Medical Committee
The University of Jordan

PHARMACOLOGY

Slide # :10-Cholinoceptor-Blocking Drugs

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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)**

Muscarinic Receptor-blocking Drugs

- **Also called antimuscarinic drugs, or parasympatholytic agents.**

Include (but not limited to):

1. Naturally occurring: Atropine (hyoscyamine) – prototype, and Scopolamine (hyoscine).

Antimuscarinic Drugs

2. **Tertiary amines for peripheral applications: Pirenzepine (peptic disease), Tropicamide (mydriatic).**
3. **Quaternary ammonium for use in bronchial asthma: Ipratropium bromide.**

Antimuscarinic Drugs

- **Atropine is found in the following plants:**

1. ***Atropa Belladonna*, or deadly nightshade.**
2. ***Datura stramonium* or jimsonweed.**

- **Scopolamine (hyoscine) is found in:**

1. ***Hyoscyamus niger* or henbane.**

- **The other drugs are either semisynthetic or fully synthetic.**

Atropa Belladonna

Datura stramonium

Hyoscyamus niger

Antimuscarinic Drugs

Pharmacokinetics:

- **The natural alkaloids and most of the tertiary antimuscarinic agents are well absorbed from the gut and conjunctival membranes.**
- **Only 10-30% of the dose of a quaternary antimuscarinic drugs is absorbed after oral administration.**

Antimuscarinic Drugs

- **Atropine and tertiary agents are widely distributed in the body including CNS (more so for scopolamine). Quaternary derivatives are poorly distributed to the brain.**
- **Atropine t½ is ~ 2 hours, 60% of dose is excreted unchanged in urine. The effect on the eye last ~ 72 hours.**

Antimuscarinic Drugs

Pharmacodynamics:

A. Mechanism of Action:

Atropine causes reversible and competitive blockade of muscarinic receptors, preventing acetylcholine from binding.

Antimuscarinic Drugs

- **Salivary, bronchial and sweat glands are most sensitive, and acid-secreting gastric cells are least sensitive (?) to atropine compared to other tissues.**
- **Atropine blocks M_1, M_2 & M_3 muscarinic receptors, while pirenzepine and dicyclomine block mainly M_1 receptors.**

Antimuscarinic Drugs

B. Organ System Effects:

1. **CNS:**

   a. Atropine has minimal stimulant effect on parasympathetic medullary centers, and a slower, longer-acting sedative effect on the brain.

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

Antimuscarinic Drugs

At toxic doses, both can produce excitement, agitation, hallucinations and coma.

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

d. Prevention or reversal of the vestibular disturbances of motion sickness – Scopolamine.

Antimuscarinic Drugs

2. **Eye:**

   A. Dilation of the pupil (mydriasis) due to block 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 through stimulation (?!) of acetylcholine release by blocking presynaptic M_1 autoreceptors.

Antimuscarinic Drugs

B. Moderate to high doses of atropine produce tachycardia through block of postsynaptic muscarinic receptors in the SA node in the heart.

C. The same mechanism operates in the AV node (enhances conduction).

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 (mechanism unknown) → 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 sweating and elevate body temperature.

Antimuscarinic Drugs

Therapeutic Uses:

1. **Parkinson's disease: Benztropine.**
2. **Motion Sickness: Scopolamine (PO, parenteral and transdermal patch).**
3. **To produce mydriasis for eye examination and to prevent adhesions in inflammatory conditions in the eye: Tropicamide.**

Antimuscarinic Drugs

4. **To prevent airway secretions and laryngospasm associated with general anesthesia (premedication): Atropine, scopolamine (also produces amnesia).**
5. **Bronchial asthma and chronic obstructive pulmonary disease (COPD): Ipratropium by inhalation.**

Antimuscarinic Drugs

6. **Bradycardia associated with excessive vagal stimulation: Atropine.**
7. **Peptic ulceration: Pirenzepine.**
8. **Diarrhea.**
9. **Urinary incontinence: Tolterodine.**
10. **Cholinergic poisoning (insecticides, mushrooms, chemical warfare): Atropine.**

Antimuscarinic Drugs

Adverse Effects:

1. **Mydriasis and cycloplegia.**
2. **Hallucinations, agitation, delirium.**
3. **Dry mouth.**
4. **Tachycardia.**
5. **Hot flushed skin, fever.**

Contraindications:

1. **Glaucoma.**
2. **Prostatic hyperplasia with urine retention.**