically to prevent the formation of clots in the vasculate.it activates **anti thrombin III** which inhibits thrombin and clotting factor IX, X, XI, XII, consequently conversion of fibrinogen to fibrin does not occur and the formation of a fibrin clot is prevented

Therapeutic Uses

Heparin sodium, LMWH, fondaparinux sodium

- In conditions necessitating prompt anticoagulant activity (evolving stroke, pulmonary embolism, massive deep venous thrombosis)
- As an adjunct for clients having open heart surgery or renal dialysis
- As low-dose therapy for prophylaxis against postoperative venous thrombosis (for example, hip/knee replacement surgery, abdominal surgery)
- In conjunction with thrombolytic therapy when treating an acute myocardial infarction
- Treatment of disseminated intravascular coagulation

Administration

- These medications cannot be absorbed by the intestinal tract and must be given by subcutaneous injection or IV infusion.
- Heparin sodium: Subcutaneously every 12 hr., continuous or intermittent IV infusion
- Enoxaparin, dalteparin sodium, tinzaparin: Subcutaneously every 12 hr. for 2 to 8 days
- Fondaparinux sodium: Subcutaneously every 12 hr. for 5 to 9 day.

Side/Adverse Effects

- Hemorrhage secondary to heparin overdose
- thrombocytopenia,
- Hypersensitivity reactions (chills, fever, urticaria)
- Administer a small test dose prior to the administration of heparin. Toxicity/overdose
- Administer **protamine sulfate**, which binds with heparin and forms a heparin-protamine complex that has no anticoagulant properties.
- Protamine sulfate should be administered slowly intravenously, no faster than 20 mg/min or 50 mg in 10 min.

Enoxaparin

- **Hemorrhage** Monitor vital signs • Advise clients to observe for signs and symptoms of bleeding, such as increased heart rate, decreased blood pressure, bruising, petechiae, hematomas, black tarry stools. • Monitor platelet count. Instruct client to avoid aspirin.
- **Neurologic damage** from hematoma formed during spinal or epidural anesthesia
- **Thrombocytopenia**, as evidenced by low platelet count , Monitor platelets. Discontinue medication for platelet count less than 100,000/mm3 .
- **Toxicity/overdose;** Administer **protamine sulfate**

- **Contraindications/Precautions**
- Parenteral anticoagulants are contraindicated in clients with low platelet counts (thrombocytopenia) or uncontrollable bleeding.
- These medications should not be used during or following surgeries of the eye(s), brain, or spinal cord; lumbar puncture; or regional anesthesia.
- clients who have **hemophilia**, increased capillary permeability, dissecting **aneurysm**, **peptic ulcer disease**, **severe hypertension, hepatic** or **renal disease**, or **threatened abortion**

Medication/Food Interactions

- Anti-platelet agents such as aspirin, NSAIDs, and

Nursing Administration; Heparin sodium:

- Obtain the client's baseline vital signs.
- Obtain baseline and monitor complete blood count (CBC), platelet count, and hematocrit levels.
- Read label carefully. Heparin is dispensed in units and in different concentrations.
- Check dosages with another nurse before administration.
- Use an infusion pump for continuous IV administration. Monitor rate of infusion every 30 to 60 min.
- Monitor PTT every 4 to 6 hr. until appropriate dose is determined, then monitor daily.
- For subcutaneous injections, use a 20 to 22 gauge needle to withdraw medication from the vial. Then, change the needle to a smaller needle (gauge 25 or 26, 1/2 to 5/8 in length).
- Administer deep subcutaneous injections in the abdomen ensuring a distance of 2 inches from the umbilicus. Do not aspirate.
- Apply pressure for 1 to 2 min after the injection. Rotate and record injection sites.
- Instruct clients to monitor for signs of bleeding (bruising, gums bleeding, abdominal pain, nose bleeds, coffee-ground emesis and tarry stools).
- Instruct clients not to take over-the-counter NSAIDs, aspirin, or medications containing salicylates.
- Advise clients to use an electric razor for shaving and a soft toothbrush.

ORAL ANTI COAGULANTS

- These are the most commonly used oral anti coagulants;
- Warfarin,
- Dicoumarol,
- Acenocoumarol

Mechanism of action

Vitamin K antagonist; these agents inhibit the liver synthesis of vitamin K clotting factor II,VII, IX, X.

Advantages over heparin

- Bioavailability is almost 100 percent.
- Low volume distribution,
- Long half life.

Pharmacokinetics

- Produces delayed action,
- possibility of genetic resistance

Clinical indications

- Treatment deep venous thrombosis.
- Pulmonary embolism
- Prevent blood clotting in patients with thrombophlebitis, pulmonary embolism and embolism from arterial fibrillation.

Contraindication /precaution

- Not given to pregnant women because it crosses the placenta barrier, it is teratogenic, and can cause an a abortion.
- Not given to patients with bleeding disorders e.g. hemophilia, peptic ulcer, sever renal/ liver disease and eclampsia.

Monitoring

- Monitor prothrombin time usually done before administering the dose.
- The PT SHOULD BE 1.5-2.5 times the reference value to be therapeutic
- If it is below the recommended range warfarin should be increased.
- If it above the recommended range warfarin should be decreased.

Adverse effects of warfarin

- Hematologic effects: increased bleeding, thrombocytopenia
- Anorexia, nausea, vomiting, diarrhoea and dermatitis.
- Hemorrhage
- Interference with bone formation in early pregnancy

Drug interaction

Potentiation activity

- Inhibition of metabolism: chloramphenicol, ciprofloxacin, cotrimoxazole, cimetidine.
- Displacement from plasma protein; ethacrynic acid.
- Platelet function inhibition; NSAIDs (Aspirin)

retarded activity

- inhibition of absorption; Sucralfate
- Enzyme induction; barbiturates, carbamazepine, rifampicin

acenocoumarol

- take 2-3 DAYS.

