Pharmacokinetic II

Distribution in pharmacokinetics refers to the process by which a drug is dispersed throughout the body compartments after absorption. It involves several factors, mechanisms, and considerations:

Body Compartments for Distribution:

1. **Vascular Compartment:** Small volume of distribution (around 4 liters in a 70 kg person). Drugs here are hydrophilic, ionized at plasma pH, and have high molecular weight (e.g., Heparin).
2. **Vascular and Interstitial Compartment:** Moderate volume of distribution (around 14 liters in a 70 kg person). Drugs are hydrophilic, have smaller molecular weight, and are less ionized at plasma pH (e.g., Neostigmine).
3. **Vascular, Interstitial, and Intracellular Compartment**: Large volume of distribution (around 40-42 liters in a 70 kg person). Drugs are non-ionized and lipophilic (e.g., Barbiturates).

Key Factors Influencing Distribution:

1. **Blood-Brain Barrier (BBB):** Only lipid-soluble and non-ionized drugs can pass through the BBB. Inflammation (e.g., meningitis) can increase the permeability of the BBB, allowing drugs like penicillins and cephalosporins to reach higher concentrations in cerebrospinal fluid (CSF).
2. **Placental Barrier**: Drugs that cross the placental barrier can cause teratogenic effects during pregnancy or neonatal issues such as asphyxia or jaundice during labor.
3. **Redistribution:** Highly lipid-soluble drugs, such as thiopental, initially distribute to the central nervous system (CNS) but then redistribute to less perfused tissues (e.g., skeletal muscle and fat), which ends their action.

Volume of Distribution (Vd):

- **Theoretical Concept**: Vd relates the amount of drug in the body to its plasma concentration. It's used to:
    1. Calculate the loading dose.
    2. Calculate the corrective dose.
    3. Treat drug toxicity.

- **Effect on Dialysis**: Hemodialysis is useful for drugs with low Vd (mostly in the blood), but less useful for drugs with high Vd (mostly in tissues). Peritoneal dialysis can be useful for drugs with moderate Vd.

Factors Influencing Distribution:

1. **Lipophilicity (Diffusion):** Lipophilic drugs diffuse more easily across cell membranes.
2. **Tissue Binding (Tissue Affinity):** Some drugs concentrate in specific tissues due to affinity. For example:
    - Chloroquine is concentrated in the liver.
    - Iodides are concentrated in the thyroid.
3. **Plasma Protein Binding (PPB):**
    - Drugs in the blood exist as a **bound form** (inactive, non-diffusible, can't be metabolized or excreted) and a **free form** (active, diffusible, can be metabolized or excreted).
    - The bound form acts as a reservoir. When the free form is metabolized or excreted, more drug is released from the bound form to maintain equilibrium.
    - Displacement from PPB can be clinically significant, especially for drugs with high PPB capacity and small Vd, as small changes in the free form can lead to toxicity. For example, aspirin can displace warfarin, leading to an increased free concentration of warfarin, which may cause bleeding.

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