Pharmacokinetics Administration, Travel, Metabolism and Elimination of Psychoactive Drugs

Psychology 472

Pharmacology of Psychoactive Drugs

Listen to the audio lecture while viewing these slides

1

Neuropharmacology

- Is the scientific study of drug effects on the nervous system.
- Is an all encompassing term
- Is applied to ALL drugs that influence the nervous system
- Includes
  - Sensory systems
  - Motor systems
  - Cognitive functioning
  - Others

2

Some Terms and Definitions

- Psychopharmacology
  - Usually used to describe drug effects on psychological parameters such as emotion and cognition (Nestler)
- Psychotropic
  - Drugs that influence behavior
- Pharmacokinetics
  - Is the study of how drugs enter, are distributed, metabolized, and removed (excreted) from the body
- Pharmacodynamics
  - Is the study of what drugs do various structures in the body.

3

Pharmacokinetics

- Four variables to examine (ADME)
  - How drugs enter are Absorbed into the system
  - How drugs are Distributed throughout the system
  - How drugs are Metabolized in the system
  - How drugs are Eliminated from the system.

4

1: How Drugs Enter or are Absorbed

- Influences
  - How fast a drug reaches its target organ
  - Which structure(s) the drug influences
  - Risk of acquiring BBPs

5

Oral

- Has a slow onset of action
  - Minutes
  - Can take longer if time release or has special coatings
- Advantage
  - Easy to take
  - Low risk for BBPs

6

Issues

- Drug must be soluble and stable in stomach fluid.
- Drug is absorbed through upper intestine through passive diffusion.
- Drugs must generally be somewhat lipid soluble.
- Disadvantages:
  - Vomiting and stomach distress
  - Hard to know how much of drug will be absorbed due to genetic differences.
  - Stomach acid destroys some drugs.

First Pass Metabolism

- Blood goes from the gastrointestinal (GI) tract to the liver before the body
- Some amount of the drug will be inactivated or metabolized as it goes through the liver.
  - Important for steroid use
- Reason for other routes of ingestion

Rectal

- Used if a person is vomiting, unconscious, or unable to swallow.
- Absorption is often irregular, unpredictable, and incomplete.
- Rarely used for illicit drugs
  - Takes to long
  - Other issues

Other Routes of Administration

- Faster routes (Seconds)
  - Respiratory (Nasal/Oral) Nicotine Cocaine
    Intravenous (Venous system) Meth. Opiates
  - Intraarteral (Arterial system) Meth. Opiates
- Problem – Risk of BBPs
- Slower routes (Minutes)
  - Intramuscular (muscle groups) Steroids
  - Mucus Membranes Cocaine
  - Subcutaneous (under the skin) Some Halluc.
  - Cutaneous (Dermal) ACh. Nerve Agents, Nicotine Patches

Mucous Membranes

- Absorbed through membranes in mouth or nose.
- Examples:
  - Nitroglycerine, cocaine, nicotine gum.

Inhalation

- Popular for recreational drugs (e.g., tobacco, marijuana, cocaine, heroin).
- Lung tissues' large surface area allows for rapid absorption into blood.
- Pulmonary capillaries carry drug directly into left side of heart and then directly into the aorta and arteries going to the brain.
- Even faster onset than injection.

Transdermal

- Provides continuous, controlled release.
- Allows for slow continuous absorption
- Decreases side effects.
- *Examples:*
  - Nicotine patches
  - Birth control medications
  - Pain medications
- Not usually used for illicit drugs
- Can be dangerous if used with combinations of other drugs
  - Opiates for pain plus injection or oral = overdose

Injection

- Intravenous - IV
  - Drug is introduced directly into bloodstream.
    - Dosage can be extremely precise.
    - (most dangerous route).
- Intramuscular – IM
  - Drugs injected into skeletal muscle.
    - More rapid than absorption from stomach
    - Slower than intravenous.
- Subcutaneous – Sub Q
  - Injected under the skin.
  - Slower than IV or IM

Additional Medical/Scientific Routes

- Intraperitoneal (peritoneal-abdominal cavity)
- Intracerebroventricular (cerebral ventricular)
- Intracerebral (brain parenchyma)
- Takes seconds or minutes
- Can be dangerous
- Minimal risk of BBPs due to sterile techniques used.