Indication

- Arterial fibrillation,
- pulmonary embolism,
- prophylaxis following insertion of heart valve.

adverse drug reaction

Alopecia, diarrhoea, hepatic dysfunction, pancreatitis vomiting

Nursing Administration of warfarin

- Administration is usually oral, once daily.
- Obtain the client's baseline vital signs.
- Monitor PT levels (therapeutic level 18 to 24 sec) and INR levels (therapeutic levels 2 to 3). INR levels are the most accurate. Hold dose and notify the provider if these levels exceed therapeutic ranges.
- Obtain baseline and monitor CBC, platelet count, and Hct levels.
- Instruct clients that anticoagulant effects may take 8 to 12 hr and full therapeutic effect is not achieved for 3 to 5 days. For clients in the hospital setting, explain the need for continued heparin infusion when starting oral warfarin.

Nursing Administration of warfarin

- Advise clients that anticoagulation effects can persist for up to 5 days following discontinuation of medication because of long half-life.
- Advise clients to avoid alcohol and over-the-counter and non-prescription medications to prevent adverse effects and medication interactions, such as risk of bleeding.

Nursing Administration of warfarin

- Advise clients to employ nonmedication measures to avoid development of thrombi, including avoiding sitting for prolonged periods of time, not wearing constricting clothing, and elevating and moving legs when sitting.
- Advise clients to wear a medical alert bracelet indicating warfarin use.

Nursing administration of warfarin

- Be prepared to administer vitamin K for warfarin overdose.
- Teach clients to self-monitor PT and INR at home as appropriate.
- Advise clients to record dosage, route, and time of warfarin administration on a daily basis.
- Plan for frequent PT monitoring for clients who are prescribed medications that interact with warfarin. The client is at greatest risk for harm when the interacting medication is being deleted or added. Frequent PT monitoring will allow for dosage adjustments as

Thrombolytic /Fibrinolytic Medications

Two phenomena which causes hemostasis include,

- Coagulation of blood .
- Formation of a thrombus

formation of a thrombus is restricted through:

1. **Fibrin inhibition:** anti thrombin III, Ant plasmin, Antitrypsin, Macroglobulin
2. **Fibrinolysis:** tissue plasminogen activator and CF XII activate fibrin bound plasminogen to active plasmin, restrict formation of a thrombus.

Mechanism of action of fibrinolytic

Thrombolytic/fibrinolytic medications dissolve clots that have already formed. Clots are dissolved by conversion of plasminogen to plasmin, which destroys fibrinogen and other clotting factors. The result is clot disintegration.

The commonly used fibrinolytic include:

- Streptokinase (Streptase)
- Urokinase
- Alteplase (Activase, tPA),
- Anistreplase
- Reteplase (Retavase)

streptokinase

Mechanism of action:

- streptokinase is a semi synthetic that acts systematically to dissolve the blood clot by activating plasminogen to plasmin.

Clinical indication

- Acute myocardial infarction
- Deep vein thrombosis (DVT)
- Massive pulmonary emboli
- thrombo embolic stroke (alteplase)
- Peripheral arterial thrombosis
- To open clotted iv catheters

Adverse reaction

- Allergic reaction (urticaria, itching, flushing, bronchospasms); possible severe anaphylactic reaction.
- Serious risk of bleeding from different sites (within brain, needle puncture sites, wounds)
- Hypotension
- Arrhythmias

Contraindications/Precautions

- Any prior intracranial hemorrhage (hemorrhagic stroke)
- Active internal bleeding
- History of significant closed head or facial trauma in the past 3 months
- Acute pericarditis
- Brain tumors
- Use cautiously in clients who have severe hypertension, a recent episode of ischemic stroke (6 months prior to start of treatment), or a recent major surgery (2 to 4 weeks prior to start of treatment).

urokinase

- Isolated from human renal cells from tissue cultures.
- Helps in direct conversion of plasminogen to plasmin.

Therapeutic uses

- Myocardial infarction.
- Venous thrombosis.
- Pulmonary embolism.

Adverse reaction

- Fever.
- Hemorrhage.

alteplase

Mechanism of action

- Recombinant tissue plasminogen activator (t-PA)
- helps in Critical activation of plasminogen bound in fibrin clot. Reduces the risk of systemic bleeding to an appreciable extent.
- Half life 4-8 minutes
- More efficacious than others

Therapeutic use

Lysis of occlusive coronary artery thrombi associated with myocardial infarction.

Deep venous thrombosis.

Ischemic cerebrovascular disease

Adverse reaction

- Nausea
- Fever
- Rash, pruritic
- Mild hypertension
- Localized bleeding

Nursing Administration of thrombolytic agents

- Use of thrombolytic agents must take place within 4 to 6 hr. of onset of symptoms
- monitor in a setting that provides for close supervision and continuous monitoring during and after administration of the medication.
- Obtain baseline platelet counts, hemoglobin (Hgb), hematocrit (Hct), a PTT, PT, INR, and fibrinogen levels, and monitor periodically.
- Obtain baseline vital signs (heart rate, blood pressure) and monitor frequently per protocol.
- Nursing care includes continuous monitoring of hemodynamic status to assess for therapeutic and adverse effects of thrombolytic (relief of chest pain, signs of bleeding). Follow facility protocol.
- Provide for client safety per facility protocol.
- Ensure adequate IV access for administration of emergency medications and availability of emergency equipment.
- Do not mix any medications in IV with thrombolytic agents.

Nursing administration cont.’

- Minimize bruising or bleeding by limiting venipunctures and subcutaneous/intramuscular injections.
- Discontinue thrombolytic therapy if life-threatening bleeding occurs. Treat blood loss with whole blood, packed red blood cells, and/or fresh frozen plasma. IV aminocaproic acid (Amicar) should be available for administration in the event of excessive fibrinolysis.
- Following thrombolytic therapy, administer heparin or aspirin as prescribed to decrease the risk of rethrombosis.
- Following thrombolytic therapy, administer beta blockers as prescribed to decrease myocardial oxygen

Medication/Food Interactions

- Decreased folate levels with concurrent use of sulfonamides, sulfasalazine, or methotrexate.

