

Chapter- 4 DRUG ACTING ON CENTRAL NERVOUS SYSTEM

4.1 SEDATIVES AND HYPNOTICS

Sedative:

These are the drugs which reduce anxiety without producing normal sleep.

Hypnotics:

These are the drugs which produces sleep natural sleep.

Sedative act as hypnotic and vice-versa the main difference is in the dose about 1/3 dose of a hypnotics willacts as sedatives

Normal sleeps are of two types:

- Non-rapid eye moment (NREM): The eyeballs are motionless.
- Rapid eye moments (REM): The eye shows rapid moment person awakened during this phase saythat they were dreaming.

A normal sleep begins with NREM (about 90mints) and then passed to a short duration of REM sleep (about20mnts) after making with NREM sleep and this cycle goes on both NREM and REM are essential for normal sleep.

CLASSIFICATION:

1) Barbiturates:

- a. **Long action barbiturates** (duration of action in 8hrs or more) Ex: Barbitone, Phenobarbitone.
- b. **Intermediate acting barbitone** (4 hrs or more) Ex: Amylobarbitone, Cyclobarbitone
- c. **Short acting barbitone** (less than 4 hrs) Ex: Hexobarbitone.
- d. **Ultra-short acting barbiturates.** (less than 1 hrs) Ex: Thiopentone Sodium

2) Non- barbiturates:

- a. **Benzodiazepines:** Ex: Diazepam, Nitrazepam, Alprazolam.
- b. **Alcohol:** Ex: Chlorhydrate, Ethanol
- c. **Aldehydes:** Ex: Paraldehyde
- d. **Carbamates:** Ex: Ehinamate

e. Inorganic:

Ex: KBr, NaBr

3) Newer Agent:

Ex: Zolpidem

Barbiturates:

Barbiturates are the derivative of barbituric acid act as general depressant. They are not preferred nowadays as sedatives and hypnotics because of development of relatively safer benzodiazepines.

PHARMACOLOGICAL ACTIONS:

- 1) **CNS:** barbiturates produce CNS depression such that from mild sedation to even coma.
- 2) **Sleep:** barbiturates induce sleep resembling natural sleep but it decreases the time spent on REM sleep.
- 3) **Respiratory system:** in higher doses they depress the respiratory center in the brain and may produce death.
- 4) **CVS:** they depress cardiac activity and in higher doses cause a fall in B.P.
- 5) **Liver:** large doses may produce hepatic dysfunction.
- 6) **Kidneys:** large doses decrease urinary output due to a decrease in glomerular filtration and release of ADH (anti-diuretic hormone)

Mechanism of action:

Barbiturates have a GABA (Gamma-Amino Butyric Acid) like action or enhance the effect of GABA which is an inhibitory neurotransmitter. Barbiturates may also inhibit the neuronal uptake of GABA or may stimulate its release.

PHARMACOKINETICS:

Barbiturates are rapidly absorbed after oral as well as parenteral administration, they are widely distributed in the body. They are mainly metabolized in the liver and to a small extent in the kidney and brain excretion is through urine.

ADVERSE EFFECTS:

- **Tolerance:** with duration of treatment tolerance develops and it requires to increase the dose to produce the same effect.
- **Drug dependence:** repeated use develops both psychological and physical dependence
- **Intolerance:** excitement, vomiting, nausea, headache, diarrhea.

ACUTE BARBITURATE POISONING:

Acute barbiturate poisoning occurs due to accidental overdose or consumption with suicidal intention, leads to hypotension, respiratory depression, and coma. If not treated properly death results due to respiratory arrest.

Uses:

- As a sedative and hypnotics
- Anaesthesia : ultra short acting barbiturates like thiopentone
- Preanaesthetic medication
- Anticonvulsant (specially long acting barbiturates)

Non - barbiturates

Benzodiazepines: These classes of drugs are safer and also possess better sedative hypnotic activity.

PHARMACOLOGICAL ACTIONS

- 1) **CNS:** benzodiazepines causes sedation, hypnotics, muscle relaxant and anticonvulsant
- 2) **C.V.S:** toxic dose may produce fall in B.P
- 3) **Respiratory system:** Hypnotic does not affect the respiration in normal person but higher doses cause respiratory depression.
- 4) **Pharmacokinetics:** given orally but IV or IM. can also be used. They are widely distributed in the body. They can cross placental and secreted in the milk. They are metabolized in liver and excreted in urine.
- 5) **Pharmacodynamic:** benzodiazepines facilitate the action of GABA in C.N.S

ADVERSE EFFECTS

- Drug dependence
- Fatigue, memory loss
- Blurring of vision
- Benzodiazepines are contraindicated in respiratory depression, hepatic impairment also sleep apnea syndrome

USES

It is used as sedative, hypnotic, anti-anxiety muscle relaxant, anticonvulsant.