ISSUES OF THE OBESE CRITICAL CARE PATIENT: DOSING

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Learning Objectives

- Recognize potential limitations of some routes of administration
- Determine optimal dosing for anticoagulation and antimicrobials
Medication Administration

- Appropriate medication therapy for obese patients begins with the route of administration
- Preferred route is oral or intravenous
  - Intramuscular injections should be avoided due to the possibility of subcutaneous administration
  - Subcutaneous and cutaneous administration may be limited by unpredictable blood supply causing a delayed onset of action

Pharmacokinetic Alteration

- Obesity changes all aspects of pharmacokinetics
  - Adsorption
  - Distribution
  - Metabolism
  - Excretion
Adsorption

- Predicted increases in adsorption have not been proven in studies
- Changes in adsorption are based on anatomy changes
  - S/p Roux-en-Y gastric bypass
  - S/p Gastric banding
  - No surgical interventions

Lee J. Orthopedics 2006;29:984-988
Distribution

- Obesity increases:
  - Adipose tissue
  - Organ mass
  - Lean body mass
  - Blood volume
  - Alpha-1 acid glycoprotein

- Dose adjustment based on distribution depends on the properties of the drug
  - Aminoglycosides – dosed on adjusted body weight
  - Propofol – dosed based on actual body weight

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Metabolism

- Increased blood volume seen in obesity, leads to increased blood delivery to the liver and kidneys
- Both phase I and phase II reactions are increased in obesity
  - Subtherapeutic drug levels may result from standard dosing – Ex LMWH are recommended to be dosed BID
- Fatty infiltration of the liver may or may not affect drug metabolism

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Excretion

- Conventional equations to estimate CrCl may be inaccurate in obesity.
- Cockcroft-Gault does not account for the changes in the muscle mass to body weight ratio seen in obesity.
- Salazar-Corcoran may be more accurate and has demonstrated a 24% increase in clearance.
- Dosing adjustments based on the increased clearance should be medication specific.

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What Weight Should I use to Choose a Drug Dose?

- Which weight is used to dose a medication is based on the drug’s properties
- Vancomycin is dosed based on total body weight
- Ideal body weight (IBW) should be used for aminoglycosides until the patient exceeds 120% of their ideal weight, then use adjusted weight
  - Adjusted body weight for aminoglycosides = (total body weight-IBW)x0.4 + IBW
Anticoagulation – Prophylaxis dosing

- Dalteparin has demonstrated efficacy up to a BMI of 40 kg/m²
- Bariatric surgery literature has recommended
  - Enoxaparin 40 mg SQ q12 for a BMI of 40-50 kg/m²
  - Enoxaparin 60 mg SQ q12 for a BMI >50 kg/m²
- A single study in medical patients showed that enoxaparin 0.5 mg/kg SQ daily demonstrated peak anti-Xa levels within in the target range.
  - Despite being a small study they did not demonstrate a correlation between anti-Xa levels and body weight or BMI

Anticoagulation – Therapeutic dosing

- Retrospective review of heparin dosing without dosing limits found
  - No difference in percentage of patients within range at the first aPTT between obese and non-obese patients
  - A higher BMI predicted a supratherapeutic first aPTT
- A subgroup analysis of CRUSADE (enoxaparin for NSTEMI) found that patients weighing >150kg were significantly more likely to bleed than patients weighing <150 kg
- American College of Chest Physicians has no firm recommendations regarding dosing in obesity
  - They do recommend monitoring anti-Xa levels as necessary

Antimicrobial Medication

- Proper dosing of antimicrobial medications is necessary for eradication and to prevent resistance
  - Obese patients in multiple studies appear to be at higher post-surgical infection risk

- A small pilot study found that cefuroxime 1.5g pre-operatively did attain adequate tissue concentrations for gram positive organism but not for gram negative organisms
  - Cefazolin 2g IV pre-operatively has also been recommended due to serum levels below the organism’s MIC with a 1g dose

Flouroquinolones are another class that may require adjustment based on body weight
- Cipro has been dosed at 5 mg/kg/dose based on both adjusted and total body weight with success

Vancomycin should be dosed based on total body weight and consideration should be given to q8h dosing due to increased clearance

Aminoglycosides should be dosed on adjusted body weight
- AdjBW = (total body weight-IBW)x0.4 + IBW

Summary

- Based on changes in the obese patient
  - Routes of medications may be less appropriate
  - Standard dosing may be excessive or under dosing may occur
  - Patients should be monitored closely for therapeutic effects of drugs and toxicities

- Future needs
  - More clinical trials determining the best dose for obese patients to maximize effectiveness and minimize toxicity
  - Possible need for more pre-made dosage strengths to accommodate larger patients


References


- Schentag JJ. Antibiotic dosing – does one size fit all? *JAMA*. 2998;279:159-160.
