Pharmacology Review

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The speaker has signed a disclosure form and indicated she has no significant financial interest or relationship with the companies or the manufacturer(s) of any commercial product and/or service that will be discussed as part of this presentation.

Session Summary

This presentation will provide a general overview of pharmacokinetics, pharmacodynamics, and common medications used in neonatal medicine to help prepare the participant for certification exams.

Session Objectives

Upon completion of this presentation, the participant will be able to:

- describe the principles of pharmacology;
- identify drugs used antenatally that affect the fetus;
- identify medications needed for resuscitation in the delivery room;
- name common medications used in the NICU.

Test Questions

1. Which of the following is not a complication of chronic Lasix chronic therapy?
   - a. Nephrocalcinosis
   - b. Metabolic alkalosis
   - c. Metabolic acidosis

2. How are aminoglycosides eliminated from the newborn baby?
   - a. Biotransformation
   - b. Glomerular filtration
   - c. Via metabolism by the liver

3. Which drug can be used in combination with Amphotericin B to increase efficacy of eradicating fungal meningitis?
   - a. Nystatin
   - b. Flucytosine
   - c. Flovent

4. Long term Dexamethasone use suppresses which hormone?
   - a. Adrenocorticotropic (ACTH) hormone
   - b. Insulin
   - c. Parathyroid (PTH) hormone
5. Volume of distribution is increased for a preterm infant due to:
   a. Increased extracellular fluid
   b. Decreased intravascular volume
   c. Limited renal function

References


Session Outline

See presentation handout on the following pages.
I. Principles of Pharmacology

- Not only about giving medications and it’s expected results
- Divided into 2 sectors:
  - Pharmacokinetics
  - Pharmacodynamics

Pharmacodynamics

- This is the ACTION part
- “what the drug does to the body”
- Definition: the activity of the drug at the receptor tissue site
- The free drug binds to a specific receptor site causing desired response

Pharmacokinetics

- “medication” “movement”
- “what happens to the drug once it enters the body”
- Definition: movement of a drug IN, THROUGH and OUT the body
- Four parameter of pharmacokinetics
  - Absorption
  - Distribution
  - Metabolism
  - Excretion
Absorption

- Getting the drug from the site of administration into the blood circulation
- Modes of medication administration:
  - PO, SQ, IM, IV, rectal, Percutaneous, endotracheal, inhalation

Bioavailability

- Amount of drug dose that reaches the systemic circulation
- IV route is the greatest!!! 100% bioavailable

So your baby is getting Lasix (IV) at 1 mg/kg/dose

He’s full feeds and someone orders Lasix @ 2 mg/kg

WHY???
Oral Administration

- Delayed absorption via po route:
  - Delayed gastric emptying
  - Stomach pH is more neutral
  - NPO status
  - Increased transit time
  - First pass metabolism

IM Route of Administration

- Erratic absorption secondary to low muscle mass
- Decreased absorption in states of vasoconstriction
  - Hypoxia
  - Hypoperfusion
  - Cold

Percutaneous Medication Administration

- Topical: localized effect
- Increased absorption secondary to:
  - Higher surface area to body weight:
  - Increases permeability of skin.
  - Decreased stratum corneum
- Advantage: can administer meds that work locally rather than systemically, i.e. EMLA
- Risk: greater risk of toxicity; esp. in PT infants

Hazardous Percutaneous Administration

- Aniline Dye: on fresh cloth diapers resulted in cyanosis
- Hexachlorophene: skin disinfectant used during bathing to prevent staph infection
- Topical steroids: causes systemic problems: cessation of growth, adrenal failure from steroid withdrawal
- Betadine: causes transient hypothyroidism
- Rubbing alcohol: has caused skin burns
Back to Components of Pharmacokinetics: Absorption, DISTRIBUTION, Metabolism and Excretion

- Distribution: transport of the drug from the bloodstream to the site of action

Route ➔ small intestine ➔ portal vein in liver ➔ bloodstream ➔ SVC intravascular compartment ➔ interstitial fluid ➔ intracellular fluid

Dependent on:

