UNIVERSITY OF ILORIN, ILORIN, NIGERIA

FACULTY OF PHARMACEUTICAL SCIENCES

DEPARTMENT OF CLINICAL PHARMACY AND PHARMACY PRACTICE

400 LEVEL PHARM. D PRACTICAL MANUAL

Biopharmaceutics and Pharmacokinetics

CLI 301

UNIVERSITY OF ILORIN

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CLI 301 PHARMACOKINETICS AND BIOPHARMACEUTICS PRACTICAL

WEEK ONE

SCHEDULE 1

NOMOGRAMS AND ALGORITHMS

Title: NOMOGRAMS AND ALGORITHMS

Introduction: Several algorithms and nomograms have been developed to individualize patients' pharmacokinetic monitoring for drugs e.g. antibiotics like aminoglycosides (AG). Three major methods of dose individualization for AG commonly used to target specific pharmacokinetic parameters are (i) linear regression analysis (one compartment model), (ii) population methods and, (iii) Bayesian estimation procedures. Although the population methods require minimal resources and are easy to use they can recommend clinically inappropriate doses as they have constant pharmacokinetic parameters and are not valid or do not represent their pharmacokinetic profile well, as seen in special population groups, that is, renal impairment. The Bayesian and linear regression methods recommend more accurate dosage regimens. However, they require additional resources, such as information technology and clinical pharmacists with background training in pharmacokinetics.

Aim: To understand the different pharmacokinetics nomograms and algorithms.

WORK SCHEDULE

1. Write notes on i. Bayesian pharmacokinetics modelling, ii. Population pharmacokinetics modelling iii. Sawchuk-Zaske pharmacokinetics modelling
2. Write notes on C_{max}, C_{min}, AUC, Vd and Cl, *a-priori* dosing method, *posteriori* dosing method

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WEEK TWO

SCHEDULE 2

CALCULATING BODY WEIGHT

Title: Calculating body weight for antibiotics like aminoglycosides

Introduction: Aminoglycosides weight-based dosing should be based on Ideal or Adjusted body weight. The following criteria are used to determine an aminoglycoside dosing weight. In normal weight patients (BMI 18.5-24.9 kg/m^2) the **actual body weight** is used, while in overweight patient (100-120% ideal weight) the **ideal body weight** is used. However in obese patients (>120% of the ideal body weight) the **adjusted body weight** is used.

Aim: To understand how to calculate aminoglycoside dosing based on body weight

Ideal body weight by Devine (1974)

Ideal Body Weight (men) = 50 + 2.3 x (height over 60 inches)

Ideal Body Weight (women) = 45.5 + 2.3 x (height over 60 inches)

Adjusted body weight = Adjusted BW=IdealBW + (0.4 x (ActualBW−IdealBW))

WORK SCHEDULE

1. JM is a 50-year-old, 110-kg (5ft 10 in) male with gram-negative pneumonia. His current serum creatinine is 3.5 mg/dL, and it has been stable over the last 5 days since admission. Is the body weight ideal? If not compute
2. BE is a 49-year-old, 90-kg (5ft 10 in) female with gram-positive pneumonia. Her current serum creatinine is 1.5 mg/dL, and it has been stable over the last 3 days since admission. Is the body weight ideal? If not compute

3. BE is a 59-year-old, 90.8-kg (5ft 10 in) female with gram-positive pneumonia. Her current serum creatinine is 1.0 mg/dL, and it has been stable over the last 3 days since admission. Is the body weight ideal? If not compute

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WEEK THREE

SCHEDULE 3

Body surface area (BSA)

Title: Body surface area (BSA)

Introduction: Like BMI, BSA uses both height and weight to describe a patient's body habitus. BMI is commonly used to calculate the dose of chemotherapy agents. While there are a number of different BSA equations, the simplest and most commonly used in the hospital setting is a simplified equation by Mosteller 1987.Of note, the Mosteller simplified BSA equation has been validated in both adults and children.

$$\text{BSA } (m^2) = \sqrt{\frac{\text{Height (cm)} \times \text{Weight (kg)}}{3600}}$$

$$\text{Childs dose} = \frac{\text{child's BSA}}{\mathbf{1.73m^2}} \times \text{Normal adult dose}$$

WORK SCHEDULE

1. Your patient weighs 180 lbs. and is 6 feet 2 inches. What is the patient's body surface area (BSA)?
2. Your patient weighs 42 lbs. and is 3 feet. What is the patient's body surface area (BSA)?
3. Your patient weighs 30 kg and is 93 cm. What is the patient's body surface area (BSA)?
4. Your patient weighs 19.3 kg and is 82 cm. What is the patient's body surface area (BSA)?
5. A pediatric patient is ordered a medication dose of 100 mg/ m^2 a day by mouth for 5 days. The patient weighs 55 lbs. and is 4 feet 5 inches. What is the daily dose of medication the patient will receive?
6. A pediatric patient is ordered a medication dose of 25 mg/ m^2 twice a day. The patient weighs 46 lbs. and is 3 feet 10 inches. How many mg will the patient receive at each dose?
7. A pediatric patient is 80 lbs. and 4 feet 9 inches. The physician orders an oral medication that has a normal adult dose of 50 mg. How many mg of this medication will be administered to the patient?

