

CLINICAL DATA TEXT

Dose

Clinically the expression dose is self-explanatory. Throughout prescription of proper dose for any patient, so many things must be well thought-out. Some antibiotics are obtainable in tablet, capsule or suspension form for oral route. So doctors should prefer the formulation suitable for the patients. It is significant because it influences the bioavailability of the drug. For instance, bioavailability of digoxin is 62 when given in oral route on the other hand, the bioavailability of digoxin elixir administered orally is 0.08. In the following tables, in case of dose it is oral route. And when another route is more usual, this has been indicated in tables.

Therapeutic Concentration

Following absorption, drug reaches the plasma or blood to produce therapeutic effect. The concentration that needs to be reached for drug to exert a significant therapeutic benefit without any side effect is called therapeutic concentration.

Penetration to CNS

The majority of the drugs are either weak acid or weak base and remain in non-ionized and lipid soluble form. Presence of hydrocarbon chain, steroid nucleus, benzene ring or halogen favor lipid solubility. On the other hand, water solubility is favored by the possession of alcohol (-OH), amide (-CONH₂), carboxyl group (-COOH), and conjugated products. Within any closely related series of compounds more lipid soluble will show better penetration to the central nervous system (CNS). Lipid soluble drugs can pass through the blood brain barrier(BBB). CSF/PI is the ratio which indicate the ability of drug to penetrate the CNS.

Lactation

Breast-feeding mothers may deliver substantial amount of some drugs to her child whose ability to handle the foreign compound is very low. So, this parameter is extremely important and this parameter is depend on the time of sampling breast milk in relation to drug administration. (Table 1.1)

T_{1/2} in Renal and Hepatic failure

Understanding in renal failure case, or decrease in renal function with age, can be related to creatinine clearance.

In some case of hepatic disease, increased bioavailability can be observed. This is due to the reduction of first-pass effect diseased liver. (Table 1.2)

Risk in Pregnancy

During first trimester, many drugs are known to damage the developing fetus, resulting malformations. There are some drugs which can exert toxic effects during second and third trimester, giving rise to retarded growth and poor functional development of certain tissues.

Table 1.1 Concentration of Various Drugs in Maternal Blood and Breast Milk under Normal pH Conditions

Drug Levels (Units/100 ML)			
Drug Administered (Therapeutic Dosage)	Plasma or Serum (pH 7.4)	Milk (pH 7.0)	Administered Drug Appearing in Milk (%day)
Aspirin	1-5 mg	1-3 mg	0.5
Bishydroxycourmarin	11-16.5 mg	0.2 mg	0.5
Chloral hydrate	0-3 mg	0-1.5 mg	0.6
Chloramphenicol	2.5-5 mg	1.5-2.5 mg	1.3
Chlorpromazine	0.1 mg	0.03 mg	0.07
Colistin Sulfate	0.3-0.5 mg	0.05-0.09 mg	0.07
Cycloserine	1.5-2 mg	1-1.5 mg	0.6
Diphenylhydantoin	0.3-4.5 mg	0.6-1.8 mg	1.4
Erythromycin	0.1-0.2 mg	0.3-0.5 mg	0.1
Ethanol	50-80 mg	50-80 mg	0.25
Ethyl biscoumacetate	2.7-14.5 mg	0-0.17 mg	0.1
Folic acid	3 µg	0.07 µg	0.1
Imipramine hydrochloride	0.2-1.3 mg	0.1 mg	0.1
Iodine 131	0.002 µc	0.13 µc	2-5
Isoniazid	0.6-1.2 mg	0.6-1.2 mg	0.75
Kanamycin sulfate	0.5-3.5 mg	0.2 mg	0.05
Lincomycin	0.3-1.5 mg	0.05-0.2 mg	0.025
Lithium carbonate	0.2-1.1 mg	0.07-0.4 mg	0.12
Meperidine hydrochloride	0.07-0.1 mg	Trace (<0.1 mg)	<0.1
Methotrexate	3 µg	0.3 µg	0.01
Nalidixic acid	3-5 mg	0.4 mg	0.05
Novobiocin	1.2-5.2 mg	0.3-0.5 mg	0.15
Penicillin	6-120 µg	1.2-3.6 µg	0.03
Phenobarbital	0.6-1.8 mg	0.1-0.5 mg	1.5
Phenylbutazone	2-5 mg	0.2-0.6 mg	0.4
Pyrilamine maleate	-	0.2 mg	0.6
Pyrimethamine	0.7-1.5 mg	0.3 mg	0.3
Quinine sulfate	0.7 mg	0.1 mg	0.05
Rifampicin	0.5 mg	0.1-0.3 mg	0.05
Streptomycin sulfate	2-3 mg	1-3 mg	0.5
Sulfapyridine	3-13 mg	3-13 mg	0.12
Tetracycline hydrochloride	80-320 µg	50-260 µg	0.03
Thiouracil	3-4 mg	9-12 mg	5