<table>
<thead>
<tr>
<th>Distribution Variables</th>
<th>Effects on drug availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. CIRCULATION</td>
<td>Increased blood flow = increased drug delivery to tissue</td>
</tr>
<tr>
<td>Rate of blood flow to tissues</td>
<td></td>
</tr>
<tr>
<td>2. TOTAL BODY WATER CONTENT</td>
<td>Increased TBW= more drug needed</td>
</tr>
<tr>
<td>Vd= volume of distribution</td>
<td></td>
</tr>
<tr>
<td>3. PROTEIN BINDING</td>
<td>Increased protein binding= less free drug available</td>
</tr>
<tr>
<td>4. LIPID SOLUBLE</td>
<td>Lipid soluble drugs move better across membranes</td>
</tr>
<tr>
<td>5. TISSUE RECEPTOR AFFINITY</td>
<td>Increased affinity= increased delivery of drug to site</td>
</tr>
</tbody>
</table>

Volume of distribution

Two compartment model

Before Administration ➔ Immediately after Administration ➔ After distribution equilibration

Volume of distribution

Two compartment model

Before Administration ➔ Immediately after Administration ➔ After distribution equilibration

GENTAMICIN
4 mg/kg
Q24
5 mg/kg
Q48
Protein bound vs. free meds

Drugs prefer to be free => not bound up

>85% = highly protein bound
<30% = low protein bound
Dilantin, Rifampin, Bacitracin

Free & Unbound Drugs

• Too much protein binding prevents a drug from having the ability to reach the tissue
• Which protein is it bound to??
• Problem is preemies
  Are hypoproteinemic

Lipid soluble drugs can pass
Sample questions

• An edematous infant will have what effect on distribution of a given drug?
  a. Increase the rate
  b. Decrease the rate

A preterm infant encounters what issues related to distribution?

Metabolism

Most drugs are metabolized to a less active form which is ready to be excreted

3 Actions of Metabolism
  • Biotransformation: the drug is chemically altered to an inactive
  • Change to water soluble drug
  • Change into active metabolite

Majority occurs in the liver (cytochrome P450 enzyme complex)

Liver metabolism usually matures by 6 months to 2 yrs

Factors that Decrease Metabolism

• Prematurity
• Decreased Cardiac Output
• Renal Insufficiency

Elimination

• Excretion of drug
  – Kidney, liver, intestine
• Dependent on renal system:
  – GFR and tubular function
• PT infants have immature renal function
  • GFR is decreased
  • Tubular function is decreased but matures over several months
1st order elimination

- A constant fraction of a drug is eliminated over time
- Proportional to amount given

Definitions to Know

- Steady State: the equilibrium point where amount of drug in equals amount of drug excreted
- Clearance: degree of efficiency a drug is removed from body over time

Half Life

HALF LIFE: time necessary for the blood concentration of a drug to fall by 50% during the elimination phase.
- Entire drug is eliminated in 5⅓ half lives
- And also takes 5⅓ half lives to reach steady state
- Loading dose: needed for drugs with long ½ life
Therapeutic Drug monitoring

• Narrow therapeutic range
  • Gentamicin, Vancomycin, Amikacin,
• Peak level: drawn after the dose is given
  • Depends on dosage and infusion rate
  • If peak high → decrease dose
• Trough level: drawn prior to dose
  — Dependent on interval of drug
  — If trough high → extend interval
• Therapeutic window: a range in where the dose of the drug will produce desired effect and minimal toxicity
  — Serum levels → Caffeine, Digoxin, Phenobarbital

Antenatal Drug Expose to Fetus

• Many drugs cross placenta antenatally
• Effect determined by:
  • Lipid solubility
  • Molecular weight of drug
  • Protein bound

Antenatal Tocolytic Exposure

• Magnesium Sulfate (IV) → muscle relaxant
• Calcium antagonist
  — Used for tocolysis in PTL & pre-eclampsia
  — Fetal transfer is RAPID & levels equal to maternal levels
  — Fetal Effect
    • Causes decreased FHR variability & decreased fetal breathing
  — Neonatal Effects:
    • Respiratory depression
    • Hypotonia and apnea
    • Decreased peristalsis
    • Treatments: resuscitation and/or assisted ventilation and check Magnesium levels.