Nursing Administration

- Assess clients for signs and symptoms of megaloblastic anemia (pallor, easy fatigability, palpitations, paresthesia of hands or feet).
- Obtain the client's baseline folic acid levels, RBC and reticulocyte counts, Hgb, and Hct levels. Monitor periodically.
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- Advise clients with folic acid deficiency to concurrently increase intake of food sources of folic acid, such as green leafy vegetables and liver. Monitor clients for risk factors indicating that folic acid therapy may be needed, such as heavy alcohol use and child-bearing age.

NB :vitamin B12 will be covered in nutrition.

MUSCLE RELAXANT/ NEUROMUSCULAR BLOCKING AGENTS

- Neuromuscular blocking agents have various uses including assisting with:

✓ sedation during general anesthesia,

✓ control of seizures during electroconvulsive therapy,

✓ suppression of gag reflex during endotracheal intubation**.**

- Medications include **succinylcholine (Anectine)** and **vecuronium (Norcuron)**

Neuromuscular agents cont.’

Muscle relaxants and antispasmodic agents can affect both the central and peripheral nervous systems.

- These agents are used with spasticity related to muscle injury, cerebral palsy, spinal cord injury, and multiple sclerosis.
- Agents include **diazepam** (Valium), **baclofen** (Lioresal), and **dantrolene** (Dantrium).
- **Bethanechol (Urecholine),** a muscarinic agonist, is used for urinary retention.
- **Oxybutynin (Ditropan),** a muscarinic antagonist, is used for neurogenic bladder

Muscle relaxant/ Neuromuscular Blocking Agents cont.’

Depolarizing neuromuscular blocker: succinylcholine (Anectine)

Nondepolarizing neuromuscular blockers: pancuronium (Pavulon)

Other Medications:

Nondepolarizing neuromuscular blockers: atracurium (Tracrium), Vecuronium (Norcuron)

Expected Pharmacological Action

Neuromuscular blocking agents block acetylcholine (ACh) at the neuromuscular junction, resulting in muscle relaxation and hypotension. They do not cross the blood-brain barrier, so complete paralysis can be achieved without loss of consciousness or decreased pain sensation.

Neuromuscular agents cont.’

Therapeutic Uses

- Neuromuscular blocking agents are used as adjuncts to general anesthesia to promote muscle relaxation.
- These agents are used to control spontaneous respiratory movements in clients receiving mechanical ventilation.
- These agents are used as seizure control during electroconvulsive therapy.
- Neuromuscular blocking agents are used during endotracheal intubation and endoscopy

Side effect

- Respiratory arrest from paralyzed respiratory muscles
- Hypotension
- Low pseudo cholinesterase activity can lead to prolonged apnea
- Signs of malignant hyperthermia include muscle rigidity accompanied by increased temperature, reaching levels as high as 43° C (109.4° F).
- After 12 to 24 hr. postoperative, clients may experience muscle pain in the upper body and back.
- Hyperkalemia

Drug interaction

General anesthetics are often used concurrently in surgery.

- Dosage of tubocurarine should be reduced to prevent extreme neuromuscular blockade.

Aminoglycosides and tetracyclines can increase the effects of neuromuscular blockade.

- Take complete medication history of clients who are to receive neuromuscular blockade.

Neostigmine and other cholinesterase inhibitors increase the effects of depolarizing neuromuscular blockers, such as succinylcholine.

- Monitor clients during neuromuscular blockade reversal after surgery

Nursing Administration

- Clients must receive continuous cardiac and respiratory monitoring during therapy.
- Monitor clients for respiratory depression and have life support equipment available.
- Carefully monitor clients for return of respiratory function.

LOCAL ANAESTHETICS

- local anesthetic bind reversibly to a specific receptor site within the pore of the sodium channels in nerves and block ion movement when applied locally to nerve tissues in appropriate concentration.
- Local anesthetic can act on any part of the nervous system, on every type of nerve fibers, reversibly blocking the action potentials responsible for nerve conduction.
- Thus a local anesthetic in contact with a nerve trunk can cause both sensory and motor paralysis in the area innervated

Mechanism of action

- Local anesthetic block conduction by decreasing or preventing the large transient increase in the permeability of excitable membranes.
- This action is due to direct interaction with voltage gated sodium channels.
- As the anesthetic action progressively develops in the nerve ,the threshold for electrical excitability increase. The rate of rise of the action potential also declines, impulse conduction slows, and nerve conduction eventually fails

Local anesthetics

Drug	Duration of action
lidocaine	medium
Bupivacaine (Marcaine),levobupivacaine (chirocaine)	long
Ropivacaine (naropin)	long
Mepivacaine (carbocaine, isocaine)	medium
articaine	medium
benzocaine	Surface use only
Cocaine	medium
Procaine	short

Neuromuscular agents

The action of non depolarizing muscle relaxant is antagonized, once muscle paralysis is no longer desired with an acetylcholinesterase inhibitor such as **neostigmine** or **edrophonium**

Skeletal muscle relaxants

Succinylcholine

- Succinylcholine mimics ACh by binding with cholinergic receptors at the neuromuscular junction. This agent fills the cholinergic receptors, preventing ACh from binding with them, and causes sustained depolarization of the muscle, resulting in muscle paralysis.

