

- Cholinergic agonists
- Classify & describe cholinergic agonists including actions, therapeutic uses & adverse reactions.
- Describe myasthenia gravis & its management
- Explain Organophosphorous poisoning & treatment

- Cholinergic agonist- **Classification**

Direct Acting Cholinergic Drug

- Acetylcholine
- Bethanechol.
- Pilocarpine.
- Methacholine

Indirect Acting Cholinergic Drugs (Cholinesterase Inhibitors)

- **Reversible: *water soluble-***
Neostigmine, Edrophonium

Pyridostigmine,
Lipid soluble- Physostigmine,
Donepezil, Tacrine,
Gallantamine

- **Irreversible**.- Organophosphorous
Compounds, Echothiophate,
malathion, parathion, tabun

Reactivation of acetylcholinesterase-
Pralidoxime

- *Actions of acetylcholine*

Muscarinic actions:

Heart: it decreases the heart rate and cardiac output.

Blood vessels: it causes vasodilatation and decreases
BP.

GIT: It increases the salivary & intestinal secretion.

Increases intestinal motility and relaxes sphincters

Respiratory system: bronchoconstriction &

Increased secretions.

Eyes: it causes:

- Miosis.
- Accommodation of near vision.

- Decrease the IOP due to increase in the out flow of aqueous humor.

Genitourinary tract: it causes:

- Urination.
- Erection of genital in male.
- *CNS:* it causes excitatory effect and effect on the learning, short term memory and arousal.

- **The nicotinic actions:**

NMJ: contraction of skeletal muscles.

- Stimulates both sympathetic and parasympathetic ganglia.
- Stimulates the release of adrenaline from the adrenal medulla and chromaffin.
- **In CNS:** stimulates the release of ADH at the hypothalamus.

Therapeutic uses:

- Uses as eye drop to produce rapid and complete miosis after cataract surgery.

- **BETHANECHOL**

- Not hydrolyzed by acetylcholinesterase but it is hydrolyzed by other esterase.
- It has no nicotinic actions.
- It is longer duration of action than acetylcholine.
- ***Therapeutic uses:***
 - Post operative non-obstructive urinary retention.
 - Post-operative ileus.

- **PILOCARPINE**

It is natural alkaloid, not hydrolyzed by acetylcholinesterase.

It has marked muscarinic actions.

Actions:

- **Eye:** loss of accommodation, miosis and lowering the intraocular pressure (IOP).
- **Other actions:** it stimulates the secretory glands and causes sweating, salivation and lacrimation.

Therapeutic uses of pilocarpine:

- In the treatment of GLAUCOMA.
- To reverse cycloplagic and mydriatic effect of atropine.

Side effects:

- CNS disturbance because it is crossing the BBB.
- Sweating and salivation.

• PHYSOSTIGMINE:

- It is an alkaloid.
- Well absorbed and penetrate the BBB.

Therapeutic uses:

- Glaucoma.
- Atropine poisoning
- Alzheimer s disease.

Side effects:

- **CNS: convulsions.**
- **Heart: bradycardia.**
- **Paralysis of skeletal muscles which it is rare seen in the therapeutic dose.**
- **Lid muscles twitching.**
 - **It is synthetic anticholinergic drug.**
 - **It is poorly absorbed.**
 - **It is polar compound and so that not cross to the CNS.**

Therapeutic uses:

- As antidote for tubocurarine poisoning
- Management of Myasthenia Gravis:

it is an autoimmune disorder due to antibodies against Ach receptor,

- **. Organophosphorous compounds**
- They are irreversible anticholinesterase:
- They are insecticides and nerve gases.

- They include: parathion, malthion, and sarin.
- They are highly lipid soluble compounds. So that they cross the BBB.
- Management of myaesthesia gravis
- Management of myaesthesia gravis(contd.)
- Toxicity / poisoning of organophosphorous compounds:
- *Mechanism of toxicity:*
- They inactivate enzyme ACHE irreversibly and increase the level of acetylcholine.

Actions:

- **Acute toxicity:** paralysis of respiratory muscle and excessive bronchial secretion.
- **Chronic toxicity:** neuropathy and demyelination of axons.

- *Treatment of organophosphate poisoning*
- **Maintenance of vital signs:** aspiration of bronchial secretions, endotracheal intubations and artificial respiration.
- **Decontamination:** to prevent further absorption, removal of the contaminated clothes and washing the skin, gastric lavage if need.
- **atropine:**
- **Cholinesterase reactivator Examples:** pralidoxime (PAM).
- Diazepam.

•References

- Lippincott's Illustrated review of pharmacology – 4th edition
- Basic & clinical pharmacology, Bertram G Katzung-12th edition
- Goodman & Gilman's –pharmacology
- Internet resource