Antenatal Tocolytic Exposure

• Indomethacin (PO) → prostaglandin synthase inhibitor
  — Used for short term tocolysis
  — Long term use can cause
    • Renal failure of fetus leading to oligohydramnios
    • Constriction of ductus arteriosus
    • Neonatal PPHN, NEC, renal insufficiency
• Terbutaline (PO) (SQ)(IV) → β2 agonist, decreases Ca
  — For PTL or tetanic contractions
  — Fetal effects: tachycardia
  — Neonatal Effects:
    • tachycardia and transient hypoglycemia, hypocalcemia
**Antenatal Tocolytic Exposure**

- Nifedipine: Calcium Channel blocker
  - Used as antihypertensive
  - Maternal -> hypotension

**Antenatal Exposure**

- Epidural Analgesia
  - Most common pain relief method
  - Lumbar catheter placed between L2-L5 space
  - Little passage to fetus
  - Risks:
    - Maternal hypotension -> fetal hypo perfusion and/or fetal bradycardia
    - Maternal temperature: If used >4hr

- Anesthesia -> NUMBING
  - Spinal:
    - Injection of local anesthetic into CSF
    - Fetal drug levels low
  - General
    - Emergent situations or contraindication to regional anesthesia
    - Uses anesthetic inducer + muscle relaxant + inhaled agent +O2
      - Inducing agents: Thiopental, Ketamine, Propofol, methohexital,
      - Muscle relaxants: Rocuronium, Succinylcholine, Vecuronium
        - do NOT affect fetus, rarely cross placenta
      - Inhaled agent: nitrous oxide or halogenated agents
    - Anesthetic agents and nitrous oxide rapidly cross placenta
    - Deliver within 10 minutes

**Antenatal Anesthesia and Analgesia Exposure**

- Maternal Analgesia and Anesthesia
  - Analgesia -> FEEL GOOD MEDS
    - **Opioids**: Demerol, Stadol, Morphine, Nubain
      - Rapidly transferred to fetus
      - Causes respiratory depression, decreased oxygenation
    - **Sedatives**: Valium, Versed, Ketamine, Ativan
      - Cross placenta rapidly
      - Fetal levels usually > than maternal levels
      - Cause respiratory depression, decreased peristalsis
Problems with General Anesthesia

- Maternal hypotension → fetal hypoxia
- Maternal hypoxia from failed intubation
- Delayed time from anesthesia to uterine incision

Teratogens

<table>
<thead>
<tr>
<th>Substance</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitors</td>
<td>Captopril → oligo, skull hypoplasia, limb deformities</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Fetal alcohol syndrome</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Mutagenic</td>
</tr>
<tr>
<td>Carbamezepine</td>
<td>Craniofacial &amp; NTD</td>
</tr>
<tr>
<td>DES</td>
<td>Multiple deformities</td>
</tr>
<tr>
<td>Folic acid</td>
<td>Cleft lip/palate, nail hypoplasia cardiac</td>
</tr>
<tr>
<td>Retin A</td>
<td>Abortion, cardiac, neuro, renal</td>
</tr>
<tr>
<td>Lithium</td>
<td>Epilepsies, anomaly, seizure, goiter</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Cranial dysplasia, low ears, flat nasal bridge</td>
</tr>
<tr>
<td>Phenobarbitil</td>
<td>Cleft lip/palate</td>
</tr>
<tr>
<td>Salicylate</td>
<td>Thrombocytopenia, bleeding, PDA closure</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>Teeth discoloration</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>Cardiac &amp; NTD</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Nail hypoplasia, seizure, mental deficiency, stippled bone epiphysis, flat nasal bridge</td>
</tr>
</tbody>
</table>

Antenatal Exposure to Street Drugs

- Reported Illicit drug use during pregnancy is estimated at 4.4%
- Still on an upward trend affecting teenagers at a higher rate
- These drugs readily cross placenta affecting fetus in various ways

Common Street Drugs

- Cocaine
- Amphetamines
- Opiates/Heroin/Methadone
- Marijuana
- Alcohol
- Benzodiazepine
- Tobacco
Cocaine