Reversal agent: Pseudo cholinesterase enzyme

- **Pancuronium, atracurium, vecuronium**
- These agents block ACh from binding with cholinergic receptors at the motor end plate. Muscle paralysis occurs because of inhibited nerve depolarization and skeletal muscle contraction.
- **Reversal agent:** Neostigmine (Prostigmin)

General anesthetics

- General anesthetics depress the CNS sufficiently to permit surgery and other noxious or unpleasant procedures.
- Gas have a low therapeutic indices and are require great care in administration.
- The consideration of patients age, associated medical condition and medication use is important.
- The physiological state induced by general anesthesia include; **analgesia**, **amnesia, loss of consciousness**,

a)Parenteral anesthetics

Pharmacokinetic principle

- After a single intravenous bolus these drugs preferentially partition into the highly perfused and lipophilic tissues of the brain and the spinal cord where they produce anesthesia within a single circulation.
- Blood levels falls rapidly, resulting in drug redistribution out of the cns back into the blood.
- The anesthetics then perfuse into less perfused tissues such as muscle and viscera , and at a slower rate into the

Parenteral anesthetics

- **Thiopental** and **Propofol** are the two most commonly used parenteral agents.
- **thiopental** has a long established track record of **safety.**
- **Propofol** is advantageous for procedures where **rapid return** to a preoperative mental status is desirable.
- **Etomidate** usually is reserved for patients at risk for **hypotension** and /**myocardial ischemia**
- **Ketamine** is best suited for patients with **asthma**, **children** undergoing short ,painful procedures

Pharmacological characteristics of parenteral anesthetics (IV)

DRUG	INDUCTION AND RECOVERY	COMMENTS
etomidate	Rapid onset and moderate fast recovery	Provides cardiovascular stability, causes decreased steroidal genesis and involuntary muscle movement
ketamine	Moderate onset and recovery	Causes cardiovascular stimulation, increase cerebral blood flow and emergence reaction that impair recovery
midazolam	Slow onset and recovery; flumazenil reversal available	Provides cardiovascular stability and marked amnesia, used in balanced anesthesia and conscious sedation.
Propofol	Rapid onset and recovery	Used in induction and maintenance can cause hypotension ,has useful antiemetic action.
thiopental	Rapid onset and recovery (bolus dose) slow recovery following infusion.	Standard induction agent, causes cardiovascular depression, avoid in porphyria's
fentanyl	Slow onset and recovery. Naloxone reversal available	opioid used in balanced anesthesia and conscious sedation produces marked analgesia

Inhalation anesthetics

- They have a low safety margin.
- The selection of inhalation anesthetic is often marching a patient pathophysiology with drug side effects.
- The inhalation anesthetics also vary widely in their physical properties, which govern the pharmacokinetics of the inhalation agents
- They produce a rapid induction of anesthesia and a rapid recovery following discontinuation.
- Examples are: **nitrous oxide, halothane,** desflurane, sevoflurane, enflurane, and methoxyflurane.

Side effect of anesthetics

- Hemodynamic effect e.g. decrease in systemic arteria BP.
- respiratory effects; elimination of both ventilatory drive and reflex that maintain airway patency, gag reflex is lost, no cough stimulus, lower esophageal sphincter tone is reduced.
- Hypothermia, nausea and vomiting.

Other emergence Postoperative effects

- Hypotension and tachycardia,
- myocardial ischemia,
- post anesthesia shivering, (give small dose of **meperidine** 12 mg lowers the shivering triggers temperature.
- Airway obstruction
- Respiratory suppression
- Hypoxemia may occur
- Negative pressure pulmonary edema may occur due to strong inspiratory efforts against a closed glottis
- pain control can be complicated
- These emergence phenomena can be greatly reduced when opioids are employed as part of the intraoperative regimen

Drugs acting on the GIT system

GIT DRUGS (**PEPTIC ULCER DISEASE)**

acid peptic disease includes:

- peptic ulcers (gastric ulcer, duodenal ulcer , NSAIDS induced ulcers)
- gasro oesophageal reflux disease,
- hypersecretory states like Zollinger Ellison Syndrome (ulcerogenic tumour of the islets of Langerhans.

Principles of therapy

The aim of therapy is to;

- relieve symptoms,
- induced ulcer healing and cure in the long run
- Decreased risk of complications
- Stopping reoccurrence .

Classification of agents used in treatment of peptic ulcer:

- **Inhibition of acid secretion**
  - H2 receptor agonist e.g. cimetidine, ranitidine, famotidine roxatidine.
  - Proton pump inhibitors e.g. omeprazole, pantoprazole, esomeprazole, lansoprazole.
  - Anticholinergics e.g. pirenzepine.
  - Prostaglandin analogue e.g. misoprostol.
- **neutralization of gastric acids**
  - Sodium bicarbonate systemic
  - Non systemic: magnesium hydroxide, aluminium hydroxide, magnesium trisilicate.

- **Mucosal protective agents** e.g. sucralfate, colloidal bismuth.
- **Anti helicobacter pylori drugs (ANTIBIOTICS)** e.g. Clarithromycin, Ampicillin, Metronidazole, Tetracycline, Tinidazole

anti H. pylori drugs

- Amoxicillin (Amoxil)
- Bismuth (Pepto-Bismol)
- Clarithromycin (Biaxin)
- Metronidazole (Flagyl)
- Tetracycline

Expected Pharmacological Action

- Eradication of H. pylori bacteria
- Therapy should include: Combination of 2 or 3 antibiotics for 14 days

Two weeks regimen

- Tetracycline 500mg QID and metronidazole 200mg BID and Bismuth sub salylicylate.
- Amoxicillin 100mg BID and clarithromycin 500mg BID+ Lansoprazole 30mgs BID.
- Clarithromycin 500mg TDS +Omeprazole.

ONE WEEK REGIMEN

Clarithromycin 250mg BID + Metronidazole 400mgs + Omeprazole 20mgs BID.

Amoxicillin 500mg Bid + Clarithromycin 250mg Bid+ Omeprazole 20mg

Histamine2 -Receptor Antagonists

- ranitidine hydrochloride (Zantac)
- Cimetidine (Tagamet)
- Nizatidine (Axid)
- Famotidine (Pepcid)

Expected Pharmacological Action: Histamine2-receptor antagonists suppress the secretion of gastric acid by selectively blocking H2 receptors in parietal cells lining the stomach

- **Therapeutic Uses**
- gastric and peptic ulcers,
- gastroesophageal reflux disease (GERD),
- hypersecretory conditions, such as Zollinger-Ellison syndrome.
- Histamine2-receptor antagonists are used in conjunction with antibiotics to treat ulcers caused by H. pylori.

