School of Studies in Pharmaceutical Sciences, Jiwaji University

B. Pharmacy

Pharmaceutics

Dr. Suman Jain

Posology

- **Posos:** How much
- **Logos:** Science
- **Definition:** Posology is a branch of medical science which deals with dose or quantity of drugs which can be administered to a patient to get the desired pharmacological action.

Factors Influencing Dose

- Age
- Gender
- Body weight
- Route of administration
- Time of administration
- Environmental factors
- Emotional factors
- Presence of disease

- Accumulation
- Additive effect
- Synergism
- Antagonism
- Idiosyncrasy
- Tolerance
- Tachyphylaxis
- Metabolic disturbances

1) Age:

a) New Born:

- ✓ **Chloramphenicol** cause grey baby syndrome because of inadequate metabolism resulting drug accumulation.
- ✓ Absorption of Amoxycillin is higher because of less gastric acidity.

b) Children (Paediatrics):

- ✓ Need lesser dose than the normal adult dose, because of their pharmacokinetic profile (metabolism & excretion).

- Children can tolerate relatively larger amounts of **belladonna, digitalis and ethanol** whereas, elderly patients are more sensitive to **hypnotics and tranquillizers** which may produce confusion states in them.
- The blood brain barrier (BBB) of children are not well developed so more sensitive to **CNS stimulants**.

c) Adults: Age (18 yrs), weight (70 kg) and BSA (1.7-1.8 m^2)

d) Old people (Geriatrics, age > 60 yrs):

✓ Need lesser dose because of their pharmacokinetic profile

✓ More sensitive to diazepam and morphine

2) Gender:

- **Morphine and barbiturates** produce more **excitement** before sedation in women. Special care must be taken when drugs are administered during menstruation, pregnancy and lactation.
- Drugs which may stimulate the **uterine smooth muscles** e.g. drastic purgatives, antimalarial drugs and ergot alkaloids are contraindicated during pregnancy.
- During lactation drugs like antihistamines morphine and **tetracycline** are excreted in milk, should be avoided or use cautiously.
- **Alcohol, barbiturate, narcotic** drugs acts on fetus through placenta

3) Body weight:

- The average dose is mentioned either in terms of mg/kg body wt or as total single dose for an adult weighing between **50-100 kg**.
- However, in cases of **obese** patients, **children** and **malnourished** patients the dose differs. It should be calculated according to the body weight.

4) Route of administration:

- Route of administration affects therapeutic efficacy of drug
- **Intravenous** dose of drugs are usually smaller than the oral doses, because drug administered directly into blood stream.
- The onset of action is quick and there may be chances of drug toxicity is higher in IV route.

5) Time of administration:

- **Food** in the stomach delays the absorption of drugs.
- The drugs are more rapidly absorbed on empty stomach.
- So the amount of drug which is effective when taken on empty stomach may not be as effective after meals.
- The irritating drugs are better tolerated if administered after meals e.g. **Iron, Arsenic and cod liver oil** should always be given after meals
- **Antacid** drugs taken before meal

6) Environmental factors:

- **Daylight** is stimulant, enhancing the effect of stimulating drugs and diminishing the effect of hypnotics.
- **Darkness** is sedative. Hypnotics are more effective at night.
- The amount of barbiturate required to produce sleep during daytime is much higher than the dose required to produce sleep at night.

7) Emotional Factors:

- Females are more emotional than males and require less dose of certain drugs.
- Inert dosage forms called **placebos** which resemble the actual medicament in the physical properties are known to produce therapeutic benefit in diseases like angina pectoris and bronchial asthma.

8) Presence of disease:

- Drugs like **barbiturates** and chlorpromazine may produce unusually prolonged effect in patients having **liver cirrhosis**.
- Streptomycin which is excreted mainly by **kidney** may prove toxic for patients having kidney failure.

9) Accumulation:

- The drugs which are **slowly excreted** may build up a sufficient high concentration in the body and produce toxic symptoms if it is repeatedly administered for prolonged time.
- E.g. digitalis, emetine and **heavy metals**.

10) Additive effect:

- When the total pharmacological action of two or more drugs administered together is equivalent to the sum of their individual pharmacological action. This phenomenon is called as additive effect
- **Ephedrine & aminophylline** in the treatment of bronchial asthma

11) Synergism:

- When two or more drugs are used in combination form, their action is increased. This Phenomenon is called synergism.
- E.g. **Procaine and adrenaline** combination increases the duration of action of procaine.