Table 1.2 Drugs whose Dosage Regimen should be Changed in Various Degrees of Renal Impairment

Mild Impairment	Moderate Impairment	Severe Impairment
Acetohexamide	Acetazolamide	Acetaminophen*
Cefazolin	Acetasalicyclic acid	Acetazolamide*
Chlorpropamide	Acetohexamide *	Amphotericin B
Clofibrate	Allopurinol	Azathioprine
Colistimethate	Aminosalicylic ac id *	Cephalexin
Gentamicin	Amoxicillin	Cephalothin
Kanamycin	Ampicillin	Colchicine
Methadone	Carbenicillin	Digitoxin
Streptomycin	Chlordiazepoxide	Diphenhydramine
Tetracycline	Chlorpropamide*	Fthaccrynic acid*
Vancomycin	Cyctophosphamide	Glutethimide
	Digoxin	Hydralazine
	Ethambutol	Lincomycin
	Flucytosine	Methicillin
	Gertamicin	Neostigmine
	Gold sodium thiromalate*	Nitrofurantoin
	Guanethidine	Penicillin G
	Insulin	Phenformin*
	Lithium carbonate*	Phenobarbital
	Meprobamate	Quinine
	Mercurials*	Spirolactone*
	Methenamine mandalate*	Sulfamethoxazole-trimethoprim *
	Methotrexate	Thiazides*
	Methyldopa	Triamterene*
	Minocyc line	Tolbutamide
	Neomycin	
	Ouabain	
	Penicillamine	
	Pentamidine	
	Phenazopyridine	
	Phenylbutazone*	
	Primidone	
	Phenothiazines	
	Probenecid*	
	Procainamide	
	Propylthiouracil	
	Sultamethoxazole-trimethoprim	
	Sulfisoxazole	
	Trimethadone	

Table 1.3 Potential Bioequivalency Problems of Some Drugs

Acetazoiamide	Hydrochlorothiazide	Promethazine
Acetyldigitoxin	Hydroflumethiazide	Propylthiouracil
Alseroxylon	Imipramine	Pyrimethamine
Aminophyllin	Isoproterenol	Quinethiazide
Aminosalicic acid	Liothyronine	Quinidine
Bendroflumethiazide	Menadione	Rauwolfia serpentin
Benzthiazide	Mephentoin	Rescinnamine
Betamethasone	Methazolamide	Reserpine
Bishydroxycoumarin	Methyclothiazide	Salicylazosulfapyridine
Chlorambucil	Methylprednisolone	Sodium sulfoxone
Chlorodiazepoxide	Methyltestosterone	Spirolactone
Chlorothiazide	Nitrofurantoin	Sulfadiazine
Chlorpromazine	Oxtriphylline	Sulfadimethoxine
Cortisone acetate	Para-aminosalicylic acid	Sulfamerazine
Deserpidine	Para-methadione	Sulfaphenazole
Dexamethasone	Perphenazine	Sulfasomidine
Dichlorphenamide	Phenacemide	Sulfasoxazole
Dienestrol	Phensuximide	Theophylline
Diethylstilbestrol	Phenylaminosalicylate	Thioridazine
Dyphylline	Phenytoin	Tolbutamide
Ethinylloestradiol	Phytonadione	Triamcinolone
Ethosuximide	Polythiazide	Trichlormethiazide
Ethotoin	Prednisolone	Triethyl melamine
Ethoxzolamide	Primidone	Trifluoperazine
Fludrocortisone	Probenecid	Triflupromazine
Fluphenazine	Procainamide	Trimeprazine
Fluprednisolone	Prochlorperazine	Trimethadione
Hydralazine	Promazine	Uracil mustard Warfarin