Side/Adverse Effects

- Cimetidine may block androgen receptors, resulting in decreased libido and impotence.
- Cimetidine may cause CNS effects (lethargy,

Contraindications/Precautions

- These medications are Pregnancy Risk Category B
- Use in older adults can cause antiadrenergic effects (e.g., impotence) and CNS effects (e.g., confusion).
- H2-receptor antagonists decrease gastric acidity, which promotes bacterial colonization of the stomach and the respiratory tract. Use cautiously in clients who are at a high risk for pneumonia, such as clients with chronic obstructive pulmonary disease (COPD).

Medication/Food Interactions

- Cimetidine can inhibit medication metabolizing enzymes and thus increase the levels of warfarin, phenytoin (Dilantin), theophylline, and lidocaine.
- Concurrent use of antacids can decrease absorption of histamine2 -receptor antagonists.

Nursing Administration

Cimetidine, ranitidine, and famotidine can be administered IV for acute situations.

Advise clients to practice good nutrition. Suggest eating six small meals rather than three large meals a day.

Inform clients that adequate rest and reduction of stress may promote healing.

Clients should avoid smoking, because smoking can delay healing.

Encourage clients to avoid aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) unless taking low-dose aspirin therapy for prevention of cardiovascular disease.

If alcohol exacerbates symptoms, advise clients to stop drinking.

- Availability of these medications OTC may discourage clients from seeking appropriate health care.
- Encourage clients to see the provider if symptoms persist.
- The medication regimen can be complex, often requiring clients to take two to three different medications for an extended period of time. Encourage clients to adhere to the medication regimen and provide support.
- Ranitidine can be taken with or without food

Proton Pump Inhibitor

- omeprazole (Prilosec)
- Pantoprazole (Protonix)
- Lansoprazole (Prevacid)
- Rabeprazole sodium (AcipHex)
- Esomeprazole (Nexium)

Expected Pharmacological Action

- Proton pump inhibitors reduce gastric acid secretion by irreversibly inhibiting the enzyme that produces gastric acid.
- Proton pump inhibitors reduce basal and stimulated acid production.

Therapeutic uses

- gastric and peptic ulcers,
- GERD,
- hypersecretory conditions such as Zollinger-Ellison syndrome.

Complications

- Insignificant side effects and adverse effects with short-term treatment
- Low incidence of headache, diarrhea, and nausea/vomiting

- **Contraindications/Precautions**
- These medications are Pregnancy Risk Category C.
- Use cautiously with children and women who are breastfeeding.
- Contraindicated for clients hypersensitive to medication
- These medications increase the risk for pneumonia. Omeprazole decreases gastric acid pH, which promotes bacterial colonization of the stomach and the respiratory tract. Use cautiously in clients at high risk for pneumonia, such as clients with COPD.
- Long-term use of proton pump inhibitors increases the risk of gastric cancer and osteoporosis.

- **Medication/Food Interactions**
- Digoxin (Lanoxin) levels may be increased when used concurrently with omeprazole.
- Monitor digoxin levels carefully if prescribed concurrently.
- Absorption of ketoconazole (formerly Nizoral), itraconazole (Sporanox), and atazanavir (Reyataz) is extremely decreased when taken concurrently with proton pump inhibitors.

Nursing Administration

- Do not crush, chew, or break sustained-release capsules.
- Clients may sprinkle the contents of the capsule over food to facilitate swallowing.
- Clients should take omeprazole once a day prior to eating in the morning.
- Encourage clients to avoid alcohol and irritating medications such as NSAIDs.

- Active ulcers should be treated for 4 to 6 weeks.
- **Pantoprazole (Protonix)** can be administered to clients intravenously. In addition to low incidence of headache and diarrhea, there may be irritation at the injection site leading to thrombophlebitis. Monitor the client's IV site for signs of inflammation (redness, swelling, local pain) and change the IV site if indicated.
- Teach clients to notify the provider for any sign of obvious or occult GI bleeding such as coffee-ground emesis.

ANTICHOLINERGICS

Piperazine :

- it is a selective M1 receptor blocker
- Produces less effects.
- Reduces acid secretion by 40 to fifty percent
- Has a small therapeutic window

Prostaglandins analogue

- They have o cytoprotective role by inhibiting acid secretion by increasing mucus and bicarbonate secretion.
- Inhibit gastrin secretion and increase mucosal blood flow.

misoprostol

- a synthetic pge1 analogue and inhibits acid output.
- ulcer heal in 4 to six weeks but relieving pain

Therapeutic Use

prevent ulceration and bleeding induced by NSAIDS

MUCOSAL PROTECTANT

sucralfate (Carafate)

Expected Pharmacological Action

The acidic environment of the stomach and duodenum changes sucralfate into a thick substance that adheres to an ulcer. This protects the ulcer from further injury that may be caused by acid and pepsin.

This viscous substance can stick to the ulcer for up to 6 hr.

Therapeutic Uses

- promotes healing of duodenal and gastric ulcers
- Poorly absorbed systemically, not used frequently due to a large doses.
- Should not be used with antacids, H2 Antagonist, PPIs as it is dependent on gastric PH.

colloidal bismuth compounds

- promote healing of duodenal and gastric ulcers.
- Act by binding to an ulcer, denaturing the protein and creating a physical barrier.
- Inhibition of pepsin, activation of mucous production, increase of prostaglandins.
- It is effective in healing of duodenal and gastric ulcers.
- Effective in non ulcer gastritis, caused by H.pylori

considerations

- take before meals and at bed time for 4 to 8 weeks.
- Poor acceptance due to blackening of tongue, dentures and stool
- inconvenience of dosing used as a regimen of multiple therapy for H.Pylori not used alone.

