WMRMC West Michigan Regional Medical Consortium

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Lesson Plan: General Pharmacology

West Michigan Regional Medical Consortium

Topic: General Pharmacology

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Location: https://wmrmcc.thinkific.com/courses/general-pharmacology

Credit Category: Preparatory

License Level: PARAMEDIC

Credits: 1

Format: 1 hour lecture

Objectives: Upon completion of this CE, the participants will be able to:

Cognitive

1. Define pharmacology as it applies to prehospital settings.
2. Identify pharmacokinetics based on route of administration.
3. Discuss pharmacodynamics and drug receptor interactions.
4. Discuss the four drug interactions.
5. Understand basic drug mechanisms by class.
6. Understand bioavailability and absorption.

Outline for Presentation:

- **A. Introduction**
  - a. **Pharmacology**: *The science of drugs as it deals with the interactions of exogenously administered chemical molecule (drugs) with living system.*
  - b. **Father of Pharmacology:** Oswald Schmiedeberg
  - c. Two main divisions
    - i. Pharmacokinetics: what the body does to the drug
    - ii. Pharmacodynamics: what the drug does to the body
- **B. Pharmacokinetics**
  - a. The quantitative study of drug movement in, through and out of the body.
  - b. Process:
    - i. Transportation > Absorption > Distribution-Storage > Free drug > Metabolism > Receptor Binding (Effect) > Excretion
  - c. Biological membrane photo*
  - **d. Transportation**
    - *i. Passive diffusion*
      1. Requires no energy and no carrier
      2. Rapid for lipophilic, nonionic and small molecules

3. Slow for hydrophilic, ionic or large molecules

ii. *Specialized transport (Aqueous channels)*
1. No energy, No carrier
2. Small hydrophilic drugs (< 200 mw) diffuse along concentration gradient by passing through aqueous channels (pores)

iii. *Facilitated diffusion*
1. No energy but needs a carrier
2. Drugs bind to carrier by noncovalent mechanisms
3. Chemically similar drugs compete for carrier

iv. *Active transport*
1. Needs energy and a carrier
2. Identical to facilitated diffusion, except that ATP powers drug transport against concentration gradient.

e. Absorption

i. Movement of the drug from its site of administration into their circulation

ii. Factors that affect absorption
1. ***Drug-associated factors:*** ionization state, molecular weight, solubility, formulation (solution vs tablet)
   a. Small, nonionized, lipid-soluble drugs permeate plasma membranes most readily
2. ***Patient-associated factors:*** depend on route of administration.
   a. Presence of food in the GI tract, stomach acidity and blood flow to GI tract influence absorption.

f. Bioavailability

i. The fraction of the drug that reaches to systemic circulation from a given dose in an unchanged form

ii. A term typically used for medications given via oral route

iii. IV route gives 100% bioavailability as it directly enters the circulation

iv. *Bioequivalent*:
1. Two formulation of the same drug having equal bioavailability

v. *Bioinequivalent*:
1. If formation differ in their bioavailability

g. Distribution

i. Once a drug has gained access to the bloodstream, it gets distributed to other tissue that initially had no drug. Concentration gradient being in the direction of plasma to tissue.

ii. Factors affecting drug distribution:
1. *Membrane permeability*
   a. Ex. Benzodiazepines are very lipophilic, and readily cross the gut, capillary wall and blood-brain barrier
   b. Ex. Some antibiotics cannot cross the blood-brain barrier
   c. Blood-brain barrier, Blood-testes barrier, Blood-placenta barrier (prevents fetal exposure to some drugs).
2. *Depot storage of lipophilic drugs*

a. Ex. sedative thiopental accumulates in fat, released slowly from fat stores. So, an obese person may stay sedated for a longer period of time than a skinny person
b. Ex. Tetracycline, an antibiotic, accumulates in bones and teeth.

3. *Lipid solubility (various barriers)*
4. *Ionization at physiologic pH*
5. *Extent of binding to plasma and tissue protein*
    a. Ex. Albumin – reduces the amount of "free" drug in the blood
6. *Presence of tissue specific transporter*
7. *Difference in the regional blood flow*
8. *First pass metabolism*
    a. blood from GI tract passes through the liver before entering any other organs. A fraction of the drug (in some cases, nearly all) can be metabolized to an inactive or less active derivative.

iii. Movement of the drug proceeds until an equilibrium is established between unbound drug in plasma and tissue fluids.

h. <u>Metabolism (Biotransformation)</u>

i. It means chemical alteration of the drug in the body.
ii. Primary sites of drug metabolism is the liver
iii. Others are the kidney, intestine, lungs and plasma.
iv. *<u>Biotransformation of drug may lead to the following:</u>*
    1. Inactivation
    2. Active metabolite from an active drug
    3. Activation of inactive drug (prodrug)

i. <u>Excretion</u>

i. The removal of the drug and its metabolite from the body
ii. *<u>Drugs and their metabolites are excreted in:</u>*
    1. Urine
    2. Feces
    3. Exhaled air
    4. Saliva and sweat
    5. Milk

j. Half-Life ($t_{1/2}$)
    i. The length of time required for a given blood level to decline by 50%

k. Influence of dosing regimen on plasma drug levels

i. <u>Single Dose (See figure)</u>
    1. Plasma concentration of drug rises as the drug distributes to the bloodstream, then falls as the drug is distributed to tissues, metabolized and excreted
    2. *Distribution half-life ($t_{1/2}a$)*: reflects the rapid decline in plasma drug concentration as a dose of a drug is distributed throughout the body.
    3. Drugs administered orally reach a peak plasma concentration at a later time than drugs administered IV.
ii. <u>Continuous Infusion (See figure)</u>
    1. Steady state (equilibrium) plasma drug concentration is reach after continuous infusion for 4-5 half lives

