Intravenous Drugs

Alireza Hayatshahi, PharmD, BCPS
American Board Certified Pharmacotherapy Specialist
Assistant Professor, Tehran University of Medical Sciences
Basics

• Sterility
• Final concentration
• Stability
• Administration
• Compatibility
Sterility

- Sterile IV admixture procedure in an isolated room
  - IV room
  - Sterile room
  - Clean room

- Inpatient Rx

- Home infusion Rx

- Satellite Rx in hospital
**Sterile** admixture
Sterility

• Clean room instructions for both pharmacists and technicians

• Laminar air flow hoods
  – Positive pressure room

• Horizontal for all IVs except for antineoplastic agents
  – Chemo-hood
  – Vertical hood
  – Negative pressure room
Total Parenteral Nutrition (TPN)
Candidates for receiving TPN

- Patient’s with obstruction in a part of their GI tract
- Surgery, trauma
- Chemotherapy, radiation therapy
- GI cancers
- Inflammatory bowel diseases
- Oral and enteral feeding intolerance
- Any surgery or procedure requiring patient to be NPO
Types of TPN

• Central parenteral nutrition
  – Patient must have central line (through subclavian vein to SVC) or **PICC line** (peripherally inserted central catheterization)
  – High osmolarity (**almost no limitation**) due to high speed blood flow (2500 ml/min)
  – May be concentrated if volume limitation needed
  – Good for patients who need TPN for more than 7 days
Types of TPN

• Peripheral parenteral nutrition
  – Osmolarity limitations (< 900 mOsmol/litter)
  – Risk of phlebitis (due to lower blood flow rate: 25-50 ml/min)
  – Must be changed every 2-3 days to minimize inflammatory process and damages
  – Ok for TPNs of less than 7-14 days
  – Large volume needed to decrease osmolarity
  – Lower concentration of amino acids and dextrose must be prepared
Types of TPN

• 3 in 1 (Total Nutritional Admixture) (TNA)
  – All macronutrients in one bag
  – Amino acids, dextrose, intralipids
  – Risk of missing visualization of possible precipitations (calcium phosphate)
  – Risk of fungal contaminations due to longer infusion time
  – Must use in-line filter 1.2 micron
Types of TPN

- 2 in 1
- Amino acids and dextrose in 1 bag
- Intralipid emulsion in separate bag
- No need to in-line filter for lipid emulsion
- Intralipid emulsion may be infused faster to minimize fungal growth
- Must use in-line 0.22 micron filter for AA and dextrose bag
**Sterile admixture**

- From 10 to over 40 injectable items to be mixed in a bag
- Prevention of CV or peripheral line infection and bacteremia
- Physical compatibility considerations
- Consistency
- Under pharmacist direct supervision
Sterile admixture

- Large volumes
  - Amino acids
  - Dextrose
  - Sterile water
  - Intralipids
Sterile admixture

- Electrolytes
  - Sodium chloride
  - Sodium phosphate
  - Sodium acetate
  - Potassium chloride
  - Potassium phosphate
  - Potassium acetate
  - Calcium gluconate
  - Magnesium sulfate
**Sterile** admixture

- Vitamins
  - May be in one or more vials
- Trace elements
- Insulin
Administration

• Nurses to be trained
• Infusion time
• Y-site IV drug compatibilities to be checked with pharmacists
• Storage
• Intralipid infusion time
• Hanging time
• Following daily orders
Monitoring

• Daily lab values to be checked
  – Na, K, Cl, acetate, serum creatinine, FBS
• Twice weekly labs:
  – Mg, Phos, Ca, CBC
• Weekly labs:
  – Albumin, LFTs, TG, INR

Glucose to be checked every six hours and SSI
Classification of Adverse Drug Reactions

Predictable Reactions (Type A)
- Examples:
  - Overdose
  - Side effects

Unpredictable Reactions (Type B)
- Hypersensitivity
- Immune mediated reactions
  - Humoral mediated
  - Cellular mediated
- Non Immune mediated reactions
Drug Allergy

• Criteria for a drug reaction to be considered immunologically mediated
  – reaction occurs in small number of patients receiving the drug
  – Reaction does not resemble drug’s pharmacologic effects
  – Reaction occurs even with small amount of drug
  – Reaction occurs by drug with similar structures
  – Presence of eosinophilia
  – Reaction resolves after discontinuation of the drug

Dipiro JT. Pharmacotherapy, A pathophysiologic approach, 5th edition. 2002; Chapter 89. 1583-95
Penicillin Hypersensitivity

• Adverse reactions to penicillin occurs in approximately 1% - 10% of treatment courses
• Fatal penicillin induced anaphylaxis occurs at the rate of 0.002% among general population
• Between 10%-20% of general population report PCN allergy, while about 90% of those reported cases are not truly hypersensitive to PCN
• Patients between the ages of 20-49 are at more risk of anaphylactic reactions
• Up to 80% of patients with a history of IgE mediated reactions to penicillin may have negative skin test in 10 years