• Sympathomimetic agent and powerful CNS stimulant
• Readily crosses placenta and enters fetal circulation
• Effects are proportional to degree of exposure
• Antenatal use causes effects on
  - mother
  - fetus
  - baby

Cocaine and vasoconstriction

• Cocaine induces vasoconstriction in vascular beds

Cocaine effects

In Early Pregnancy Use
- Miscarriage
- Fetal stroke
- Increase risk of IUGR, SGA, LBW
- Risk of birth defects usually affecting midline structures:
  - Limb Defects
  - Microcephaly: decrease brain growth
  - GI/GU Abnormalities
  - Neural Tube Defects
  - Facial Defects

In Late Pregnancy Use
- Risk of preterm labor
- Risk of placental abruption

Effects of Cocaine on Newborn

• Up to 25% of exposed infants have some degree of health problems
• Withdrawal- in 48 hours
• Increased risk of SIDS

<table>
<thead>
<tr>
<th>Developmental Issues</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Cognitive delays</td>
<td>Learning disabilities</td>
</tr>
<tr>
<td>Decreased motor skills</td>
<td>Lower IQ</td>
</tr>
<tr>
<td>ADD</td>
<td>Behavioral Problems</td>
</tr>
</tbody>
</table>
Methamphetamine and other amphetamines

- Hyper-stimulant drugs
  - Makes the user hyper, increased HR and BP
  - Makes the fetus hypersensitive
- Increased in numbers recently
- Infant has no withdrawal but neurobehavioral symptoms

<table>
<thead>
<tr>
<th>Crystal Meth</th>
<th>Ecstasy</th>
<th>Amphetamines</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Risks of taking during pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTL</td>
</tr>
<tr>
<td>Stillborn</td>
</tr>
<tr>
<td>Abruptions</td>
</tr>
<tr>
<td>Neonatal Heart defects</td>
</tr>
<tr>
<td>Low birth weight</td>
</tr>
</tbody>
</table>

Heroin/Methadone

- Heroine is a very common street drug
- Past heroin users are encouraged to take methadone to treat the heroine need

Methadone

- Blocks effects of heroin and decrease craving for HEROIN
- Encouraged to take methadone during pregnancy
  - Withdrawal is harmful to fetus and mother
  - Increased chance of relapse with heroine use
- >50% of neonates go through withdrawal from methadone
  - Withdrawal is usually seen in 1st 96 hrs up to 2 weeks.
  - Because it is short acting but has a longer half life
  - Does not depend on maternal dose—but plasma level

Marijuana

- Most commonly used illicit drug during pregnancy, no clinical withdrawal signs
- Fetal risk—depends on usage
  - IUGR, PTL
  - linked to hypoglycemia, hypocalcemia, sepsis
- Neonatal risk
  - sensitive to touch, sleep issues
  - NO WITHDRAWAL
FAS
3 Basic Components: The TRIAD

• I. Growth Deficiency
• II. CNS Dysfunction
• III. Facial Features

Drug screening

• Maternal urine toxicology
• Neonatal Urine toxicology:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana</td>
<td>7 days to 1 month</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Up to 4 days</td>
</tr>
<tr>
<td>Heroin</td>
<td>Up to 2 days</td>
</tr>
<tr>
<td>Methadone</td>
<td>Up to 10 days</td>
</tr>
</tbody>
</table>

• Neonatal meconium toxicology
• Neonatal hair testing

Neonatal Abstinence Syndrome

• Term used for newborns exposed to antenatal drugs who go through withdrawal
• In utero fetus adapts biochemically to drug exposure
• Once born: the abrupt cessation of the drug causes various effects in the neonate:
  - CNS disturbances
  - GI Disturbances
  - Autonomic Dysregulation
  - Respiratory Symptoms
Neonatal Abstinence Scoring System

- This is a way to have objective data re: severity of neonatal withdrawal
- Values are subjective to the examiner
- Must be used in adjunct to clinical picture
- Score >8 on 3 consecutive occasions OR if sum of 3 scores is > 24 may need pharmacological intervention.