LAXATIVES

This are drugs tha promote deafacation

*laxatives; mild action

*Purgative; strong action

*Classification

Bulk forming purgatives

- Magnesium sulphate, magnesium hydroxide, sodium phosphate, lactulose, sodium tartrate, osmotic cathartic.
- Vegetable fibres, bran
- Hydrophillic colloids, methyl cellulose

- **Irritants and stimulants**
  - Diphenylmethanes; phenolphthalein, Bisacodyl
  - Anthraquinone derivatives; senna, cascara
  - Fixed oil; castor oil
- **Stool softeners;** docusate, mineral oil, glycerin suppositories

Mechanism of action of laxatives

- Laxatives cause retention of fluid in colonic contents increasing bulk and softness of stool and its transit.
- They may decrease absorption of water and electrolyte by acting on intestinal mucosa.
- They may enhance intestinal motility reducing absorption of water.

Bulk forming purgatives

Osmotic or saline cathartics

- They are poorly absorbed hold water through osmosis.
- In addition the ions stimulate secretion and motility.
- Main used salts are; magnesium sulphate, sodium sulphate, magnesium hydroxide, sodium potassium tartrate.
- Sodium salts contraindicated in congestive heart failure.

Considerations

- Cause after constipation therefore not used routinely
- Preferred for pre-operative care before colonoscopy and in poisoning.

Lactulose

- A synthetic disaccharide containing fructose and galactose absorbed in the GIT.
- Produces soft stools within 1-3 days
- Side effects; abnominal cramps, flatulence,
- Contraindicated in patients requiring galactose free diet.

Vegetable fibres

- Dietary fibres derived from whole grains, vegetables and fruits. They contains the indigestible portion of cell wall.
- Dietary fibre act by binding water and ions in the intestine softens stool and promotes peristables. Also increases faecel mass.

Indications

- Prevention and treatment of functional constipation.
- Used for symptomatic relief of mild diarrhea

Adverse effects

Flatulance

Intestinal obstruction, oesophageal obstruction may occur.

Contraidication

Stenosis

Ulceration

Irritant and stimulant purgatives

- They promote accumulation of water and electrolytes in the lumen.
- Enhance intestinal motility
- Increased water secretion is through activation of cAMP and synthesis of prostaglandins
- Phenolpthalein and bisacodly are widely used.
- **Castor oil** is hydrolysed to glycerol and ricinoleic acid which stimulates peristalsis. Effect in the small intestines causes rapid complete evacuation.
- Side effects include; Cramping, dehydration.
- Regular use bordestroys mucosa

Stool softeners

Docusates

- Used as an emulsifying, wetting and dispersing agent.
- soften stool with 1-3days

Liquid paraffin

- It’s a mineral oil.
- Pharmacologically inert and acts as lubricants and softens stool.

Adverse effects of liquid paraffin

- Leakage of oil past anal sphincter
- Affect absorption of fat soluble vitamins.

Glcerin

- Used as a suppository, produces effects within 30mins.

Indication of laxatives

- Constipation not responding to non- pharmacological measures: fibre rich diet, regular exercise, regular bowel movements, (bulk laxatives are the 1st choice).
- Before and after surgery to produce soft stool in patients with haemorrhoids and fissures.

Contraindications

Undiagnosed abnominal pain

Appendicitis

Intestinal obstruction

Should be avoided during later stages of preganancy.

Anti- diarrhoeal agents

- Diarrhoea is marked by frequent passage of unformed or liquid stools.

Treatment of diarrhoea

- fluid and electrolyte replacement
- Nutritional management
- Drug therapy

Drug Therapy

Anti-diarrhea drugs include;

a) Antimotility drugs
b) Antisecretory drugs
c) Adsorbents
d) Antibacterial agents

Atimotility drugs

E.g loperamide, diphenoxylate

Loperamide

- Acts mainly on GIT receptor.
- Acts quickly and has a longer duration of action
- Decreases GIT motility and is excreted unchanged indicated for non infective diarrhea, mild travellors diarrhea.

Adverse effects

- Skin rash , abdominal cramps with excessive use paralytic ileus

Antisecretory drugs

Racecadotril

- Enkephalinase inhibitor that increases endogenous enkephalin level and reduce intestinal hyper tension of water and electrolytes.
- Used for systematic treatment of diarrhea.
- Has no side effects like bloating and after constipation.
- Should not be used in pregnancy, lactation and children.

Adsorbents

- Include kaolin, pectin, methylcellulose , magnesium aluminium silicate.
- They act by absorbing microorganisms and/ toxins by altering normal flora or by protecting the mucosa of the intestines.
- Their efficacy is doubtful

Antimicrobial agents

- Cholera; tetracyclines, norfloxacin/ciprofloxacin
- Infections with camphylobacter; erythromycin and flouroquinolones
- Amoebiasis or giardiasis; metronidazole, diloxanide furoate, ornidazole
- Shigella spcs, ciprofloxacin, norfloxacin or cotrimoxazole.

Miscellaneous

- Contain viable lactic acid bacilli.
- Improve intestinal microflora
- Known as probiotics
- Useful in rotavirus diarrhoea and anti biotic induced diarrhoea

D.ANTI EMETICS

- Vomitting is reflex action that results in forceful evacuation of gatric contents.
- Conditions pregnancy, ulcers, motion sickness, chemotherapy.

Anti emetics

Applied to suppress or prevent vomiting.

Classification

Anti muscarinic: scopolamine (hyoscine), dicyclomine

H1 antagonist: promethazine, doxylamine,

Prokinetic drugs; metoclopramide, domperidone, cisapride, mosapride.

Neuroleptics; phenothiazines, chlorpromazine

Adjuvant antiemetics; dexamethasone, benzodiazepines

1. Prokinetic drugs

a. Metroclopramide

- Effective for all types of vomiting, post- operatively, radiation, chemotherapy.
- Less effective in motion sickness.
- Blocks dopamine receptors, enters CNS

Side effects: extrapyramidal effects, dystonia, dyskinesia.