2. Increasing the rate of infusion will NOT decrease the time needed to reach steady state.
3. Increasing the rate of infusion WILL, however, increase the plasma drug concentration at steady state.

iii. Intermittent Dose (See figure)

1. A drug must be administered for 4-5 half-lives before steady state (equilibrium) is reached.
2. Peaks: high points of fluctuation. Toxic effects are most likely to occur here
3. Troughs: low points of fluctuation. Lack of drug effect most likely to occur here.

C. Pharmacodynamics

a. The study of drug effects
b. It attempts to elucidate the complete action-effect sequence and dose-effect relationship.

c. Principles of drug action:

i. Drugs do not impart new function to any system, organ or cell they only alter the pace of ongoing activity.
ii. Types of drug action:
   1. Stimulation
   2. Depression
   3. Irritation
   4. Replacement
   5. Cytotoxic action

d. Mechanism of drug action

i. Majority of the drugs produce their effect by interacting with a discrete target biomolecule
ii. There are four major target of drug:
   1. Enzymes
   2. Ion-channel
   3. Transporters
   4. Receptors
      a. Generally, proteins or glycoproteins that are on the cell surface, on an organelle within the cell or in the cytoplasm.

D. Drug

a. According to the WHO: Drug is any substance or product that is used or is intended to be used to modify or explore physiological system or pathological states for the benefits of the recipient.

E. Various physiochemical properties of drugs

a. Lipid and water solubility
b. Molecular size
c. Particle size
d. Degree of ionization
e. Physical forms
f. Chemical nature
g. Dosage form

h. Formulation
i. Concentration
j. Shape

F. Drug receptor interaction

a. Receptors are specific protein and have specificity and selectivity
b. No drug is truly specific, but many have a relatively selective action on one type of receptor
c. Drug + receptor --> Drug – receptor complex --> response
d. ***Definitions***:
    i. ***Affinity***: The strength of binding between a drug and its receptor
    ii. Intrinsic activity: The ability of the drug to produce a pharmacological action after combining with the receptor.
    iii. ***Agonist***: A drug that is capable of producing pharmacological action after binding to the receptor.
        1. ***Strong Agonist***: An agonist which causes maximal effects, even though it may only occupy a small fraction of receptors on a cell.
        2. ***Weak Agonist:*** An agonist which must be bound to many more receptors than a strong agonist to produce the same effect.
        3. ***Partial Agonist:*** A drug which fails to produce maximal effects, even when all the receptors are occupied.
    iv. ***Antagonist***: Drugs that bind to receptor, but are not capable of producing pharmacological action. These produce receptor blockade.
        1. ***Competitive Antagonist:*** Compete with agonists for receptors.
            a. Surmountable as large amounts of agonists can overcome this
        2. ***Noncompetitive Antagonist:*** Bind to a site other than the agonist-binding domain. Induces a conformational change in the receptor such that the agonist no longer "recognizes" the agonist-binding domain.
            a. Insurmountable in that larger amounts of agonists cannot overcome this antagonism
        3. ***Irreversible Antagonist***: Compete with agonist for the agonist-binding domain, but the binding is permanent. Cannot be "reclaimed" by an agonist.
        4. ***Physiological Antagonism***: Two agonists, in unrelated reactions, cause opposite effects and cancel each other out.
        5. ***Antagonism by neutralization:*** Two drugs bind to one another, and become inactive.

G. Drug Interactions

a. <u>Addition</u>
    i. The response elicited by combined drugs is EQUAL TO the combined responses of the individual drugs (Mathematical Model: 1+1=2)
b. <u>Synergism</u>
    i. The response elicited by combined drugs is GREATER THAN the combined responses of the individual drugs (Mathematical Model: 1+1=3)
c. <u>Potentiation</u>
    i. A drug which has no effect enhances the effect of a second drug (Mathematical Model: 0+1=2)

d. **Antagonism**
    i. Drug inhibits the effect of another drug. Usually, the antagonist has no inherent activity (1+1=0)

H. Routes of drug administration

a. **Parenteral** = "around the GI tract"
b. Intravenous
    i. Rapid onset
    ii. Insoluble drugs cannot be administered IV
c. Intramuscular
    i. Rate of absorption depends on formulation
        1. Oil based = absorb slowly
        2. Aqueous preparations = absorb rapidly
d. Subcutaneous
    i. Absorption can be controlled by drug formulation
e. Topical
    i. local effect (good for meds that have systemic toxic effects)
f. Inhalation
    i. rapid and targeted
g. Per Os (PO)
    i. Most compatible with drugs that are self-administered
    ii. Must be able to withstand the acidic environment for the stomach and must permeate the gut lining before entering the blood-stream.
    iii. Absorption affected by gastric emptying and intestinal motility
    iv. portal circulation --> liver --> first pass metabolism
h. Rectal
    i. 50% first pass
    ii. Absorption is unreliable
    iii. Useful for unconscious, vomiting or small children
i. Sublingual
    i. Rapid absorption
    ii. no first pass
j. Intrathecal
    i. Into the CSF
k. Transdermal
    i. sustained effect