15

2: How Drugs are Distributed in the Body

- Circulatory system
- Blood goes from the Heart to the
- Lungs to
- Heart to
- Body structures via arteries
- Arteries to smaller blood vessels
- Small blood vessels to Heart via veins
- Repeat

16

Distribution Methods

- Plasma–more likely with water soluble drugs
- Platelets–more likely with lipid soluble drugs
- Attached to proteins (e.g., albumin)–bound vs. free

Capillaries

- Tiny cylindrical blood vessels
- Have small pores (between 90 and 150 angstroms), which are larger than most drugs.
- Allow transport of drugs regardless of lipid-solubility.
- Blood and protein are too big for pores; drugs that bind to plasma proteins cannot pass through.

Bioavailability

- Determines how much of a drug that actually reaches a target.
- Effects can depend on
  - Gastrointestinal loading (decreases absorption)
  - Liver metabolism (First Pass)
  - Binding to plasma proteins that makes the drug unavailable to the target
  - Cannot penetrate the Blood-Brain Barrier
  - Cannot penetrate other cell membranes

Cell Membranes

- Membranes made of a phospholipid layer.
- The membrane is only permeable to small, lipid-soluble molecules.
- Important as barriers to absorption and distribution of drugs.

Effects on Target Binding Site

- All drugs bind on some receptor site
- Causes some effect on the target site
- Creates some behavioral effect
  - Called Main Effect
- Also has other unintended effects
  - Called Side Effect
- Called Pharmacodynamics

Pharmacodynamics

- Generally is defined as effects of drugs on neurological systems.
- Can be associated with any system
  - Heart, Liver, Endocrine System, etc.
- Lots of issues influence pharmacodynamics
  - Amt. of drug available
  - Past drug use - Tolerance
  - Drug Stability
    - How long a drug lasts in the body before it is metabolized
  - Drug Consistency
    - Does it need metabolized before it can be used L-Dopa vs. Dopamine

3: Metabolism and Elimination of Drugs

- Drugs can be removed many ways
- Breathing
- Sweat
- Feces
- Liver metabolism
  - Have specific enzymes that break down drugs to inactive compounds
- Can be influenced by
  - Liver disease
  - Other compounds that are present
    - Multiple drugs
    - Fluid levels
  - Other health effects

Breathing, Sweat, Feces

- Removes trace amounts of some drugs
- Alcohol
  - Is removed multiple ways
  - Reason for breathalyzer

Liver

- Protects the body from toxic substances.
  - Uses enzymes/proteins to change from toxic to non-toxic states
    - Physically located in liver cells.
    - Most are nonspecific.
    - Referred to as the microsomal enzymes (main category = *cytochrome P450*).

Factors influencing P45O Activity

1. Disease, especially of the liver
2. Species
3. Age, changes in young and old
4. Genetics
5. Environment
6. Past experience with drugs

Kidneys

- Also metabolizes some drugs (Ibuprofen)
- Removes other waste products from the blood
- Can be influenced by fluid levels and other compounds (salt)
- Also removes other drugs and products
  - BCPs, Lithium, some hallucinogens, metabolites
  - Can cause problems in other organisms

Other issues

- Genetics and Age
  - Have major influences in how the body absorbs and eliminates drugs
- Additive and Synergistic Effects
  - Different drugs can combine to create a greater effect than before
    - Alcohol and Barbiturates vs Alcohol and Benzodiazepines

Drug Half-Life

- Definition

  Time it takes for the body to eliminate half of a given blood level of a drug.

  Varies by type of drug

  Influences potential for overdose

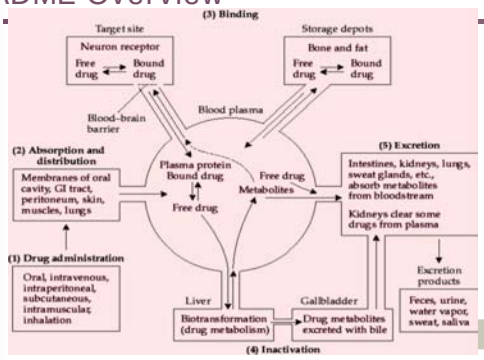
Blood Brain Barrier

- Designed to protect neurons from toxins.
- Brain capillaries do not allow drugs to pass as easily as capillaries in rest of body.

Steady State Dynamics

- Is the balance point at which the rate of drug administration approximates the rate of excretion.
- Used when providing drugs to achieve some effect
- Important for medicine
- Also important for withdrawal issues

ADME Overview



Conclusions

- Many variables can influence drugs in the body
- Is important for the clinician to be aware of them
  - Reason psychopharmacology is important
  - Reason medical exams are a important component for drug/alcohol treatment

33