Finnegan Score

Treatment for Newborn Withdrawal

I. Nutritive: optimal nutrition, hyper caloric formula
II. Environmental: swaddling, decrease stimuli, quiet environment
III. Pharmacologic
   - Pharmacological
     - Opiods
       - Morphine
         - No ETOH
     - Phenobarbital
       - Polysubstance users
       - NAS seizures
       - Maximized on morphine
   Other agents
   Clonidine, Methadone

Drugs that can cause NAS

<table>
<thead>
<tr>
<th>Opiates</th>
<th>Hyper stimulant</th>
<th>Psychotropic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>Cocaine</td>
<td>Benzodiazepines</td>
</tr>
<tr>
<td>Codeine, Percocet</td>
<td>Methamphetamines</td>
<td>SSRI</td>
</tr>
<tr>
<td>Heroin</td>
<td>Crystall Meth</td>
<td></td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>Demerol/Dilaudid</td>
<td></td>
</tr>
<tr>
<td>Subutex</td>
<td></td>
<td></td>
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</tbody>
</table>
Drugs Used for Resuscitation

• Epinephrine
• Volume Expanders

10% of all Newborns Require Support in the delivery room
<1% will require full resuscitation with medication
Most important factor is effective ventilation

Epinephrine in the DR

• Epinephrine: 1:10,000 concentration
  Used when adequate ventilation oxygenation and chest compressions fail to bring HR>60 bpm
  Mechanism: Increases HR by Peripheral vasoconstriction
  Dose:
  1st dose via Endotracheal: 0.5-1 ml/kg
  2nd/3rd Dose via IV/UVC: 0.1 to 0.3 ml/kg
  Give dose 3-5 minutes apart
  Give as a rapid push followed by Normal Saline
  IV route is preferred !!!!

Volume Expanders

• O neg blood
• Normal Saline
• Ringers lactate
  Used for hypovolemia
  10 ml/kg via UVC
  Give SLOWLY over 5-10 min
  Fast infusion linked to IVH

• Overt bleeding
  • Placenta previa
  • Vaso previa
  • Abruption

• Occult blood loss
  • Maternal hemorrhage
  • Fetal-placental hemorrhage (e.g. nuchal cord, snapped cord)

Side Note: Delivery blood loss will not result in low HCT on initial CBC
Naloxone – “Narcan”

- Dose: 0.1ml/kg IV or IM
- Use: reversal of narcotic effect in neonate
- Not necessary during the acute phase of resuscitation – VENTILATE!
- Indications for use:
  - Continued respiratory depression after PPV has restored a normal heart rate and color AND
  - History of maternal narcotic administration in the 4 hours prior to birth
- Contraindicated in presence of maternal narcotic dependence
- Monitor infant for 6 hrs post med

Respiratory Drugs

- Surfactant
- Nitric Oxide
- Bronchodilators
- Steroids

Respiratory Distress Syndrome (RDS) or (HMD)

- RDS develops due to lung immaturity in preterm infants
- Due to SURFACTANT deficiency

Surfactant

FUNCTIONS
- REDUCES ALVEOLAR SURFACE TENSION !!
- It concentrates on the lining of the alveolar cells during exhalation
- Reduces collapsing of alveoli
- Decreases minimum pressure to open lung
- Reduces neonatal mortality by 50%
- Minimizes air leaks
- Stabilize lung volumes & Promote gas exchange
Survanta vs. Curosurf

- Beractant
- 4 ml/kg
- Cow lung extract
- Used since 1991
- Repeat dosing every 6 hrs

- Poractant
- 2.5 ml/kg
- Pig lung extract
- More concentrated
- Repeat dosing 1.25mg/kg in 12 hrs

Nitric Oxide (NO)

- **Use:** Treatment of PPHN by decreasing pulmonary vascular resistance
- **Dose:** 5-20 ppm of continuous inhaled gaseous NO
- **Mechanism of Action:** Potent selective pulmonary vasodilator. Relaxes smooth muscles
- **Side Effects:** Methemoglobinemia
- **Advantage:** Will not cause systemic hypotension as in previous PPHN treatment modalities