I. Tolerance, Dependence and Withdrawal

a. Tolerance:
    i. Represents a decreased response to a drug.
    ii. Clinically seen when the dose of a drug must be increased to achieve the same effect.
    iii. Metabolic – drug metabolized more rapidly after chronic use
    iv. Cellular – Decreased in number of drug receptors (downregulation)
    v. Behavioral – an alcoholic learns to hide the signs of drinking to avoid being caught by his colleagues
b. Dependence
    i. Occurs when a patient needs a drug to "function normally"

ii. Clinically, it is detected when cessation of a drug produces withdrawal symptoms.

c. Withdrawal
   i. Occurs when a drug is no longer administered to a dependent patient.
   ii. Symptoms are often opposite the effect achieved by the drug.
   iii. Ex: severe hypertension in a patient after cessation of antihypertensive meds

d. Cross tolerance/Cross Dependence
   i. Occurs when tolerance or dependence develop to different drugs which are chemically or mechanistically related.
   ii. Ex: Methadone relieves the symptoms of heroin withdrawal because patients develop cross dependence to these two drugs.

1. **Part 2 - Medications Objectives**
   a. Understand basic drug mechanisms by class
   b. Understand bioavailability, absorption
2. **Critical Care Drugs**
   a. Cardiovascular Drugs
      i. **Anti-arrhythmics**
         1. **Use:** Treatment and cardioversion of Atrial Fibrillation or Atrial Flutter Treatment and prophylaxis of refractory Ventricular Tachycardia
         2. **Adverse Effects:** Hypotension, QT prolongation, Torsades, Ventricular Tachycardia AV Block
         3. **Dosing:**
            a. **Magnesium Sulfate**
               i. Bolus: 1-2 grams over 5 minutes Infusion: 6-12 grams over 24 hours
         4. **Special Considerations:**
            a. Use infusion pump for drips.
            b. May not be compatible with heparin, lidocaine, amiodarone or bicarb
            c. Frequent BP checks for hypotension
            d. Increased risk for ventricular dysrhythmias if on certain antihistamines or anti-nausea medications
      ii. Beta Blocker
         1. **Uses:** Slow ventricular response in SVT, Atrial Fibrillation and Atrial Flutter Slow sinus node rate
         2. **Adverse Effects:** Hypotension, bradycardia, Hypoglycemia (diabetics on medications); usual signs and symptoms are masked, Bronchospasm, Sinus node arrest
         3. **Dosing:**
            a. **Atenolol (Tenormin)**
               i. Infuse: 5 mg over 5 minutes
                  May be repeated in 10 minutes
            b. **Esmolol (Brevibloc)**
               i. Bolus: 500 mcg/kg (0.5 mg/kg) over one minute
                  Infusion: 50 mcg/kg/minute for 4 minutes

ii. If inadequate response, repeat bolus and increase drip rate by
50 mcg/kg/minute up to 3 times **(total dose of 2000 mcg bolus and infusion @ 200 mcg/kg/minute)**
iii. Drug comes in a 100 mg (10 mg/ml) vial or 2500 mg ampule into 250 ml (10 mg/ml) or 500 ml (5 mg/ml) NS or D5W

c. **Labetalol (Normodyne)**
i. Infusion: 2 mg/minute (concentration 1mg/ml; 2ml/min) duration from 25 minutes to 2.5 hours

d. **Metoprolol (Lopressor)**
i. Inject: 2.5 mg IV slow push over 2 minutes May repeat dose up to 5 every 5 minutes for a **total dose of 15 mg**

e. **Sotolol (Betapace)**
i. Bolus: 1-1.5 mg/kg; followed by
ii. Infusion: 0.008 mg/kg/minute = 8 mcg/kg/min

4. **Special Considerations:**
a. Use infusion pump
b. Check BP frequently; monitor heart rate
c. Carefully monitor for hypotension, excessive bradycardia or new AV blocks
d. Patient with DIABETES may have symptoms of hypoglycemia masked; watch carefully for mental status changes
e. Contact MC if develop adverse reaction

iii. Anti-Hypertensives

1. **Uses:** Short term parenteral treatment when oral treatment is not feasible Nitroprusside may be used in CHF to reduce both preload and afterload (reduces work of the heart)
2. **Adverse Effects:** Hypotension, bradycardia, dysrhythmias, Palpitations, flushing, angina, Headache, restlessness, drowsiness, confusion or slurred speech
3. **Dosing:**
a. **Hydralazine**
i. Inject: 5- 40 mg IV push over 1-2 minutes
Usually given as repeat bolus doses every 20-30 min
ii. Rarely given as drip: 1-10 mg/hour

b. **Nicardipene (Cardene)**
i. Dilute to: 0.1 mg/ml
Infusion: Start @ 50 ml/hr (5 mg/hr)
ii. May increase rate by 2.5 mg/hr every 15 minutes until desired BP is reached for a **maximum dose of 15 mg/hr**

c. **Nitroprusside**
i. Infusion: Continuous to maintain BP
ii. **See dosage chart below; amount listed is in *ml/hr***
iii. **ADD NITROPRUSSIDE DOSING CHART**

d. **Nesiritide (Natrecor)**
i. Inject: 2 mcg/kg IV push over 60 seconds Infusion: 0.01 mcg/kg/min maintenance infusion

