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Pharmacology
Chapter 4 : Drugs Acting on the Central Nervous System

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Chapter 4

Drugs Acting on the Central Nervous System

General Anaesthetics

- → The drugs which produce reversible loss of all sensation , conscious ness and Movement .
- → there are three component of anaesthesia :
  - Analgesia (pain killer)
  - Amnesia (loss of memory)
  - Immobolisation (loss of movement)

Anaesthetics are of two types :

1. Local Anaesthetics : These act locally and eliminate the sensory perception over a local area.
2. General Anaesthetics : These eliminate the sensation of complete body and are used as an adjunct to surgical operations to make patient unaware and unresponsive to painful conditions.

- → General anaesthetics are drugs producing analgesia, unconsciousness, reversible loss of all sensation, and relaxing the patient's muscles.

Stages of Anaesthesia

Stage -1 :

Analgesia :

- It starts with administration of anaesthetics
- Beginning of loss of consciousness , reflexes and respiration remain normal , and feel dream like condition.
- loss of pain sensation.

Stage -2 :

Excitement or Delirium :

- It starts with unconsciousness to beginning of irregular respiration.
- Patient may shout , struggle for movement , jaws are tightly closed.
- Heart rate and BP may rise , and pupils dilate
- Involuntary Urination , and defecation.
- No operative procedure carried out in this stage.

Stage -3 :

Surgical Anaesthesia :

- All the surgical procedures are done in this stage.
- plane 1 : respiration becomes regular , and eyes become fixed.
- plane 2: loss of corneal and laryngeal reflexes
- plane 3 : pupils start dilating and light reflexes
- plane 4: Dilated pupils , decrease muscle tone , BP falls.

Stage 4:

Medullary paralysis :

- This stage must be avoided , otherwise patient may be died . In this stage medulla depresses and leads to stop respiration and then death .

Classification of General Anaestheics

1) Inhalation Anaestheics
    - Enflurane
    - Desflurane
    - Halothane
    - Ether
2) Intravenous Anaestheics
    - Thoipental sodium
    - ketamine hydrochloride
    - Diazepam
3) Gaseous Anaestheics
    - Nitrous Oxide

Pharmacological Action Of general anaestheics

→ These drugs work on central nervous system and depress it , and induce sleep , loss of pain sensation and unconsciousness.

Indication , Contraindication and doses of some commonly used general anaesthetics

Inhalation Anaestheics

Halotane

- **Indication :** It is used for general Anaesthesia in combination with other anaesthetic agents .
- **contraindication :** It should not be used in patient having intracranial hemorrhage .
- **Dose :** 2-3 % in oxygen vapor .

Intravenous Anaestheics

Thiopental sodium

- **Indication :** It is used for general Anaesthesia in combination with other anaesthetic agents .
- **Contraindication :**
    - It is contraindicated in myasthenia gravis .
    - in Prolonged asthma
    - in low blood pressure
    - in porphyria
- **Dose:** 2.5 % solution for IV

Gaseous Anaestheics

Nitrous Oxide

- **Indication** : It is used to maintain surgical anaesthesia in combination with other anaesthetic agents.
- **Contraindication :**
    - It is contraindicated in patients suffering from chronic respiratory problems.
    - In pregnancy
    - In vitamin B12 deficiency patients
- **Dose :** It should be mixed with at least 30% oxygen .

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Sedative & Hypnotics

- → **Sedatives :** Sedatives are those drugs which reduce excitement,emotions, tension and induce calmness . It is also used as antianxiety.
- → **Hypnotics :** hypnotics are those drugs which produce sleep , just like natural sleep.
- → When we increase sedative drugs dose then they produce hypnotics effects.
- → Sedative-hypnotic agent is a chemical substance which reduces tension and anxiety and induces calmness (sedative effect) or sleep (hypnotic effect). Low doses of these drugs exert a calming effect and higher doses have a sleep- inducing effect.
- → Sedative-hypnotic drugs depress the CNS.

Classification

1) Urea derivatives : Barbiturate
    - Long acting barbiturate : Phenobarbitone , Mephobarbitone.
    - Short acting barbiturate : Butobarbitone , secobarbitone.
    - Ultra short acting barbiturate : Thiopentone , hexobarbitone
2) Benzodiazepines :
    - Sedative and hypnotics : diazepam , clonazepam , Alprazolam , flurazepam.
3) Newer Non Benzodiazepine Hypnotics : Zopiclone , zolpidem.
4) Miscellaneous : Chloral hydrates, Triclofos.