12) Antagonism:

- When the action of one drug is opposed by the action of other drug on the same pharmacological system is known as drug antagonism.
- The use of antagonistic response to drugs is valuable in the treatment of poisoning e.g. milk of magnesia is given in acid poisoning where alkaline effect of milk of magnesia neutralizes the effect of acid poisoning.

a) **Competitive/Reversible antagonism:** Both agonist and antagonist have same binding site.

- Acetylcholine and atropine

b) **Noncompetitive/Irreversible antagonism:** Antagonist inactivate receptor so that effector complex with agonist cant be formed. Phenoxybenzamine and adrenaline at α-receptor.

c) **Physiological antagonism:** Binding of agonist and antagonist to two different receptors but their action is opposite. Adrenaline (bronchodilatation) and histamine (bronchoconstriction).

13) Idiosyncrasy (Allergy):

- Extraordinary pharmacological response to a drug. The word idiosyncrasy has been replaced by allergy. Ex.,
- Small quantity of **aspirin** may cause gastric hemorrhage
- **Penicillin** sensitivity is observed in many individuals.

14) Tolerance:

- When unusually large dose of drug is required to produce pharmacological action which could have been otherwise produced by normal dose, is termed as tolerance.
- e.g., **Smokers** can tolerate nicotine etc.
- True tolerance is produced by oral and parenteral administration of drug while Pseudo is produced only by oral route of administration.

15) Tachyphylaxis:

- It is observed that when certain drugs are administered repeatedly at short intervals, the cell receptors are blocked up and pharmacological response to that particular drug is decreased.
- e.g., Ephedrine when given in repeated dose at short interval in the treatment of bronchial asthma may produce very less response due to tachyphylaxis

16) Metabolic disturbances:

- Changes in water electrolyte balance and acid base balance, body temperature and other physiological factors may modify the effects of drugs.
- **Salicylates** reduce the body temperature only in case an individual has rise in body temperature. They have no antipyretic action

17) Drug dependence/ Addiction:

- Euphoria; Tolerance; Dependence/Habituation

a) Physical Dependence: Tea, Nicotine

- Depend on drug to function normally
- Occurrence of withdrawal syndrome
- when stop taking drug abruptly
- ✓ Vary from one class of drug to another
- ✓ Compensating mechanisms produce imbalance

b) Psychological Dependence: LSD, Marijuana, Opiates

- Behavioral dependence
- High rate of drug use, craving for the drug & tendency to relapse after stopping use
- Related to drug reinforcing properties

Dose Calculation for Child

1) Young's formula:- Child below **12** years

$$\frac{\text{Age (years)}}{\text{Age (years)} + 12} \times \text{Adult dose}$$

2) Fried's rule: Infant max upto **2** years

$$\frac{\text{Age (months)}}{150} \times \text{Adult dose}$$

3) Dilling's Formula: 4-20 years

$$\frac{\text{Age in Years}}{20} \times \text{Adult dose}$$

4) Catzel's rule:

$$\frac{\text{Body surface area of child}}{\text{Body surface area of adult}} \times \text{Adult dose}$$

$$\frac{\text{Body surface area of child } (m^2)}{1.73\ m^2} \times \text{Adult dose}$$

5) Clark's formula: When weight is given in kg or pounds

$$\frac{\text{Child's weight in kg}}{70} \times \text{Adult dose}$$

$$\frac{\text{Child's weight in pounds}}{150} \times \text{Adult dose}$$

Dose From Body Surface Area

No.	Weight (kg)	Surface Area (m^2)	Approx % of Adult Dose
1	2	0.15	9
2	4	0.25	14
3	6	0.33	19
4	8	0.40	23
5	10	0.46	27
6	15	0.63	36
7	20	0.80	46
8	25	0.95	55
9	30	1.08	62
10	35	1.20	70
11	40	1.30	75
12	45	1.40	81
13	50	1.51	87
14	55	1.58	91

CALCULATING PEDIATRIC DOSAGES USING FRIED'S RULE

EXAMPLE 5.9 An infant, 15 months old and weighing 20 pounds, needs Streptomycin Sulfate, which is usually administered to adults as 1 gm (1000 mg), as a daily IM injection. What is the appropriate dosage for the infant?

To calculate the pediatric dosage based on a child's age in months, simply use the formula for Fried's Rule. Using the information provided, you can set up the calculation as follows:

$$\text{Pediatric Dose} = \frac{15\ (\text{Age in months})}{150} \times 1000\ \text{mg (Adult Dose)}$$

$$\text{Pediatric Dose} = \frac{15}{150} \times 1000$$

$$\text{Pediatric Dose} = 0.1 \times 1000$$

$$\text{Pediatric Dose} = 100\ \text{mg}$$

So, according to Fried's Rule, the pediatric dosage appropriate for a 15-month-old would be 100 mg.