4. **Special Considerations:**
    a. Use infusion pump
    b. Dedicated IV line-should not administer in same IV line as other meds
5. **Nicardipene**:
    a. If hypotensive (BP<60) or tachycardic (HR>140), discontinue drip.
    b. May resume when stable @ 3-5 mg/hr
    c. Infusion site must be changed after 12 hours
    d. Use with caution in patients with liver failure, since it is metabolized in the liver.
    e. May be contraindicated in severe Aortic Stenosis as may decrease preload.
6. **Nitroprusside**:
    a. Small boluses or slight increases in infusion rate may produce profound hypotension
    b. Solution must be wrapped in foil to protect it from light
    c. Do not mix other medications in the same line
    d. Check BP and heart rate every 5 minutes
    e. Hypotension can be alleviated by decreasing the infusion rate
7. **Nesiritide**:
    a. Caution in pregnant or lactating patients
    b. Contact MC for worsening signs/symptoms, significant BP change or if BP<90

iv. Calcium Channel Blockers

1. **Uses:** Ventricular Rate Control in A Fib, Atrial Flutter, MAT or SVT
2. **Adverse Effects:** May cause Atrial Flutter, AV Block, Bradycardia, Chest Pain, CHF, Ventricular Arrhythmias, nausea/vomiting, dyspnea or hypotension
3. **Dosing:**
    a. **Diltiazem (Cardizem)**
        i. Bolus: 0.25 mg/kg over 2 minutes (20 mg for average patient) If needed may repeat bolus in 15 minutes @ 0.35 mg/kg (25 mg in the average patient) over 2 – 5 minutes
        ii. Infusion: Dilute 125 mg (25ml) in 100 ml NS/D5W Drip @ 5 – 15 mg/hour titrated to heart rate

    b. **Nicardipene (Cardene)**
        i. Dilute to: 0.1 mg/ml
        ii. Infusion: Start @ 50 ml/hr (5 mg/hr) May increase rate by 2.5 mg/hr every 15 minutes until desired BP is reached for a **maximum dose of 15 mg/hr**
4. **Special Considerations:**
    a. Carefully monitor for hypotension/excessive bradycardia/ new A/V block
    b. PVC's can occur with conversion to NSR

c. Don't use in the presence of a WIDE COMPLEX TACHYCARDIA

v. Glycoprotein IIb/IIIa Inhibitors
   1. **Use:** Unstable Angina Non Q-wave MI Percutaneous Coronary Intervention
   2. **Adverse Effects:** Bleeding (usually at cath sites) possible allergic reactions to ReoPro
   3. **Dosing:**
      a. **Abciximab (ReoPro)**
         i. Loading bolus: 0.25 mg/kg over 10-60 minutes
         ii. Maintenance infusion: 0.125 mcg/kg/min for 12 hours following PCI or 18-24 hours for unstable angina
         iii. Should be administered through a 0.2 or 0.22 micron filter
         iv. Drip rates will vary depending on concentration that was mixed.
         v. Verify drip rates/dosage calculations with the transferring facility staff prior to transport.
      b. **Tirofiban (Aggrastat)**
         i. Loading infusion: 0.4 mcg/kg/min for 30 minutes
         ii. Maintenance infusion: 0.1 mcg/kg/min
         iii. Rate will be halved for patients with renal insufficiency.
      c. Eftifibatide (Integrilin)
         i. Loading bolus: 180 mcg/kg over 1-2 minutes
         ii. Maintenance infusion: 2 mcg/kg/min up to 72 hours
   4. Special Considerations:
      a. Use infusion pump
      b. Should always be given WITH heparin
      c. If bleeding occurs, need to turn off heparin as well as the GPIIb/IIIa drug.
      d. All settings on this medication are to be determined by the ordering physician.

i. Heparin gtt
   a. **Uses:** Prevents blood clotting, especially in the following situations: Acute MI, Pulmonary Embolus, Deep Vein Thrombosis
   b. **Adverse Effects:** Hemorrhage from various sites including needle sticks, GI tract, CNS bleeds
   c. **Dosing:**
      i. Bolus: 15-18mg/kg
      ii. Infusion: 800-1600 mg/hour
      iii. Infusion rates may be outside this range and should not require adjustment during transport

d. **Special Considerations:**
    i. Use infusion pump
    ii. D/C immediately for onset of major bleeding or acute mental status change
    iii. Contact MC for any bleeding such as IV sites or gums