Indications;

- Anti emetic
- Dyspesia
- facilitate lactation

b. Domperidone

- Peripheral D2 receptor agonist .
- Causes less extra pyramidal effects, doesnot cross the blood brain barrier.
- Lower efficacy than metoclopramide

Uses; levodopa or bromocriptine induced vomiting.

Side effects; increased prolactin, galactorrhoea, dry mouth, rashes. Headache.

2. **Anti muscarinic**

Scopolamine (hyoscine)

- Alkaloid related to atropine
- Most effective in prophylaxis of motion sickness
- Antimuscarinic action blocks afferent pathways for vomiting reflex.
- Has short duration of action
- Produces anticholinergic effects; blurred vision, dry mouth, sedation.
- Not effective with vomiting of other aetiologies.

3. Neuroleptics

- Phenothiazines**:** chlorpromazine
- potent anti emetics in vomiting due to drug toxicity, chemotherapy.
- They act by blocking the D2 receptors in the medulla oblongata chemoreceptor trigger zone.
- Not effective in motion sickness
- Dosage is lower than antipsychotics

Side effects; sedation, extrapyramidal effects; dyskinesia, dystonia

4. H1 antagonist

- Doxylamie useful in motion sickness
- Modest effect on chemotherapy
- Reduce extra pyramidal effects of D2 receptor antagonist.
- Are antagonist therefore avoided in pregnancy.

Adjuvant antiemetics

Corticosteroids; dexamethasone, methylprednisolone, used to control chemotherapy vomiting.

- Act by blocking prostaglandins.
- Cause insomnia and hyperglycemia

Cannabinoids; tetrahydrocannabinol

- active principle of marijuana
- Reduce chemotherapy emesis.
- For patients intolerant or refractory to others antiemetics

Side effects; hallucinations. Disorientation, vertigo, sedation

DRUGS acting on the endocrine system

Insulin, oral hypoglycemic agents

- Overview
- Diabetes mellitus is a chronic illness that results from an absolute or relative deficiency of insulin.
- Various insulins are available to manage diabetes. These medications differ in their onset, peak, and duration.
- Oral hypoglycemic agents work in various ways to increase available insulin or modify carbohydrate metabolism.
- Newer injectable medication are used to supplement insulin or oral agents to manage glucose control.

- Review regulation of insulin secretion and its function in control of blood glucose level from A/P.

diabetes mellitus and effects of insulin

- DM consists of agroup of disorders characterized hyperglycemia, altered metabolism of lipids, carbohydrates and proteins and increased complications from vascular diseases.
- Most patients can be classified clinically as having either type1 or type 2 DM.
- The criteria for the diagnosis of DM include symptoms (e.g.polyuria, polydipsia, and unexplained weight loss)and a random plasma glucose concentration of greater than 200ml/dl)11.1mmol.

Insulin Therapy

- Insulin polypeptide hormone is the mainstay for treatment of all types of diabetes.
- Insulin may be administered **IM , IV, SC**.
- long term treatment relies on subcutaneous injections of the hormone.

Expected Pharmacological Action

- ✓ Promotes cellular uptake of glucose (decreases glucose levels)
- ✓ Converts glucose into glycogen
- ✓ Moves potassium into cells (along with glucose)

Therapeutic Uses

- Insulin is used for glycemic control of diabetes mellitus (**type 1, type 2, gestational**) to prevent complications.
- Clients with type 2 diabetes mellitus may require insulin when:

✓ Oral hypoglycemic, diet, and exercise are unable to control blood glucose levels.

✓ Severe renal or liver disease is present.

✓ Painful neuropathy is present.

✓ Undergoing surgery or diagnostic tests.

✓ Experiencing severe stress such as infection and trauma.

✓ Undergoing emergency treatment of diabetes ketoacidosis (DKA) and hyperosmolar hyperglycemic nonketotic syndrome (HHNS).

✓ Requiring treatment of hyperkalemia.

Classification of insulin; classified according to duration of action

classification	Generic (trade name)	Onset	Peak	duration
Rapid acting	Lispro insulin (Humalog), Insulin aspart (NovoLog) , Insulin glulisine (Apidra)	Less than 15 min	Less than 15 min 0.5 to 1 hr.	3 to 4 hr.
Short acting	• Regular insulin (Novolin R)	0.5 to 1 hr.	2 to 3 hr.	5 to 7 hr.
Intermediate acting	neutral protamine Hagedorn(NPH) insulin (Humulin N) , lente insulin	1 to 2 hr.	4 to 12 hr.	18 to 24 hr.
Long acting	Ultra lente, Insulin glargine (Luntus)	1 hr.	None	10.4 to 24 hr.

Premixed insulins

- 70% NPH and 30% Regular (Humulin 70/30) – mixture of intermediate acting and short-acting insulin
- 75% insulin lispro protamine and 25% insulin lispro (Humalog 75/25) – mixture of intermediate acting and rapid-acting insulin Complications

SIDE/ADVERSE EFFECTS NURSING INTERVENTIONS/CLIENT EDUCATION

Risk for hypoglycemia (too much insulin)

- Monitor clients for signs of hypoglycemia. If abrupt onset, client will experience sympathetic nervous system (SNS) symptoms **(tachycardia**, **palpitations, diaphoresis, shakiness).** If gradual onset, client will experience parasympathetic (**PNS)** symptoms (**headache, tremors, weakness).**
- Administer glucose. For conscious clients, administer a snack of 15 g of carbohydrate (4 oz. orange juice, 2 oz. grape juice, 8 oz. milk, glucose tablets per manufacturer's suggestion to equal 15 g).

- If the client is not fully conscious, do not risk aspiration. Administer glucose parenterally such as IV glucose, or SC/IM glucagon.
- Encourage clients to wear a medical alert bracelet.

Lipohypertrophy

- atrophy of the sub cutaneous fat at the site of insulin injection is probably an immune response to insulin.
- It may occur with human insulin if patients inject themselves repeatedly in the same site
- Instruct clients to systematically rotate injection sites and to allow 1 inch between injection sites.