- **Where do preemies fit in this equation??**

Bronchodilators

- **Albuterol**
  - ACUTE bronchospasm and improve lung capacities in BPD infants
  - **Mechanism of Action:** Causes bronchodilation by acting on B2 adrenergic receptors and B agonist
  - **Side Effects:** Rebound tachycardia, hypokalemia and HTN

- **Atrovent**
  - Used to treat bronchospasm related to CLD
  - **Mechanism:** Inhibits parasympathetic bronchoconstriction
  - Not as potent as Albuterol but more effective when used together

Dexamethasone

- **Potent glucocorticoid that suppresses inflammation**
  - Increases permeability of lung capillaries
- **Side Effects:** Suppress immune response, hyperglycemia, hypertension, growth retardation

- Reports of neuro-developmental compromise
  - Adrenal insufficiency if weaned too fast

Airway Edema

Vent Weaning

- 3 doses in 24 hours
- Long 7-10 day tapering course
Cardiovascular Drugs

Dopamine
- Dose: 5-20 mcg/kg/min IV drip
- Use: treat hypotension and renal hypo-perfusion
- Mechanism:
  - low doses work on dopaminergic receptors to produce renal perfusion
  - higher doses works on alpha and ß1 adrenergic receptors to produce inotropic effect on heart
- Side effects: tachycardia

Dobutamine
- Dose: 5-20 mcg/kg/min IV drip
- Use: treat low output heart failure & poor cardiac contractility
- Mechanism:
  - ß1 agonist increasing cardiac output
- Side effects: tachycardia, arrhythmias

Cardiovascular Agents

DIGOXIN
- Treat CHF and arrhythmias
- Long half life loading and maintenance dose
- Mechanism: increase intracellular calcium improves cardiac contractility
- Caution: Dig toxicity: vagal response - bradycardia, vomiting, hypokalemia,

ADENOSINE
- Treat SVT - supraventricular tachycardia
- 0.05-0.2 mg/kg/dose RAPID IV push then normal saline
- Mechanism: slows down SA node firing decreases AV node conduction converts to normal heart rhythm
- Side effects: don’t use with 2nd or 3rd degree heart block
- Give closest IV to heart...half life of 10-15 seconds

PDA
- Fetal connection b/w pulmonary artery and aorta remains and causes L→R shunt
- Treatment: inhibits prostaglandin synthesis
- After delivery Oxygen in lungs and prostaglandin inhibitor causes PDA to begin closing

Ibuprofen | Indomethacin
--- | ---
< renal dysfunction | Renal dysfunction
GI perforation | GI perforation
Repeat/extended course | Decreased plt aggregation
IVH protection
Alprostadil

- **Prostin (Prostaglandin E)**
  - **Dose:** 0.05-0.4 mcg/kg/min IV drip
  - **Use:** keep ductus arteriosus patent in life threatening ductal dependent cardiac disorders
  - **Mechanism of action:** relaxes the smooth muscle of the ductus
  - **Side Effects:** apnea, bradycardia, fever, hypotension, thrombocytopenia
  - **Advantage:** results seen within 30 minutes

Gastroesophageal Reflux

- **Rx Treatment**
  - Histamine 2 Receptor Agonist
  - Proton Pump Inhibitor
  - Gastro-Prokinetics

### GI problems- GER

<table>
<thead>
<tr>
<th>Medication</th>
<th>Type</th>
<th>Use</th>
<th>Mechanism</th>
<th>Dose</th>
<th>Warnings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zantac</td>
<td>H2 Receptor Antagonist</td>
<td>GER</td>
<td>Inhibits gastric acid secretion</td>
<td>2-4 mg/kg/day</td>
<td></td>
</tr>
<tr>
<td>Reglan</td>
<td>Prokinetic</td>
<td>GER motility</td>
<td>Contraction of smooth muscle in GI tract</td>
<td>0.1-0.2 mg/kg/day (IV/PO)</td>
<td>Tardive dyskinesia</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Prokinetic</td>
<td>GER motility</td>
<td>Motilin receptor agonist</td>
<td>10 mg/kg/dose q8h (IV/PO)</td>
<td>Cardiac issues with high and prolonged use</td>
</tr>
<tr>
<td>Prevacid</td>
<td>Proton Pump Inhibitor</td>
<td>GER</td>
<td>Blocks production of gastric acid secretion</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Infectious Disease