ii. Inotropes
a. **Uses:** Short term intravenous treatment of patients with acute decompensated heart failure Severe CHF/Cardiogenic Shock To increase cardiac output by increasing myocardial contractility and stroke volume Hemodynamically significant hypotension not resulting from hypovolemia
b. **Adverse Effects:** May develop hypokalemia resulting from increased cardiac output and/or diuresis. May have tachycardia, ventricular dysrhythmias or ectopy, hypertension, angina or ischemic chest pain. Dobutamine may also cause hypotension. Dopamine may cause nervousness, headache, palpitations, dyspnea, nausea or vomiting
c. **Dosing:**
    i. **Inamrinone (Inocor):**
        1. Loading dose over 2-3 minutes: 0.75 mcg/kg
        2. Maintenance infusion: 5-10 mcg/kg/min
    ii. Milrinone (Primacor)
        1. Loading dose over 10 minutes: 50 mcg/kg
        2. Maintenance infusion: See dosing chart
    iii. Dobutamine
        1. Infusion: 2.5-20 mcg/kg/min continuous
        2. Onset may be 10 minutes
    iv. Dopamine
        1. Infusion: 1-20 mcg/kg/min continuous
        2. Onset may be 10 minutes
    v. Epinephrine
        1. Infusion: 1-10 mcg/min titrated to effect
    vi. Norepinephrine (Levophed)
        1. Infusion: 0.5-1.0 mcg/min; titrated up to 30 mcg/min
d. Special Considerations
    i. Use infusion pump
    ii. For Inamrinone/Milrinone: do not mix with Lasix or dextrose-containing solutions
    iii. Monitor for cardiac dysrhythmias; these may be caused by hypokalemia, pre-existing arrhythmias, abnormal drug levels, catheter placement, etc.
    iv. Check blood pressure and heart rate frequently.
    v. Discontinue briefly if develop hypotension secondary to vasodilatation.

vi. Contact MC for any adverse affects

iii. Thrombolytic Therapy

a. **Uses:** Dissolves clots in blood vessels Generally used in the setting of Acute MI or CVA; occasionally used Pulmonary Embolus

b. **Adverse Effects:** Minor hemorrhages from IV sites and gums Major hemorrhage from GI and intracranial or spinal sites Reperfusion dysrhythmias often occur about 30-60 minutes after staring infusion.

5. **Dosing**:
   a. tPA
      i. Dose to be determined by transferring physician
      ii. Rate should not require adjusting en route
6. **Special Considerations:**
   a. Use infusion pump
   b. Monitor heart rhythm
   c. Check BP and HR frequently
   d. Do not mix with other medications in the same line
   e. D/C infusion immediately if there is cardiac arrest, major hemorrhage, anaphylaxis or change in mental status **AND call MC**.

b. Sedation and Paralytic Agents

i. Benzodiazepine gtt

1. **Uses:** Sedation for patients who are intubated (and often concurrently on a paralytic drip) May be used to treat Status Epilepticus
2. **Adverse Effects:** May be more prone to hypotension if used with an opioid drug Can cause paradoxical agitation, hypertension or tachycardia
3. **Dosing:**
   a. **Lorazepam (Ativan):**
      i. Loading dose: 0.5-4.0 mg IV bolus; may be repeated in 10 min
      ii. Infusion: 0.02-0.1 mg/kg/hour
   b. **Midazolam (Versed):**
      i. Loading dose: 0.01-0.1 mg/kg IV bolus
      ii. Infusion 0.02-0.1 mg/kg/hour
4. **Special Considerations:**
   a. Only to be used in intubated patients

ii. Moderate Sedation Agents

1. **Uses:** Sedation for patients who are intubated (and often concurrently on a paralytic drip) May also be used for refractory seizures or therapeutic coma

2. **Adverse Effects:** May be more prone to hypotension if used with an opioid drug. Can cause paradoxical agitation, hypertension or tachycardia
3. **Dosing:**
    a. **Propofol:**
        i. Loading dose: 0.5-5 mg/kg
        ii. Maintenance infusion: 2-10 mg/kg/hour
    b. **Barbiturates:** *Pentobarbital* is most commonly used
        i. Loading dose: 10 mg/kg; infuse up to 25 mg/min
        ii. Maintenance: 1-2 mg/kg/hour
    c. **Ketamine:**
        i. Loading dose: 1-5 mg/kg
        ii. Maintenance infusion: 0.01-0.05 mg/kg/hour
4. **Special Considerations:**
    a. Only to be used in intubated patients

iii. Opioid gtt

1. **Uses:** *Typically **part of** a sedation combination* for patients who are intubated. Occasionally for pain control
2. **Adverse Effects:** May cause hypotension, especially in volume depleted patients or those with right-sided heart failure
3. **Dosing:**
    a. Morphine
        i. Bolus: 0.5-10 mg
        ii. Infusion: 2-30 mg/hr
    b. Fentanyl
        i. Bolus: 1-3 mcg/kg
        ii. Infusion: 25-250 mcg/hr
4. **Special Considerations:**
    a. Not advisable to give patients on narcotic drips Naloxone, as this may precipitate acute withdrawal
    b. Antihistamines (both H1 and H2) may counteract hypotension.

iv. Paralytic Agents

1. **Uses:** Total muscular paralysis when patient movement may:
    a. Compromise airway control (e.g. causing unwanted extubation)
    b. Exacerbate a real or potential illness or injury (e.g. spinal cord injury from a spine fracture)
    c. Endanger the patient, EMS care provider or others
2. **Adverse Effects:** Bronchospasm, flushing, hypotension and tachycardia have been rarely reported
3. **Dosing:**
    a. **Pancuronium:**
        i. Loading dose: 10 mg/kg

ii. May repeat dose every 1-2 hours as needed

b. **Vecuronium:**
   i. Initial dose: 10 mg IV push
   ii. Repeat dose of 10 mg IV push every 20-40 minutes as needed
   iii. Maintenance infusion may be an alternative: 0.01mg/kg/min

c. **Rocuronium:**
   i. Loading dose 0.6 mg/kg
   ii. May rebolus 0.2 mg/kg every 30-45 minutes
   iii. Maintenance infusion may be an alternative: 0.01–0.15 g/kg/min