Insulin allergy resistant

- identify the underlying cause.
- If allergic reaction to porcine insulin human insulin should be used.
- Antihistamines may provide relieve in patients with cutaneous reaction.
- Glucocorticoids are used in patients with resistant to insulin or more severe systemic reactions

Drug interaction

- Drug interaction is often caused by ethanol, adrenergic receptor antagonist, and salicylates.
- Adrenergic receptor antagonist pose a risk of hypoglycemia due to inhibition of catecholamine effects on gluconeogenesis and glycogenolysis.
- These agents may also mask he autonomic symptoms associated with hypoglycemia.
- Salicylates enhance cell sensitivity to glucose and potentiate insulin secretion and also have a weak insulin – like action in the periphery.
- Epinephrine, glucocorticoid, atypical antipsychotic drugs such as clozapine and olanzapine, and ARVS (protease inhibitors) have direct effects on peripheral tissues that counter the effect of insulin.
- Phenytoin, clonidine, ca2+channel blockers cause hyperglycemia by inhibiting insulin secretion directly or in directly via depletion of K+ (diuretics).

Nursing education

- Ensure proper storage of insulin.
- ✓ Unopened vials of a single type of insulin may be stored in the refrigerator until their expiration date.
- ✓ Vials of premixed insulins may be stored for up to 3 months.
- ✓ Insulins premixed in syringes may be kept for 1 to 2 weeks under refrigeration. Keep the syringes in a vertical position, with the needles pointing up. Prior to administration, the insulin should be resuspended by gently moving the syringe.
- ✓ Store the vial that is in use at room temperature,

- Administer NPH by subcutaneous route.
- Instruct clients to administer SC insulin in one general area to have consistent rates of absorption. Absorption rates from subcutaneous tissue increase from thigh to upper arm to abdomen.
- Use only insulin-specific syringes that correspond to the concentration of insulin being administered. Administer U-100 insulin with a U-100 syringe; administer U-500 insulin with a U-500 syringe.
- Select an appropriate needle length to ensure insulin is injected into subcutaneous tissue versus intradermal (too short) or intramuscular (too long).

- For insulin suspensions, the nurse should gently rotate the vial between his or her palms to disperse the particles throughout the vial prior to withdrawing insulin.
- Do not administer short-acting insulins if they appear cloudy or discolored.
- Insulin glargine and insulin detemir are both clear in color, not administered IV, and should not be mixed in a syringe with any other insulin.
- Administer lispro, aspart, glulisine, and regular insulin by subcutaneous injection, continuous subcutaneous infusion, and IV route.
- Adjust the client's insulin dosage to meet insulin needs.
- The client's dosage may need to be increased in response to the client's increase in caloric intake, infection, stress, growth spurts, and in the second and third trimesters of pregnancy.
- The client's dosage may need to be reduced in response to level of exercise or first trimester of pregnancy.

Oral hypoglycemic Classification

Medications	Expected pharmacological action
Sulfonylureas • 1st generation – tolbutamide (Orinase), chlorpropamide (Diabinese) • 2nd generation – glipizide (Glucotrol, Glucotrol XL) ,glyburide (DiaBeta, Micronase , glibenclamide) glimepiride (Amaryl)	Results in insulin release from the pancreas
Meglitinides repaglinide (Prandin) nateglinide (Starlix)	Results in insulin release from the pancreas
Biguanides metformin HCl (Glucophage)	• Reduces the production of glucose within the liver through suppression of gluconeogenesis • Increases muscles' glucose uptake and use
Thiazolidinedione's (Glitazones) , rosiglitazone (Avandia) , pioglitazone (Actos)	• Increases cellular response to insulin by decreasing insulin resistance • Results in increased glucose uptake and decreased glucose production
Alpha glucosidase inhibitors acarbose (Precose) , miglitol (Glyset)	• Slows carbohydrate absorption and digestion
Gliptins • Sitagliptin (Januvia	• Augments naturally occurring incretin hormones, which

Therapeutic Uses

- All classifications of oral hypoglycemic agents control blood glucose levels in clients with type 2 diabetes mellitus and are used in conjunction with diet and exercise lifestyle changes.

Metformin HCl is used to treat polycystic ovary syndrome (PCOS).

SIDE/ADVERSE EFFECTS

Glipizide and repaglinide

- Hypoglycemia

metformin

- Gastrointestinal effects (anorexia, nausea, vomiting, which frequently results in weight loss of 3 to 4 kg [6 to 8 lb])
- Vitamin B12 and folic acid deficiency caused by altered absorption
- Lactic acidosis (hyperventilation, myalgia, sluggishness, somnolence) – 50% mortality rate

Rosiglitazone

- Fluid Rosiglitazone retention
- Elevations in low density lipoproteins (LDL) cholesterol
- Hepatotoxicity .

Side/ adverse effects

acarbose

- Intestinal effects (abdominal distention and cramping, hyperactive bowel sounds, diarrhea, excessive gas).
- Risk for anemia due to the decrease of iron absorption
- Hepatoxicity with long-term use

Sitagliptin

- generally well tolerated

Contraindications/Precautions

- Pregnancy Risk Category C: Glipizide, repaglinide, rosiglitazone
- Pregnancy Risk Category B: Metformin HCl (Glucophage), acarbose (Precose), sitagliptin (Januvia)
- These oral agents are generally avoided in pregnancy and lactation, but the provider may decide to prescribe them.
- Use cautiously in clients with renal failure, hepatic dysfunction, or heart failure because of the risk of medication accumulation and resulting hypoglycemia. Severity of disease may indicate contraindication.
- Contraindicated in the treatment of diabetic ketoacidosis (DKA) Metformin HCl is contraindicated for clients with severe infection, shock, and any hypoxic condition.
- Acarbose is contraindicated for clients with gastrointestinal disorders, such as inflammatory disease, ulceration, or obstruction.