- **Pathogen**
  - GAIN ENTRY
  - PRODUCE TOXINS

- **Types of Infectious agents**
  - Bacterial
  - Fungal
  - Viral
Antibiotics

Each antibiotic is specific for eradicating SPECIFIC Bacteria

Timing of infections:

> EARLY ONSET:
  - 1st week of life:
    - 3 common infectious agents: GBS, E. Coli, Listeria
    - Initial Abx used is Ampicillin and Gentamicin

> LATE ONSET:
  - After the 1st week the risk of numerous nosocomial infections increase:
    - Common infectious agents: Staph, Pseudomonas,
    - This is why the choice of antibiotics has a broader spectrum of coverage

Ampicillin
- Broad spectrum penicillin
- Used to tx GBS, Listeria Streptococcus and E.Coli sepsis or meningitis
- Acts by interrupting bacterial cell wall synthesis- β-lactamase inhibitor
- GRAM (+) COVERAGE

Aqueous Penicillin G
- Used for streptococcus but also for proven bacteremia and meningitis due to GBS
- Dose: 50,000 to 400,000 units/kg/day for GBS

Aminoglycosides

- Treat gram negative bacteria
  - E. coli, Pseudomonas, Serratia, Proteus
  - Gentamicin has synergistic effect with Ampicillin against GBS, Staph, Listeria
- Gentamicin and Tobramycin
- Eliminated by renal excretion by Glomerular filtration rate
- Side Effects: renal and ototoxicity...needs therapeutic monitoring
- Inhibit bacterial protein synthesis
Cephaolsporins

- Bacteriocidal and β-lactam
- Mechanism: interferes with cell wall synthesis

<table>
<thead>
<tr>
<th>Generation</th>
<th>Example</th>
<th>Organism Coverage</th>
<th>Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>Ancef/Keflex</td>
<td>Mostly gram (+) coverage</td>
<td>Skin and Wound</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Staph and Strp</td>
<td></td>
</tr>
<tr>
<td>2nd</td>
<td>Cefoxitin</td>
<td>&lt; gram (+) coverage</td>
<td>Orthopedic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>more Gm (-) coverage</td>
<td></td>
</tr>
<tr>
<td>3rd</td>
<td>Cefotaxime</td>
<td>Has broader gram (-) coverage</td>
<td>Meningitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Crosses BBB</td>
<td>Nosocomial Infections</td>
</tr>
<tr>
<td>4th</td>
<td>Cefepime</td>
<td>Broader gr (-) and (+) coverage</td>
<td>Pseudomonas &amp; Meningitis</td>
</tr>
</tbody>
</table>

Antibiotics

- Vancomycin
  - Broad spectrum a
  - Treating gram positive cocci
    - Examples: Staph Epidermis, Staph Aureus (both MSSA and Methicillin resistant Staph Aureus (MRSA)
  - Mechanism of action: interferes with cell wall synthesis, alters membrane and inhibits RNA synthesis
  - Ototoxic & red man syndrome
  - Be careful of over use → resistance
  - Excreted by kidneys
- Clindamycin
  - Anaerobic antibiotic coverage
  - Used in perforated GI tract (NEC or SIP)

Antiviral

- Indication: to treat infections caused by virus’
- I.e…. Herpes, HIV, Varicella
- Acyclovir
  - Used to treat Herpes infection and Varicella
  - Mechanism: inhibits DNA synthesis & replication of virus
  - may cause renal dysfunction and neutropenia
- Decreases morbidity
- AZT/Zidovudine
  - Used in the treatment & prophylaxis of HIV
  - Reduces perinatal transmission to 1%
  - Side effects: anemia, granulocytosis