4. **Special Considerations:**
   a. Produces COMPLETE APNEA; therefore an intact airway (e.g. endotracheal intubation), and adequate ventilation/oxygenation **MUST BE ESTABLISHED PRIOR TO ADMINISTRATION.** Likewise, personnel and equipment with the ability to restore an airway, ventilation and oxygenation must be available during transport.
   b. Causes paralysis only; **therefore concomitant use of a sedative/hypnotic is indicated**
   c. Note: Paralysis may alter the clinical exam. For example, motor seizure activity will not be seen, but the brain will continue to undergo seizure activity, and this must be treated! Also, conditions such as shock, hypoxia, pain, intracranial injury, hypoglycemia, etc. maybe the cause of this unwanted, spontaneous patient movement in the first place. **These conditions must be addressed but may be masked by the paralytic agent!**

c. CNS Drugs
   i. Anticonvulsants
      1. **Uses:** Prevention and treatment of seizures
      2. **Adverse Effects:**
         a. If intravenous phenytoin is given too rapidly, may result in:
            i. Cardiac dysrhythmias including ventricular fibrillation or asystole
            ii. Hypotension
         b. Subcutaneous extravasations of intravenous phenytoin may cause tissue necrosis or pain at the IV site
      3. **Dosing:**
         a. **Phenytoin:**
            i. 100-1200mg IV piggyback in normal saline;
            ii. Rate not to exceed 50 mg/min
         b. **Fosphenytoin:** *dose expressed in* ***phenytoin equivalents (PE)***
            i. 15-20 PE/kg; rate up to 100-150 PE/min
         c. **Valproic Acid:**

i. 40-60 mg/kg Rate up to 3 mg/kg/min

d. Phenobarbital:

i. 5-15 mg/kg IV, then 0.5-10 mg/kg/hour

4. **Special Considerations:**
   a. Use infusion pump
   b. Monitor heart rhythm
   c. Check BP frequently; vital sign monitor recommended
   d. D/C infusion and contact MC for any adverse effects

ii. Mannitol

1. **Uses:** Treatment of increased intracranial pressure or selected fluid overload states
2. **Adverse Effects:** Hypernatremia, Volume Depletion
3. **Dosing:**
   a. 25-50 grams IV push or bolus infusion (in 50cc D5W over 20 minutes)
4. **Special Considerations:**
   a. Patients receiving mannitol should have a Foley to monitor fluid status

iii. Steroids

1. **Uses:** Spinal cord injury to decrease edema. Cerebral edema due to injury or CNS mass or lesion
2. **Adverse Effects:** GI Bleed, Electrolyte disturbance and hyperglycemia, Hypertension, Acute CHF, Agitation, Corticosteroid hormonal suppression (hypoglycemia, hypotension, hypothermia), Higher risk for infection or masking symptoms of infection
3. **Dosing:**
   a. **Methylprednisolone (Solumedrol):**
      i. Initial bolus: 30 mg/kg over 15 minutes
      ii. Start infusion 45 minutes later: 5.4 mg/kg/hour for 23 hours
   b. **Dexamethasone (Decadron):**
      i. Cerebral Edema: start with 10 mg IV x 1, then 4 mg IM/IV q 6 hrs
4. **Special Considerations:**
   a. Contact MC for question of adverse effects

d. HAL/TPN, Insulin and Electolytes

i. Hyperalimentation/TPN

1. **Uses:** Intravenous nutrition
2. **Adverse Effects:** Catheter related sepsis, Air embolism if central venous IV tubing becomes disconnected, Subcutaneous extravasations of solution can cause tissue necrosis Discontinuation of infusion may cause hypoglycemia
3. **Dosage:** Continuous infusion usually through central venous catheter but occasionally through a peripheral IV line. Rate should not require adjustment enroute.
4. **Special Considerations:**

a. Use infusion pump.
b. Do not administer any other medication through the same IV line.
c. Contact MC for any adverse effects listed above
d. Consider use of a cardiac monitor

ii. Insulin gtt
1. **Uses:** Lowers blood glucose. Used in diabetics especially with ketoacidosis or hyperosmolar nonketonic coma.
2. **Adverse Effects:** Hypoglycemia related (tachycardia, diaphoresis, mental status changes, and seizures)
3. **Dosage:** 5-15 units per hour but dosages outside this range may be used.
4. **Special Considerations:**
a. Use infusion pump
b. Do not administer medications in the same IV line except D50.
c. If symptoms of hypoglycemia develop:
i. turn off infusion, perform a D-Stick, administer 25 grams, (one AMP) D50) if glucose <80 and contact MC.
ii. Monitor blood sugar every 30 minutes during transport
iii. Cardiac monitoring required

iii. Potassium Chloride
1. **Uses:** Replacement therapy for hypokalemia
2. **Adverse Effects:** Cardiac dysrhythmias (prolonged PR interval; wide QRS complex; depressed ST segment; tall, peaked T-waves; heart block; cardiac arrest). Subcutaneous extravasations of solution can cause tissue necrosis
3. **Dosage:**
a. Usual range is up to 20 mEq / hr., continuous infusion.
b. May be mixed with various IV solutions in various sized bags including “piggy back” solutions.
c. Rate should not require adjustment en route.
4. **Special Considerations:**
a. Monitor heart rhythm
b. Often causes burning during infusion; contact MC if this is problematic
c. Contact MC for changes in EKG configuration and/or dysrhythmias.