Arroliga M E. Penicilin Allergy. Cleavland Clinic Publications; March 2005
Solensky R. Hypersensitivity reactions to beta-lactam antibiotics. Clin Revievs in Allergy & Immune; 2003(24):201-19
Cross-reactivities

• Less than 10% cross-reactivity between PCNs and Cephalosporins in general population
  – Less than 2% of general population without penicillin allergy are allergic to cephalosporins
  – Lower risk of cross-reactivity with later cephalosporin generations

• Up to 25.6% cross-reactivity between PCNs and carbapenems reported in general population
  – Minimal cross-reactivity with meropenem
  – Less than 3% of general population without penicillin allergy are allergic to carbapenems
Beta-lactam Antibiotics

- Penicillins
  - Penicillin
  - Nafcillin
  - Oxacillin
  - Piperacillin
  - Apmicillin
  - Amoxicillin
Beta-lactam Antibiotics

• Cephalosporins
  – Cefazolin
  – Cefuroxime
  – Ceftriaxone
  – Ceftazidime
  – Cefepime
Beta-lactam Antibiotics

- Carbapenems
  - Ertapenem
  - Imipenem
  - Meropenem
  - Doripenem
Imipenem

- Risk of seizures
  - 1-1.5%
- Drug-drug interaction
  - Decrease valproic acid serum levels
  - Monitor levels
  - Use alternative ABX if possible
  - Concurrent use with meperidine increases the risk of seizures
- Rate of administration
  - 20-30 minutes
  - Use lower rates if N/V occurs
Meropenem

• Risk of seizures
  – 0.7%

• Decreases valproic acid serum levels
  – Use higher doses of valproic acid
  – Monitor the levels
  – Use an alternative ABX if possible

• Intermittent infusion
  – 15-30 minutes
Vancomycin

- Infusion 10mg/minute
  - 1000mg at least over 60 minutes
- Concentration 5mg/ml
  - 1000mg in 200 ml of D5W or NS
- Faster infusion rates
  - Thrombophelebitis
    - IV site change q 2-3 days
  - Redman syndrome (usually upper torso, face and neck pruritis, chest pain, dizziness)
    - Use hydrocortisone, acetaminophen, antihistamine
Vancomycin

• Red man (red neck) syndrome:
  – Erythematous rash on face and upper body
  – To manage:
    • Administer antihistamines pre-infusion
    • Slow the infusion rate
Vancomycin

• Nephrotoxicity
  – Higher doses
  – Higher serum concentrations
  – Longer period of treatment
  – Reversible
• Drug-induces fever
  – Impurities
• Monitoring
  – Trough levels
    • Before the dose
Linezolid

• IV/PO
• Drug interactions
  – Serotonergic medications
    • Sertraline, citalopram, fluoxetine
  – Meperidine
  – Serotonergic syndrome
    • Hypertension, hyperthermia, mental status changes
  – Avoid concurrent use or monitor closely
• Myelosuppression if use longer than 2 weeks
  – Thrombocytopenia
Gentamicin

• Rate of 30-60 minutes

• Major toxicities
  – Nephrotoxicity
    • Usually reversible
    • Good hydration minimize the problem
    • Monitor drug serum levels
    • Monitor renal function
      – Serum Cr, BUN, Urine output
    • Avoid concurrent other nephrotoxic drugs if possible
Gentamicin

• Ototoxicity
  – Damages to the 8th cranial nerve
  – Sensory portions of the inner ear
  – **Hearing loss may be irreversible**
  – Once daily dosing: less toxic
  – **Drug serum levels monitoring is strongly recommended**
  – Peak level: 30-60 minutes after the dose
  – Trough level right before the dose
Amphotericin B

• Major adverse reactions
  – Hypotension, tachypnea, fever, chills, headache
  – Hypokalemia, hypomagnesemia
  – Nausea
  – Impair renal function (nephrotoxicity)

• Faster infusion rate: higher risk of adverse effects
  – Infuse over 4-6 hours to minimize ADRs

• Concentration
  – Up to 0.25mg/ml D5W
Amphotericin B

• Premedication 30-60 minutes prior to amphotericin
  – Ibuprofen
  – Acetaminophen
  – Diphenhydramine
  – Hydrocortisone
  – Meperidine (for patients who had rigors)

• Prehydration
  – Containing Mg, K
Amphotericin B

• Monitoring
  – Renal function
    • Serum Cr, BUN, Urine output
    • Electrolyte levels
      – Potassium
      – magnesium
Chemotherapy induced GI Toxicities

- Second to bone marrow in susceptibility to chemo agents
  - N/V
  - Mucositis
  - Esophagitis
  - Diarrhea
  - Constipation
CINV