Antifungal Medication

- Indication: to treat fungal infections especially Candida Albicans & Candida parapsilosis
  - Fluconazole: (PO/IV)
    - used to treat systemic Candida infection.
    - Longer half life than Amphotericin B but causes transient liver dysfunction
    - Usage for fungal prophylaxis in VLBW infants
  - Amphotericin: (IV)
    - Types: AmphoB, Ambisome, Amphotericin B Lipid Complex
    - used to treat various systemic fungal infections.
    - Mechanism: binds to fungal cell wall and causes damage
    - Side Effects: renal dysfunction, hypokalemia
    - Combine with Fluycytosine for fungal meningitis
  - Nystatin: (PO/Topical)
    - antifungal agent used to treat skin, mucous membranes and GI infections with Candida.
    - Advantage is it is inexpensive and safer
    - Mechanism: same as in Amphotericin
CNS Agents

- Caffeine
  - Use: treat neonatal apneas related to CNS immaturity
  - Mechanism of action: stimulates the respiratory center, improves respiratory muscle contraction
  - Considerations: can cause tachycardia at high levels
  - Therapeutic levels: 5-20 mcg/ml
  - Replaced the use of Theophylline because it causes less side effect, a wider therapeutic window, long half life

- Phenobarbital
  - 1st line Anticonvulsant used to control seizures
  - Also for withdrawal symptoms and sedation.
  - Mechanism: it raises the seizure threshold

Diuretics:
- Used to treat edema, fluid overload & hypertension

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism</th>
<th>Dose</th>
<th>Warnings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lasix</td>
<td>Potent loop diuretic</td>
<td>1-2 mg/kg/dose</td>
<td>Electrolyte instability, Ototoxicity, Nephrocalcinosis, Renal calculi</td>
</tr>
<tr>
<td>Aldactone</td>
<td>Potassium sparing diuretic</td>
<td>1.3mg/kg/day</td>
<td></td>
</tr>
<tr>
<td>Chlorothiazide</td>
<td>Non Calcium Wasting Diuretic</td>
<td>20-40 mg/kg/day PO</td>
<td>2-8 mg/kg/day IV</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>Inhibits sodium reabsorption in distal tubules</td>
<td>2-3 mg/kg/day PO</td>
<td></td>
</tr>
</tbody>
</table>

Diuretics: Prevent Na reabsorption in Loop of Henle

Sedative Agents or Pain Management

- Fentanyl (IV or drip)
  - Used for analgesia, sedation or adjunct to anesthesia
  - Short term narcotic agonist ...50x more potent than Morphine
  - Adv: does not cause severe hypotension
  - Major side effect: CND and respiratory depression, chest wall rigidity

- Morphine (IV or Drip)
  - Treatment of severe pain, sedation and narcotic withdrawal
  - mechanism: stimulates opioid receptors in the CNS
  - Side effects: resp depression, hypotension
CNS Meds- Benzodiazepines

- **Ativan** (Lorazepam) (PO/IV/IM)
  - Dose: 0.05-0.1 mg/kg/dose every 4-8 hrs (for sedation)
  - Use: status epilepticus refractory to other anti seizure meds & for sedation
  - Side effect: resp depression & seizure like myoclonic activity

- **Versed** (Midazolam) (PO, IV, IM or drip)
  - Dose: 0.05-0.15 mg/kg/dose every 2-8 hr (drip dose higher)
  - Use: as a sedative, anti anxiety agent for ventilated newborns
  - Rapid onset with short duration
  - Side effects: resp depression & hypotension

Muscle Relaxants

- **Common Types:** Pancuronium, Rocuronium, Vecuronium (IV dose or drips)
- Paralyzing agent used commonly for surgical procedures & maintaining assisted ventilation
- Mechanism: neuromuscular blocking agent at junction causing paralysis
- Do not paralyze without pain medication
- Side effects:
  - Immobilization of diaphragm
  - Immobilization of secretions
  - Reverse it with Atropine

• Vecuronium: longer acting—fighting the vent and cant ventilate
  - Must turn the patient frequently to mobilize secretions
• Rocuronium: rapid sequence in pediatrics for intubation...laryngeal paralysis, last only hr......limited data in PT infants
• Pancuronium; not really used
  - Longer acting
  - Increased cardiac output and ICP