e. Obstetric Drugs
i. Magnesium Sulfate
1. **Uses:** Treatment of pre-eclampsia and eclamptic seizures. Premature rupture of membranes
2. **Adverse Effects:** Lethargy, nausea, vomiting, hypotonia, respiratory depression, dysrhythmia
3. **Dosing:**
a. Loading dose: 2 – 6 grams IV over 15 minutes (may give 2 gms over 5 minutes)

b. Followed by maintenance infusion: 1 – 2 gms/hr

4. **Special Considerations:**
   a. Monitor reflexes
   b. For symptomatic toxicity: 10 mLs of 10% Calcium Chloride and contact MC
   c. MC may also request furosemide and/or NS bolus as MCO
   d. In renal failure, patient may require emergency dialysis

ii. Oxytocin (Pitocin)
   a. **Uses:** Stimulates post-partum contraction of the uterus to control bleeding
   b. **Adverse Effects:** Hypertension, tachycardia, dysrhythmias
   c. **Dosing:** 10-40 units added to 1000 mL IV Fluid to control hemorrhage. Usual rate is 10-20 milliunits/min
   d. **Special Considerations:**
      i. Use infusion pump
      ii. Monitor heart rhythm
      iii. Check BP frequently; vital sign monitor recommended
      iv. Contact MC for any adverse effects

f. Antimicrobial Therapy
   i. Antibiotics and Antiviral
      1. **Uses:** Bacterial or Viral infections (treatment and prophylaxis)
      2. **Adverse Effects:** Allergic signs and symptoms, including anaphylaxis
      3. **Dosage:** Vary depending on the antibiotic. Generally given as a "piggyback" solution. Rate should not require adjustment en route
      4. **Special Consideration:** D/C infusions if there are any allergic signs or symptoms, then contact MC.
      5. ***Most Commonly used:***
         a. ***Acylcovir***
         b. ***Azithromycin (Zithromax),***
         c. ***Cefazolin (Ancef)***
         d. ***Ceftriaxone (Rocephin)***
         e. ***Gentamicin***
         f. ***Levofloxacin (Levaquin)***
         g. ***Metronidazole (Flagyl)***
         h. ***Piperacillin/Tazobactam (Zosyn)***
         i. ***Vancomycin***
   ii. Antifungal
      1. **Uses:** Fungal infections. Often in immune-compromised patients, those on chemotherapy or chronic antibiotics
      2. **Adverse Effects:** Nausea or diarrhea. Amphotericin-fever, rigors, chills.
      3. **Dosing:**
         a. **Amphotericin B, Azoles or "Fungins":**
            i. Usually given as bolus dosing once daily to TID.
            ii. May be given as continuous bladder irrigation: 50 mg/liter Over 24 hours @ 42 ml/hour

4. **Special Considerations:**
    a. Drug interactions may occur with statins, coumadin, antivirals, benzodiazepines, oral hypoglycemic drugs and transplant anti-rejections drugs
    b. Side effects can be pre-treated with Acetaminophen or Diphenhydramine

g. Pain Control
    i. **Uses:** Control of pain
    ii. **Adverse Effects:** May cause hypotension, especially in volume depleted patients or those with right-sided heart failure Respiratory Depression
    iii. **Dosing:**
        1. **Morphine:**
            a. Loading dose: 2 mg increments given every 5-10 minutes until adequate pain control; typically max dose is 10 mg-may be higher in patients on chronic pain therapy
            b. Infusion: 1-10 mg/hour
        2. **Fentanyl:**
            a. Loading dose: 1-5 mcg/kg given IV push
            b. Infusion: 1-5 mcg/kg/hour
        3. **Hydromorphone (Dilaudid):**
            a. Loading dose: 0.5-4 mg IV slow push
            b. Continuous infusion: 1-10 mg/hour
    iv. **Special Considerations:**
        1. Avoid Naloxone as this could precipitate acute withdrawal
        2. Pump malfunction could precipitate withdrawal
        3. Antihistamines (both H1 and H2) may counteract hypotension; this is an MC option

h. PCA pumps and subcutaneous pumps
    i. **Uses:** Treatment for patients with palliative care or chronic pain conditions. Often PO analgesia is not feasible
    ii. **Adverse Effects:** Hypotension, Respiratory depression, Catheter site infection or irritation
    iii. **Dosing:**
        1. **PCA (Patient Controlled Analgesia) Pumps**
            a. **Morphine, Fentanyl and Hydromorphone are most commonly used.**
            b. Pre-programmed settings for patient
            c. Patient may require assistance to “self-administer” medication
        2. **Subcutaneous Catheter Pumps**
            a. **Morphine most commonly used.**
            b. Up to 2 mLs volume at a time regardless of concentration
            c. May also give IV fluids at a usual rate of 1-10 mLs/hour; MAX of 25 mLs/hr
    iv. **Special Considerations:**