Pharmacological Action

- ❖ **CNS Depression :** They depress the CNS and cause sedation and hypnotic effects . over dose can cause death when respiratory and vasomotor center depressed.
- ❖ **CVS :** they lower blood pressure , reduce cardiac output , and induce vasodilatation.

Indications

- They are used as sedative and hypnoti cs.
- They are as anticovusant.
- They are used as anaesthetics in combination of other anaesthetic drugs.

Contraindications

- They are contraindicated in porphyria.
- They are contraindicated in Liver and kidney diseases
- They are contraindicated in pulmonary diseases .

Dose

- **Diazepam :** Tablets 2 , 5, and 10mg and slow releasing capsule 15 mg
- **Alprazolam :** Tablets (0.25 , 0.5 , 1 , and 2 mg)
- **Clonazepam :** Injection and tablets (0.25 , 0.5 , 1 , and 2 mg)

Anti-Convusant Drugs / Antiepileptic / Antiseizure drug

- → The drugs are used to treat convulsion are called anticovulsant drugs . Convulsion is a nervous system disorder , due to abnormal electrical activity in brain cells.
- → This disorder may result involuntary muscle movement , uncontrolled shaking of the body.

Classification

1. **Hydantoin Derivatives :** Phenytoin, Methatoin, and Ethotoin.
2. **Barbiturates :** Phenobarbiturate, Primidone.
3. **GABA Transaminase Inhibitors :** Sodium Valproate, Vigabatrin.
4. **GABA agonist :** Gabapentin
5. **Benzodiazepines :** Diazepam , clonazepam
6. **Iminostilbenes :** Carbamazepine, Oxcarbazepine.

Pharmacological Action

- ⇨ These drugs stabilize cell membranes and suppress the abnormal electric impulses in the cerebral cortex.
- ⇨ They mainly work on GABA receptors , sodium and calcium channels.

Indications

- ⇨ These drugs are used to treat various types of Epilepsy.
  - Generalised (Tonic clonic , pettimal)
  - partial seizure (simple , complex)
  - Status

Contraindications

- ❖ These are contraindicated in liver diseases.
- ❖ These are contraindicated in certain blood diseases.
- ❖ These are contraindicated in narrow angle glaucoma.

Doses

- **Phenytoin :** 50 mg and 100mg tablets , 50 mg IV , and it should not exceed 50mg / minute .
- **Phenobarbitone :** 60mg 1-3 times a day . 3-6 mg /kg / day in children . It is the first effective antiepileptic drug was introduced in 1912 . and it broad spectrum antiseizure drug .
- **Sodium Valproate :** 100mg and 200 mg tablets and 200mg/5ml syrup. and in children 10mg/kg in tow divided doses .
- **Carbamazepine :** 100mg initial dose and gradually increased to 600-1200mg /day in divided dose . it is available as 100 ,200, 400 mg tablets

Anti-Anxiety Drugs / Anxiolytic Drugs

- → Anxiety is a CNS disorder.
- → Some symptoms of anxiety are below :
  - Too much worry and fear about everyday situation
  - Feeling nervous and restlessness
  - Tension , panic
  - Increased heart rate and breathing
  - Sweating
- → The antianxiety agents (or anxiolytic drugs) are used for controlling the effects of stress and the feelings of discomfort, tension, fearful anticipation of untoward events, and dysphoria in patients with neuroses and mild depressive states.
- → These agents also produce skeletal muscle relaxant effects.
- → The drugs are used to treat anxiety are called antianxiety drugs .

Classification

1. **Benzodiazepines :** Diazepam , clonazepam , alprazolam , lorazepam , oxazepam , Clobazam , chlordiazepoxide.
2. **Non Benzodiazepines anxiolytics :** meprobamate , tybamate , zopiclon , zolpidem.

Pharmacological Action

- ❖ These drugs show anxiolytic , sedative & hypnotic , anticonvulsant , and central muscle relaxant actions.

Indications

- ➢ **In Anxiety :** They are used to treat anxiety.
- ➢ **In depression :** Alprazolam is used to treat mild depression
- ➢ **In Insomnia :** They are used to treat insomnia .
- ➢ **In convulsant :** They are used to treat convulsant.
- ➢ **In drug withdrawal :** Diazepam and chlordiazepoxide are used to reduce alcohol withdrawal symptoms.

Contraindications

- ▪ These are contraindicated in liver diseases.
- ▪ These are contraindicated in certain blood diseases.
- ▪ These are contraindicated in narrow angle glaucoma.

