Drug Dosing in Special Populations

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Special Populations

A special population are persons displaying one or more of the following characteristics:

a. prone to under or over responding to usual dosing regimens
b. least able to tolerate, recognize, or communicate drug effects
c. accidentally frequently mis-dosed

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Patient conditions that may altered the dosing of most drugs:

- Renal or hepatic disease, may decrease the elimination or metabolism of the majority of drugs and change the amount of drug being cleared from the body.
- Dialysis procedures, conducted using artificial kidneys in patients with renal failure, removes some medications from the body although the pharmacokinetic of other drugs are not changed
- Heart failure, results in low cardiac output, which decreases blood flow to eliminating organs
- Obesity, adds excessive adipose tissue to the body, which may change the way that drugs distribute in the body and increase the amount of drug needed for that patient.
- Age may affect the amount of medication a person receives. Infant and pediatric patients have different dosing requirements than adult patients.

Renal Disease

- Glomerular filtration is the primary elimination route for many medications
- The most common method of estimating glomerular filtration for the purpose of drug dosing is to measure/estimate Creatinine Clearance (CrCl)

Equations:

\[ \text{CrCl} \text{ (ml/min)} = \frac{U_{Cr} \times V_{urine}}{S_{Cr} \times T} \]

- \( U_{Cr} \) = the urine creatinine concentration (mg/dl)
- \( V_{urine} \) = the volume of urine collected (ml)
- \( S_{Cr} \) = the serum creatinine collected at the midpoint of the urine collection (mg/dl)
- \( T \) = the time of urine collection (minute)

Problems with routine measurement of patient’s CrCl:

- Incomplete urine collection
- Serum creatinine concentration obtained at incorrect times
- Collection times errors
One example of an Equation to calculate creatinine clearance: Cockroft and Gault

\[
\text{CrCl}_{\text{est}} = \frac{(140 - \text{age}) \times \text{BW}}{72 \times \text{Scr}} \text{ for males}
\]

\[
\text{CrCl}_{\text{est}} = \frac{0.85(140 - \text{age}) \times \text{BW}}{72 \times \text{Scr}} \text{ for females}
\]

- \( \text{CrCl}_{\text{est}} \) = estimated creatinine clearance (ml/min)
- Age in years
- BW = body weight (kg)
- Scr = serum creatinine (mg/dl)

Modifying Doses for patients with renal impairment

- It is possible to decrease the drug dose and retain the usual dosage interval, or
- Retain the usual dose and increase the dosage interval, or
- Both decrease the dosage and prolong the dosage interval
- The choice was made depend on the route of drug administration, the dosage forms available

For drugs with narrow therapeutic index

- Measured or estimated CrCl may be used to estimate pharmacokinetic parameters for a patient based on prior studies conducted in other patients with renal dysfunction
- Estimated pharmacokinetic parameters are then used in pharmacokinetic dosing equation to compute initial dose

Hepatic Disorders

- Most lipid soluble drugs are metabolized to some degree by the liver

Two major types of liver disease

1. Hepatitis
   - Acute hepatitis: mild, transient decreases in drug metabolism required no or minor changes in drug dosing
   - Chronic hepatitis: irreversible hepatocytes damage required drug dosage changes. Patients with long term hepatocytes damage can progress to hepatic cirrhosis
2. Cirrhosis: a permanent lost of functional hepatocytes. Drug dosage schedules usually need to be modified
Heart Failure

- Is accompanied by a decrease in cardiac output results in lower liver and renal blood flow
- Decreased drug bioavailability has been reported, due to collection of edema fluid in the GI tract difficult absorption and decreased blood flow to GI tract

Age

- Children are not small adults but rather distinct individuals who have different absorption, distribution, metabolism, and excretion rates of medications than adults.

\[ \text{Age (years)} = \frac{\text{Adult dose}}{\text{Child's dose (approx)}} \]

Young's Rule example: Dosage based on Age Example

A child is 5 years old and weighs 60lbs. You want to calculate the dose of Acetaminophen for them. The recommended adult dose is 650mg. Use Young's rule to calculate a medication dose based on age.

\[
\text{Child's Estimated Dose} = \frac{\text{Adult Dose} \times \text{Age of child in years}}{\text{Age in Years} + 12 \text{ yrs}}
\]

\[
\text{Child's Estimated Dose} = \frac{650mg \times 5 \text{ yrs}}{5 \text{ yrs} + 12 \text{ yrs}} = 191mg
\]

Clark's Rule Example: Dosage based on Weight

A child is 5 years old and weighs 60lbs. You want to calculate the dose of Acetaminophen for them. The recommended adult dose is 650mg. Use Clark's rule to calculate a medication dose based on age.

\[
\text{Child's Estimated Dose} = \frac{\text{Adult Dose} \times \text{Child's weight in pounds}}{150\text{lb}}
\]

\[
\text{Child's Estimated Dose} = \frac{650mg \times 60\text{lb}}{150\text{lb}} = 260mg
\]

Weight

- Most drugs in children are dosed according to body weight (mg/kg) or body surface area (BSA) (mg/m²). Care must be taken to properly convert body weight from pounds to kilograms (1 kg = 2.2 lb) before calculating doses based on body weight. Doses are often expressed as mg/kg/day or mg/kg/dose, therefore orders written "mg/kg/d" which is confusing, require further clarification from the prescriber.

(Math Calculations for Pharmacy Technicians. Robert M. Fulcher and Eugenia M. Fulcher. Saunders, 2007.)

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