1. Encourage patient to use medication as needed
2. Avoid Naloxone as this could precipitate acute withdrawal
3. Pump malfunction could precipitate withdrawal
4. Subcutaneous catheter sites need to be changed every 7 days

i. Antidotes
   i. N-Acetyl Cysteine/NAC (Mucomist)
      1. **Uses:** Acetaminophen overdose-toxic quantities
      2. **Adverse Effects:** Anaphylactoid type reactions (urticaria, flushing, hypotension and bronchospasm)
      3. **Dosing:**
         a. Loading dose: 150 mg/kg over 15-20 minutes
         b. Maintenance infusion: 50 mg/kg over 4 hours
         c. Then: 100 mg/kg over 16 hours
      4. **Special Considerations:**
         a. Ideal time of onset of treatment is within 8-10 hours of ingestion
         b. Anaphylactoid reactions may be treated with IV diphenhydramine
         c. Maintenance infusion must be doubled at the 4 hour period
   ii. Cyanide Antidote Kit
      1. **Uses:** Cyanokit is indicated for the treatment of known or suspected cyanide poisoning.
      2. **Adverse Effects:** Allergic reaction, HTN, Hematochezia
      3. **Dosing:**
         a. The starting dose: for adults: 5 g (i.e., both 2.5g vials)
         b. Administered as an intravenous infusion over 15 minutes (approximately 15 mL/min), i.e., 7.5 minutes/vial.
         c. Depending upon the severity of the poisoning and the clinical response, a second dose of 5 g may be administered by intravenous infusion for a total dose of 10 g.
         d. The rate of infusion for the second dose may range from 15 minutes (for patients in extremis) to two hours, as clinically indicated.
      4. **Special Considerations:**
         a. Caution should be exercised when administering other cyanide antidotes simultaneously with Cyanokit,
         b. If a decision is made to administer another cyanide antidote with Cyanokit, these drugs should not be administered concurrently in the same intravenous line.
         c. Comprehensive treatment of acute cyanide intoxication requires support of vital functions.
         d. Cyanokit should be administered in conjunction with appropriate airway, ventilatory and circulatory support.
         e. Once reconstituted, hydroxocobalamin is stable for up to 6 hours at temperatures not exceeding 40°C (104°F). Do not freeze.

f. Any reconstituted product not used by 6 hours should be discarded.

iii. Thiamine
1. **Uses:** Wernicke's encephalopathy
2. **Adverse Effects:** Possible anaphylactic reactions
3. **Dosing:** 100 mg IV over 15-30 minutes
4. **Special Considerations:**
   a. Glucose administration in nutritionally depleted patients should be accompanied by thiamine

i. Bicarbonate gtt
   a. **Uses:** Tricyclic, aspirin or other acidotic overdoses. Renal protection after IV contrast or with sever e muscle breakdown (rhabdomyolysis)
   b. **Adverse Effects:** Sodium load
   c. **Dosing:** Titrated to urine pH >7 by hospital staff
   d. **Special Considerations:**
      i. Usually will have a Foley to check urine pH and output
      ii. May be associated with hypokalemia

ii. Pyridoxine
   a. **Uses:** Isoniazide (INH) Overdose
   b. **Adverse Effects:** GI upset Headache or sleepiness Tingling or burning of hands/feet
   c. **Dosing:** 5 grams IV over 3 – 5 minutes; repeat every 5-20 minutes until seizures resolve
   d. **Special Considerations:**
      i. Often patient is in status epilepticus; seizures may respond to benzodiazepines

i. Glucagon
   a. Uses: Beta-blocker reversal, Calcium Channel Blocker reversal, hypoglycemia
   b. Adverse Effects: Nausea and Vomiting, anaphylaxis, hypertension or hypotension.
   c. Dosing:
      i. Bolus: 3-10 mg IV
      ii. Infusion: 1-10 mg/hr
   d. Special Considerations:
      i. Given with an antiemetic

ii. Intralipid
   a. Uses: Beta-blocker, Calcium Channel blocker or other highly lipid soluble overdose.
   b. Adverse Effects: Hyperglycemia
   c. Dosing:
      i. Bolus: 1.5 mL/kg IV,
      ii. Infusion: 0.25 mL/kg/min
   d. Special Considerations:
      i. Fat overload syndrome may result if given too rapidly. Usually reversible upon discontinuation.

ii. Contraindicated if known allergy to egg or soybean proteins

j. GI Drugs
   i. Acid Reduction
      1. **Uses:** Decrease secretion of gastric acid or chronic reflux. Patients with UGI Bleed
      2. **Adverse Effects:** (all rare). Occasional CNS symptoms-more so in the elderly. Jaundice. GI upset
      3. **Dosing:**
         a. **Pantoprazole (Protonix**)
            i. Bolus: 80 mg over 5 minutes
            ii. Infusion: 8 mg/hr
         b. **Lansoprazole (Prevacid)**
            i. Bolus: 30 – 60 mg over 30 minutes
            ii. Infusion: 6 mg/hr
         c. **Ranitidine (Zantac)**
            i. Bolus: 50 mg over 20 -30 minutes
            ii. Infusion: 150 mg over 24 hours
      4. **Special Considerations:**
         a. May be used for antihistamine effects
   ii. GI Bleed related medications
      1. **Uses:** Variceal Upper GI Bleed
      2. **Adverse Effects:** Gall Bladder sludging or stones. Diarrhea and GI Upset. Hypoglycemia
      3. **Dosing:**
         a. **Octreotide:** 50 mcg IV bolus, then 50 mcg/hour
      4. **Special Considerations:**
         a. Alters the balance between insulin/glucagon; could result in either hypoglycemia or hyperglycemia
         b. **Vasopressin** is presently rarely used due to its potent vasoconstrictive and catecholamine inducing properties

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