Doses

- ⇨ **Diazepam :** Tablets 2 , 5, and 10mg and slow releasing capsule 15 mg
- ⇨ **Alprazolam :** Tablets (0.25 , 0.5 , 1 , and 2 mg)
- ⇨ **Clonazepam :** Injection and tablets (0.25 , 0.5 , 1 , and 2 mg)
- ⇨ **Lorazepam :** 1-4mg /day
- ⇨ **Chlordiazepoxide :** 10-30mg /day

Anti-Depressant drugs

→ Depression : According to WHO Depression is a mental disorder presents with depressed mood , loss of interest or pleasure , feeling of guilt or low self confidence , disturbed seep and appetite , low energy , and poor concentration.

→ Types of Depression

- **Unipolar depression :** In this type of depression mood swings always in the same direction.
- **Bipolar depression :** In this type of depression mood swings in two directions depression and mania . In mania condition the affected person feel more energetic , and exaggerated self confidence.

→ The drugs are used to treat depression are called antidepressant drugs.

Classification Of Antidepressant drugs

1. **Monoamine Oxidase Inhibitors (MAOIs):** Phenelzine , Isocarboxazid
2. **Tricyclic Antidepressant (Reuptake (reabsorb) Inhibitor) :** Imipramine , Amitiptyline.
3. **Selective Serotonin Reuptake Inhibitors(SSRIs) :** Fluoxetine , setraline
4. **Atypical Antidepressant :** Trazodone , Venlafexine.

Pharmacological Action

- **ANS :** They cause blurred vision , dry mouth , and constipation.
- **CVS :** they cause Hypotension (due to α blocking effect) and toxic effect on myocardium.
- They inhibit the reuptake (reabsorption) of neurotransmitter Like Dopamine , Norepinephrine , serotonin.

Indications

- They are used to treat depression.
- They are used to treat migraine, and panic disorder
- Have a high risk of suicide.

Contraindications

- In having a history of myocardial infarction , heart failure,
- Narrow angle glaucoma.

Dose

- **Phenelzine Sulphate (Nardil) :** 45-60mg/day . upto 75 mg
- **Isocarboxazid :** 10-30 mg /day , upto 50 mg
- **Imipramine :** 75 mg tablet daily , upto 150 mg a day .
- **Amitriptyline :** 75 mg tablet daily , upto 150 mg a day .
- **Fluoxetine :** initial dose is 20mg /day , up to 30-40 a day .
- **Setraline :** 50mg / day

Anti-psychotics / Neuroleptics

- → Schizophrenia is one of the major forms of psychiatric illness which affects young people, is often chronic, and high disabling.
- → Symptoms of schizophrenia
    - Hallucination (in which a person hears , sees, smell , taste ,or feel things that seems to real but only exit in his mine) and delusions.
- → The drugs are used to treat schizophrenia (mood-altering) are called antipsychotics.
- → It may be called mood stabilizing agents.

Classification

1. **Phenothiazine derivatives :** Chlorpromazine
2. **Butyrophenones :** Haloperidol
3. **Rauwolfia Alkaloids :** Reserpine
4. **Atypical Neuroleptics :** Clozapnie , Risperidone
5. **Substituted Benzamide :** Sulpiride
6. **Indole Derivatives :** Malingole.

Pharmacological Actions

- ❖ They prevent the excess of dopamine in the brain.
- ❖ In normal individuals , chlorpromazine makes them to loss interest from surroundings.
- ❖ They act as α adrenergic blocking agents.
- ❖ They cause hypotension.

Indications

- ◈ They are used to treat Schizophrenia .
- ◈ They are used to treat manic depression
- ◈ They are used for controlling aggressive and destructive behavior in children
- ◈ they are used to control vomiting and Hiccups

Contraindications

- ⅄ These are contraindicated in severe allergy
- ⅄ In severe cardiac diseases
- ⅄ In narrow angle glaucoma
- ⅄ In History of seizure disorder

Doses

- **Chlorpromazine :** 10-100 mg TDS (thrice a day) Max 800 mg a day)
- **Haloperidol :** 2-20mg/day
- **Clozapnie :** 100-300mg/day
- **Risperidone :** 2-8mg/day

Nootropic Agents / Cognitive Enhancer / Smart drugs

→ Nootropics, also known as “smart drugs” are a diverse group of medicinal substances whose action improves human thinking, learning, and memory,

Or

→ Nootropics are those substances which increase mental functions including : Memory, Motivation, Concentration, Attention

Classification

1. **Cholinergic Activators :** Piracetam
2. **Seratonergics :** Theamine
3. **Dopaminergic :** L- Dopa
4. Some other examples Aniracetam , Oxiracetam , Hydergine , Vincamine Meclofenoxate .

