Cholinoceptor-Blocking Drugs

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Cholinoceptor-Blocking Drugs

Comprise 3 groups of drugs:

1. **Antimuscarinic drugs.**
2. **Ganglion Blockers (nicotinic receptors)**
3. **Neuromuscular junction blockers (nicotinic receptors). These are NOT part of the autonomic nervous system (ANS).**

Muscarinic Receptor-blocking Drugs

- They are also called antimuscarinic drugs.

Include:

1. Naturally occurring alkaloids: Atropine (hyoscyamine) – prototype, and Scopolamine (hyoscine).
2. Quaternary amines for GIT application (peptic ulcer disease and hypermotility): Propantheline, Glycopyrrolate.

Antimuscarinic Drugs

3. Tertiary amines for peripheral applications: Pirenzepine (peptic ulcer disease), Tropicamide (mydriatic), Dicyclomine (peptic disease and hypermotility).
4. Quaternary ammonium for use in asthma: Ipratropium.
5. Tertiary amine for Parkinson's disease: Benztropine, Tiotropium
6. Tolterodine – for hyperactive bladder.

Antimuscarinic Drugs

Pharmacokinetics:

- **The natural alkaloids and most of the tertiary antimuscarinic agents are well absorbed from the gut and conjunctival membranes.**
- **They are also widely distributed in the body including CNS**
- **Quaternary antimuscarinic drugs are poorly absorbed after oral administration, and poorly transported to the brain.**

Antimuscarinic Drugs

Pharmacodynamics:

A. Mechanism of Action:

- **Antimuscarinic drugs cause reversible and competitive blockade of muscarinic receptors, preventing acetylcholine from binding.**

Antimuscarinic Drugs

B. Organ System Effects:

1. CNS:

A. Atropine has sedative effect on the brain.

B. Scopolamine has more marked central effects producing drowsiness and amnesia.

- **These actions make them useful as pre-anesthetic medications.**
- **At toxic doses, both can produce excitement, agitation, hallucinations and coma.**

Antimuscarinic Drugs

C. **Centrally acting antimuscarinic drugs reduce the tremor of Parkinson's disease**

D. **Prevention or reversal of the vestibular disturbances of motion sickness.**

Antimuscarinic Drugs

2. **Eye:**

A. **Dilation of the pupil (mydriasis) due to blockade of the pupillary constrictor muscle.**

B. **Weaken contraction of the ciliary muscle (cycloplegia) leading to loss of the ability to accommodate for near vision.**

C. **Reduction of lacrimal secretions leading to dry or sandy eyes.**

Antimuscarinic Drugs

3. **Cardiovascular system (CVS):**

A. **Small doses of atropine produce bradycardia by stimulation of acetylcholine release by blocking presynaptic M_1 autoreceptors.**

B. **Moderate to high doses of atropine produce tachycardia by blocking postsynaptic muscarinic receptors in the SA node in the heart.**

C. **Effects on atria and ventricles are minor.**

Antimuscarinic Drugs

D. **Block vasodilation (in coronary arteries and skeletal muscle blood vessels) induced by cholinomimetics despite lack of parasympathetic innervation of blood vessels (but contain endothelial muscarinic receptors).**

E. **<u>Cutaneous blood vessel dilation</u> in the upper part of the body (may be due to blocking of sweating??) → flushing at toxic doses.**

Antimuscarinic Drugs

4. **Respiratory system:**

A. Bronchodilation (M_3 receptors).

B. Reduced respiratory secretions.

C. Prevention of laryngospasm.

5. **Gastrointestinal tract:**

A. Effects on gastrointestinal function are modulated by local hormones, noncholinergic neurons and enteric nervous system.

Antimuscarinic Drugs

B. Reduce salivary secretions → dry mouth.
C. Reduction of gastric secretions – volume and amount of acid, pepsin and mucin. Basal secretion is blocked more than that stimulated by food, nicotine or alcohol.
D. Pancreatic and intestinal secretions are less (?) affected.

Antimuscarinic Drugs

E. **Relaxation of smooth muscle of GIT from stomach to colon, both tone and propulsive movements are diminished. → prolong gastric emptying time and intestinal transit time.**
F. **Constipation**

Antimuscarinic Drugs

6. **Genitourinary tract:**

A. Relaxation of smooth muscle of the ureters and bladder wall → slows voiding (urination) → urinary retention.

7. **Sweat glands (sympathetic cholinergic fibers):**

A. Suppress thermoregulatory sweating → reduce seating and elevate body temperature.