CNS Depressants
Objectives

- Describe the general signs of CNS depression.
- Discuss the definition of sedative, hypnotic, tranquilizer and anesthetic.
- Elucidate sedative – hypnotic classification.
- Understand the mechanism of barbiturate and benzodiazepine and illustrate some examples of each drug class.
Classification of CNS depressants according to their actions:

1- Sedative – hypnotics.

2- Tranquillizers.

3- Anesthetics.
General signs for CNS depressants

1- ↓ vitality.

2- ↓ excitability.

3- ↓ HR & RR.
I. Sedative – hypnotics

**Sedatives:**
Drugs which decrease the activity, calm the recipient, cause sedation and in large dose they induce sleep.

**Hypnotics:**
Drugs which induce sleep that resembles the natural sleep.

e.g. Barbiturates
Natural Sleep

<table>
<thead>
<tr>
<th>NREM</th>
<th>REM</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Non rapid eye movement.</td>
<td>▪ Rapid eye movement.</td>
</tr>
<tr>
<td>▪ Consists of 4 stages.</td>
<td>▪ Consists of one stage (dreaming stage).</td>
</tr>
<tr>
<td>▪ Lasts for 90 min.</td>
<td>▪ Lasts for 20 min.</td>
</tr>
</tbody>
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Sedative – hypnotics: Classification

**Sedative-hypnotics**

**Barbiturates**
1. Long acting (12-24 hr) e.g. Phenobarbital
2. Intermediate acting (8-12 hr) e.g. Amobarbital
3. Short acting (4-8 hr) e.g. Pentobarbital
4. Ultrashort acting (0.5-1 hr) e.g. Thiopental

**Non-barbiturates**
- Benzodiazepines
- Non-benzodiazepine
II- Tranquillizers

Definition:

Tranquillizers are drugs which relieve mental anxiety and stress without affecting the consciousness.

e.g. Chlorpromazine (CPZ)
III- Anesthetics

**Definition:**
Drugs which cause unconsciousness and generalized loss of pain sensation to permit the performance of surgery. e.g. thiopental (IV), halothane (inhalation).

**MOA:**
Decrease with propagation of nerve impulses by interfering with electrolytes conductance through the cell membrane.
1- Barbiturates

MOA:
They have GABA-like action → ↑ opening time of chloride channels → ↑ conductance of chloride ions → hyperpolarization.

Classification according to their duration of action:
1- Long-acting.
2- Intermediate-acting.
3- Short acting.
4- Ultrashort acting.
2- Benzodiazepines

MOA:

- Bind non-selectively to benzodiazepine receptors (GABA<sub>A</sub>-dependent).
  - GABA<sub>A</sub> receptors $\rightarrow$ increase Cl influx $\rightarrow$ hyperpolarization
  - GABA<sub>B</sub> receptors $\rightarrow$ Gi protein $\rightarrow$ ↓cAMP $\rightarrow$ relaxation

Examples:

- Diazepam (sedative).
- Triazolam (hypnotic).
3- Non-barbiturate Non-BZD

1. 5-HTA1 agonist e.g. buspirone.

2. Chloral hydrate (prodrug) converted to trichloroethanol.

3. Antihistamine e.g. diphenhydramine.

4. Paraldehyde.

5. Promethazine.
Specific signs of sedative-hypnotic

Drugs:

Thiopental, Phenobarbital and Chloral hydrate.

Signs:

1- Staggering gait.
2- Sleeping posture.
3- Loss of righting reflex (onset time).
4- ↓ Touch & pain reflexes (lost with thiopental).
Specific signs for CPZ

Signs:

1- No loss of righting reflex.
2- Creeping gait.
3- Abdomen touches the ground.
4- State of catalepsy (loss of muscles control) → onset time.
5- ↓ Touch & pain reflexes.
CPZ mechanism of action:

- It is D2, 5 HT, H1 and alpha 1 agonist.
## Lab work

<table>
<thead>
<tr>
<th>Drug</th>
<th>Conc.</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiopental</td>
<td>2.5 %</td>
<td>100 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>2 %</td>
<td>200 mg/kg</td>
<td>IP</td>
</tr>
<tr>
<td>Chloralhydrate</td>
<td>3 %</td>
<td>300 mg/kg</td>
<td></td>
</tr>
<tr>
<td>C.P.Z</td>
<td>0.1%</td>
<td>15 mg/kg</td>
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References