Pharmacological Actions

- They increase Metabolism in brain .
- They increase cerebral circulation .
- They protect brain from Chemical damage .

Indications

- They are used to treat alzheimer's disease.
- They are used in those who are suffering from learning and attention problems,.
- They are used to increase intelligence , smartness.
- They are used to treat amnesia.
- They are used to treat dementia (abnormalities in to remember , think , and decision)

Contraindications

- In Hypersensitivity
- In pregnancy
- In lactation

Dose

- **Piracetam :** 2-3mg /day in divided dose
- **Hydergine :** 4.5- 9 mg / day

Centrally Acting Muscle Relaxant

→ The centrally acting muscle relaxants are a group of drugs that act in the central nervous system (CNS) to mitigate tension and spasm of skeletal muscles.

OR

→ The drugs are used to relax the skeletal muscle by acting on central nervous system are called " centrally acting muscle relaxants .

→ They are used to treat spasm and pain in muscles .

Classification

1) **Barbiturates :** phenobarbitone
2) **Benzodiazepines :** Diazepam
3) **GABA derivatives :** Baclofen
4) **Mephenesin Congeners :** Mephenesin , Meprobamate ,Chlormezanon

Pharmacological actions

- **Voluntary Muscles :** They relax the voluntary muscles by depressing the CNS.
- **CNS :** They depress the CNS , Show sedative effects.

Indications

- **Muscles Spasm :** They are used to treat spasm and pain of muscles , and rheumatic disorders.
- **Anxiety and Tension :** They are used in treatment of anxiety and tension .
- **Tetanus :** They are used in treatment of tetanus in combination with other medicines .
- **Convulsion :** They are also used in treatment of convulsion.

Contraindication

- Mephenesin Congeners and Baclofen are contraindicated in hypersensitivity .

Doses

- **Diazepam :** Tablets 2 , 5, and 10mg and slow releasing capsule 15 mg
- **Phenobarbitone :** 30-120 mg /day in divided dose.
- **Mephenesin :** Ointment as required.
- **Baclofen :** 10-15 mg/day orally

Opioid (Narcotic) Analgesics

- → Analgesics are those substances which reduce pain by acting on central nervous system.
- → Opioid Analgesics are pain killers that obtained from opioids.
- → They reduce pain without disturbing other sensory functions , or without causing unconsciousness.
- → Opioid Analgesics may be natural , semi synthetic , or synthetic.

Classification

1) **Morphine :** It is a potent analgesic drug .It is also called gold standard drug for treating severe pain .It has a high potential for addiction .
   Eg : Morphine , dimorphine , Codeine.
2) **Synthetic :** Pethidine , tramadol Methadone , pentazocine , cyclazocine.

Pharmacological Action

1) CNS : It interacts with different types of brain receptors and produces following actions
   - Analgesia : It reduces pain sensation.
   - Euphoria : It produces a feeling of excitement and happiness.
   - sedation : it causes sleep .
   - vomiting : It stimulates Chemoreceptor Trigger Zone in medulla and causes vomiting.
   - respiratory depression : It depresses the respiratory volume , and may cause death.
   - antitussive : It suppresses the cough reflex by depressing cough center in medulla .
2) Action on GIT : It causes constipation , It inhibits peristaltic movement.
3) CVS : it causes Vasodilatation.
4) It causes pain in bile duct.
5) It causes urine urgency and difficulty in urination.
6) It prolongs labours.

Indications

- Analgesia : they are used to relief severe pain.
- They are used to treat Diarroea.
- They are used to relief cough.
- They are used as pre anaesthetic.

Contraindications

- In head injury .
- In Bronchial Asthma .
- Undiagnosed abdominal pain .
- Chronic lungs diseases
- In Hypothyrodism .
- In Hepatic failure.

Doses :

- **Morphine :** (10-15mg oral) 0.1 - 0.2 mg /kg (4 hours) as need to manage pain
- **Codeine :** 30 -60 mg
- **Pethidine :** 50-100 mg oral
- **Tramadol :** 50-100 mg oral
- **Methadone :** 2.5-10mg oral
- **Pentazocine :** 50-100 mg oral

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