Example: Calculate the child dose for 1-year-old baby, if the adult dose of the medicine is 400 mg.

Solution: Given
Age of child in month = 12 months
Average adult dose = 400 mg.

Child dose = (Age of child in month /150 lbs) x Average adult dose
= (12/150lbs) x 400 mg
= 32mg

CALCULATING PEDIATRIC DOSAGES USING YOUNG'S RULE

EXAMPLE 5.10 Now, let's reexamine Example 5.9 using Young's Rule, which uses the child's age in years. The age of a 15-month-old could be expressed as 1.25 years old, since he or she has lived for 12 months (1 year) + 3 months (1/4 or 0.25 of a year).

Using an age of 1.25 years and the information provided in Example 5.5, set up the calculation, using Young's Rule, as follows:

$$\text{Pediatric Dose} = \frac{1.25 \text{ (Age in years)}}{13.25 \text{ (Age of child + 12)}} \times 1000 \text{ mg (Adult Dose)}$$

$$\text{Pediatric Dose} = \frac{1.25}{13.25} \times 1000$$

$$\text{Pediatric Dose} = 0.094 \times 1000$$

$$\text{Pediatric Dose} = 94 \text{ mg}$$

So, according to Young's Rule, the pediatric dosage appropriate for a 15-month-old would be 94 mg.

Example: A 10 year old girl weighing 60 lbs. Average adult dose given for the girl is 300 mg Calculate the child‘s pediatric dose.

Solution: Given, age of child = 10 year, average adult dose = 300 mg.

Child’s pediatric dose = [Age of child/Age of child+12] x Average adult dose

= [10 / (10 + 12)] x 300 mg
= (10/ 22) x 300 mg

= 0.4545 x 300 mg

= 136.36 mg

CALCULATING PEDIATRIC DOSAGES USING CLARK'S RULE

EXAMPLE 5.11 Now, let's reexamine Example 5.9 using Clark's Rule, which uses the child's weight in pounds.

Using a weight of 20 pounds and the information provided in Example 5.5, set up the calculation, using Young's Rule, as follows:

$$\text{Pediatric Dose} = \frac{20 \text{ (Weight in pounds)}}{150} \times 1000 \text{ mg (Adult Dose)}$$

$$\text{Pediatric Dose} = \frac{20}{150} \times 1000$$

$$\text{Pediatric Dose} = 0.133 \times 1000$$

$$\text{Pediatric Dose} = 133 \text{ mg}$$

FORMULA	Weight Conversion

$$1 \text{ kg} = 2.2 \text{ lb}$$

CONVERTING WEIGHT FROM POUNDS TO KG

EXAMPLE 5.12 If the infant weighs 20 pounds, what is his or her weight in kg?

Using the weight conversion formula, you divide the patient's weight, which in this case is 20, by 2.2 to convert the weight from pounds to kg.

$$20 \div 2.2 = 9.09$$

So, the infant weighs 9.09 kg.

EXAMPLE 5.13 If a person weighs 180 lb., divide by 2.2 to find weight in kilograms.

$$\frac{180}{2.2} = 81.82 \text{ kg}$$

So 180 lb. equals 81.82 kg.

CALCULATING DOSAGES USING MG/KG/DAY

EXAMPLE 5.14 Using the infant from Example 5.9, determine the pediatric dosage if it is recommended to administer 20 mg/kg/day (maximum of 1gm) of Streptomycin Sulfate.

The infant's weight in kg has already been calculated as 9.09, so now we will multiply the recommended number of milligrams by her weight in kilograms to calculate the appropriate daily pediatric dosage.

$$20 \text{ mg} \times 9.09 \text{ kg} \times 1 \text{ day} = \text{Pediatric Daily Dosage}$$

$$20 \times 9.09 \times 1 = \text{Pediatric Daily Dosage}$$

$$181.8 = \text{Pediatric Daily Dosage}$$

So, according to mg/kg/day, the patient should be given 181.8 mg of Streptomycin Sulfate as a daily IM injection.

Using the patient from Example 5.13, an order is given for a dose stated as 20 mg/kg tid.

Step 1: The weight has been determined to be 81.82 kg.

Step 2: Multiply 81.82 by 20 mg, which equals 1634 mg.

Step 3: Divide the total number of milligrams for the day by the number of doses for the day: 1634 mg/3 = 544 mg.

Based on his weight, the patient should receive 544 mg of drug per dose.

The patient used in the preceding example weighs 180 lb. and is probably an adult. The same principles apply to calculating appropriate dosages for a child based on body weight in kilograms.