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WEEK FOUR

SCHEDULE 4

Creatinine clearance

Title: Creatinine Clearance

Introduction: While the Cockcroft-Gault equation was the first and is the most well-known estimating equation for kidney function, it has largely fallen out of favor in clinical practice due in large part to its propensity to overestimate GFR using newer creatinine assays, with both the MDRD and CKD-EPI equations performing better across a variety of populations. However, many drug dosing recommendations for patients with decreased kidney function were based on creatinine clearance calculations from the CG equation, and it remains one option for determining drug dosage and discontinuation. Evidence suggests that eGFR measured by both MDRD and CKD-EPI show better concordance with measured GFR than does the CG equation, and so the use of these equations is appropriate for determining drug dosing. The MDRD equation cannot be used for acute renal failure. It is only useful in estimating glomerular filtration rate (GFR) in stable chronic kidney disease. Despite improvements to the MDRD equation, it tends to significantly underestimate measured GFR. Underestimation of GFR is particularly significant in patients with a GFR >60 ml/min/m2. The CKD-EPI equation performs superiorly to the MDRD Equation in patients with normal or mildly reduced estimated GFR (eGFR), and just as well in patients with an eGFR of <60 mL/min/m^2. It is used most widely by nephrologists and understood to be the most accurate means of non-invasively assessing GFR in the United States.

MDRD EQUATION CKD-EPI EQUATION

GFR (mL/min/1.73 m^2) = 175 × $(S_{cr})^{-1.154}$ × $(Age)^{-0.203}$ × (0.742 if female) × (1.212 if African American)

2021 CKD-EPI EQUATION

GFR(mL/min/1.73m^2) = 141 * min(Scr/κ,1)$^{\alpha}$ * max(Scr/κ, 1)$^{-1.209}$ * 0.993^{Age} * 1.018 [if female]

* 1.159 [if black]

Creatinine clearance, CC (mL/min) = (UV/P) x (1.73/A) (Corrected)

Where U = urine creatinine

V = urine volume

P = serum creatinine

A = body surface area (m^2)

WORK SCHEDULE

1. A 48 year-old male patient weighing 90kg with height 172cm submits a 24-hour urine for creatinine clearance analysis. The volume of the sample submitted is 1580 mL. The urine creatinine is 120 mg/dL, and the plasma creatinine is 1.0 mg/dL. What is the creatinine clearance? Is it normal, decreased, or increased?
2. A 35 year-old female patient with a body surface area of 2.50 m2 has a plasma creatinine of 2.5 mg/dL, and in 1 hour produces 90 mL of urine with a creatinine concentration of 100 mg/dL. What is the creatinine clearance? Is it normal, decreased, or increased?
3. Calculate the creatinine clearance in mL/min using the following results obtained from an 18 year-old female in a creatinine clearance evaluation:
   Urine Creatinine: 84 mg/dL (U)
   Urine Volume: 1440 mL/24 hours (V = 1440/1440 = 1.0)
   Serum Creatinine: 1.4 mg/dL (P)
   Body Surface Area: 1.60 m2 (A)
4. A 60 year-old male of average height and weight is admitted to the hospital for renal function evaluation. His urine creatinine was determined from a volume of 600 mL collected over 12 hours to be 120 mg/dL, and the serum creatinine was determined to be 1.5 mg/dL. Calculate the creatinine clearance for this patient.
5. A 54 year old gentleman visiting the Abuja while on a business trip from Canada became ill and presented to the ER of a local hospital with shaking chills, a fever of 39.4°C (oral) and a productive cough. A chest x-ray showed bilateral lower lobe infiltrates and the man

was admitted to your service with a diagnosis of pneumonia. The ER physician has ordered that the patient be given ceftizoxime 2g IV q8h. You notice, upon examining the patient's labs, that his serum creatinine is 2.6 mg/dL. Upon questioning, the patient tells you that his usual weight is 13 stone. A "stone" is a commonly-used weight unit in the Commonwealth countries. One stone equals 14 pounds. He says he is 188cm in height. Cal. CrCl. Is there a need for dosage change? Suggest if yes

Facts and Comparisons ® gives you the following information about ceftizoxime:

Ceftizoxime dosage in renal impairment

CrCl (ml/min)	**severe infections**
50-79	750mg - 1.5g IV q8h
5-49	500mg - 1g IV q12h
0-4	500mg - 1g IV q48h

The order is received in the pharmacy. Ceftizoxime is carried there as a 1g vial. The technician will need to dilute this vial with 10ml sterile water, resulting in a total volume of 10.7 ml. How much fluid will the technicians need to withdraw from the vial in order to make one of the doses that you have specified?

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6. Some medications are dosed for patients according to their "ideal body weight" (IBW), but only if a patient's actual body weight (ABW) is 25% or more above their IBW. The common equation used for calculating IBW is:

   Ideal Body Weight (men) = 50 + 2.3 x (height over 60 inches)

   Ideal Body Weight (women) = 45.5 + 2.3 x (height over 60 inches)

   Please calculate the ideal body weight, in kg, for a 5'3" female who weighs 140 pounds.

   _____ kg