- One of the most distressing and frightening adverse effects of chemotherapy
- Direct effect of chemotherapy agents on CTZ
- GI mucosal damage and inflammation
  - Enterochromaffin cells
  - 5HT3 release
  - Vagal afferents
  - Stimulation of VC and NTS
Major neurotransmitters involved in this process

- Serotonin (5HT3)
- Dopamine
- Neurokinin 1
- Others: muscarinic, histamine
CINV

• Types of CINV
  – Acute
    • Within the first 24 hours of the chemo Tx
    • Usually started in 1-2 hours post Tx and peaks at 5-6 hours post Tx
    • Better control with current antiemetic regimens
  – Delayed
    • After 24 hours of chemo TX
    • Peaks in 2-3 days post Tx
    • Subsides in next 2-3 days
    • Less control with current antiemetic regimens
    • **High dose cisplatin**
    • Also with Carboplatin, anthracyclies, cyclophosphamaide
Chemotherapy Agents

• Depends on the percentage of N/V induction
  – >90% (high risk)
    • Cisplatin, cyclophosphamide dose =>1500mg/m2, ...
  – 30%-90% (moderate risk)
    • Carboplatin, cycl;ophosphamide dose<1500mg/m2, doxorubicin, irenotecan, cytarabine>1g/m2, ...
  – 10%-30% (low risk)
    • Cytarabine =<1g/m2, docetaxel, paclitaxel,...
  – <10% (minimal risk)
    • Vincristine, rituximab, bleomycin
Mucositis

• Cells with rapid division affected by chemotherapy agents
• Concurrent radiation worsens
  – Xerostomia
  – Mucositis
  – Bleeding
  – Infection
GI Toxicities

• Prevention and treatment
  – Mucositis
    • Viscous lidocaine
    • Nystatin
    • Diphenhydramine
    • Magnesium hydroxide
    • Sucralfate
    • Benzocaine
    • Hydrocortisone plus nystatin plus diphenhydramine
    • Chlorhexidine 0.12%
GI Toxicities

• Topical anesthetics
• Antacids
• Antihistamines
• Antibacterial agents
• Antifungal agents
• Routine dental checks
• Avoid spicy and salty foods
GI Toxicities

- Avoid hot tea or coffee
- Avoid rough foods
- Attention to hydration
- Attention to supportive nutrition
- Liquid and soft diet
- TPN if needed
GI Toxicities

• Diarrhea
  – Irinotecan induced diarrhea
    • Early
      – Within 24 hours
      – Cholinergic
      – Use atropine iv or sc 0.25 to 1 mg
    • Late
      – After 24 hours
      – Atropine not effective
      – Loperamide schedule, NOT PRN
GI Toxicities

• Irrinotecan induced diarrhea
  • 2mg q2h, 4 mg q4h, 4mg q2h
  • Until diarrhea free for 12 hours
  • For resistant cases
    – Sandostatin (octreotide)
    – 100-2000 mcg sc TID
Dermatologic Toxicities

- Alopecia
- Hypersensitivity reactions
- Extravasations
- Hyperpigmentations
Dermatologic Toxicities

• Alopecia
  – 7 to 10 days after chemotherapy
  – Noticeable in 1 to 2 months of therapy
  – Regeneration after a couple months of regimen completion
  – Different look

• Prevention
  – Tourniquets
  – Ice caps
Dermatologic Toxicities

• Alopecia
  – Cyclophosphamide
  – Ifosfamide
  – Paclitaxel
  – Etoposide
  – Docetaxel
Dermatologic Toxicities

- Hyperpigmentation (diffused generalized)
  - 5-FU
  - Busulfan
  - Doxorubicin

- Nail changes
  - Paclitaxel
  - Docetaxel
  - cyclophosphamide
Dermatologic Toxicities

• Hand and foot syndrome
  – Tingling, burning sensation of the palms and soles
    • Cytarabine
    • 5-FU
    • Methotrexate
  – May need to D/C the medication until recovery

• Dry skin
  – Use emollient creams
Dermatologic Toxicities

• Other dermatologic toxicities
  – Radiation recall
    • Doxorubicin
  – Photosensitivity
    • 5-FU
    • MTX (sun burn recall)
  – Radiation enhanced reactions
    • Doxorubicin
    • hydroxyurea
Dermatologic Toxicities

• Extravasation
  – Generalized vascular disease
  – Elevated venous pressure
  – Injection site over joints
  – Recent venipuncture on the same vein
Dermatologic Toxicities

• How to manage
  – Stop injection
  – Do NOT pull needle
  – Aspirate medication then pull the needle
  – Site elevation
  – Surgical consult
Dermatologic Toxicities

• How to manage
  – Cold compress (for 1 day)
    • For most agents
  – Warm compress (for 1 day)
    • For vinca alkaloids
  – Topical DMSO (dimethylsulfoxide)
    • For doxorubucin extravasation
    • Free radical scavenger
    • Apply 1-2 ml on the site for 2 weeks
    • Do not cover and allow the air dry