Anticholinergic Drugs

Lecture 12

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Atropine
Pharmacodynamics

Competitive antagonist. It competes with Ach for muscarinic receptors blocking them producing pharmacological actions opposite to muscarinic effects. It has initial agonistic actions.

Most antimuscarinic drugs are inverse agonists causing inactive state of receptor.

3ry ammonium compound.

Action 1 is via M2 blockade while actions 2-5 are mediated via M3 blockade.

1. ↑myocardial contraction, HR, AV conduction & prolongation of effective RP.
2. ↓tone & motility of GIT (peristaltic movement) & urinary bladder.
4. ↓secretions as .......
5. On eye: .......= adverse effects.
Adverse effects

1. Tachycardia.
2. Constipation.
3. Retention of urine.
4. Dryness of secretions as.....
5. All actions on eye.
   b. Cycloplegia by paralysis of ciliary muscle → loss of accommodation & reflexes.
   c. ↑IOP.
Acute atropine toxicity

More dangerous in children.

1. Adverse effects of atropine.
2. Fever: by ↓ sweating.
4. Excitation & convulsion by CNS stimulation in big dose.
   Also amnesia.

Clinical picture:
Blind as bat (mydriasis), dry as bone (↓ secretions),
hot as hare (fever), mad as hen (CNS stimulation)
and red as beet (VD).
Treatment:

1. Gastric lavage, using potassium permanganate for oxidation.
2. Physostigmine antagonizes its antimuscarinic & central adverse effects.
3. Diazepam for CNS stimulation.
4. Artificial respiration.
5. Cold dressings for fever.

Atropine antagonists on eye: 3ry amines:
Physostigmine & pilocarpine (partially) & organophosphorus compounds (completely).
Contraindications
Relative and not absolute.
1. Old age due to glaucoma & retention of urine (by enlarged prostate).
2. Thyrotoxicosis: due to tachycardia, CNS stimulation & ↑temperature.
3. Fever (↓sweating).
5. Non selective antimuscarinic drugs in PU and all antimuscarinic drugs in GU (cause slower gastric emptying).
Differences between atropine & hyoscine (scopolamine)

Hyoscine has:
1. Rapid onset.
2. Short duration.
3. Pure antagonist.
4. No cardiac effects.
6. CNS depressant e.g. ↓short term memory.
7. Used in preanesthetic medication specially in thyrotoxicosis.
Atropine substitutes (uses…)

Atropine is commonly replaced clinically by these specific drugs.

1. **Antiparkinsonism:**
   Used in Parkinsonism.
   Benzhexol & benzotropine.

2. **Mydriatic cycloplegics:**
   Used in fundus examination (eye drops).
   Short duration, less ↑IOP, less cycloplegia and easy antagonism than atropine e.g. homatropine, cyclopentolate & tropicamide.

3. **Antisecretory antispasmodic (on GIT):**
   4ry amines. more localized in GIT with less systemic effects.
   Used in intestinal colic.
   e.g. hyoscine butyl bromide, glycopyrrolate, oxyphenonium.
4. Ipratropium bromide:
By inhalation in COPD and bronchial asthma to ↓systemic toxicity.
It ↑exercise tolerance and ↑mucociliary transport but causes viscous bronchial secretions.
Tiotropium is similar with longer duration due to slow dissociation from M3 receptors (once daily).

5. Selective M1 antagonists:
   Pirenzepine:
Selective and not specific M1 receptor blocker (mainly in gastric mucosa) decreasing Hcl secretion, used in peptic ulcer.
→ dry mouth & ↓accommodation, in large doses other anticholinergic adverse effects may occur.
Telenzepine.....
6. Selective M₃ antagonists:
Used in urinary frequency, urgency, incontinence & overactive bladder.
  a. Oxybutinin.
  b. Darifenacin, solifenacin & tolterodine: more M₃ selective, longer duration, less xerostomia & constipation, used once daily.

  **Atropine is used in:**

  1. Cardiac uses:
     b. Digoxin toxicity (digoxin has vagal action, blocked by atropine).
  2. Organophosphorus poisoning.
  3. Preanesthetic medication: by:
     a. ↓secretions.
     b. Blocking of vagal reflexes e.g. vomiting & cough.
Drugs with atropine-like action

1. Pethedine.
2. Antihistaminics (1st generation H1 antagonists).
3. Quinidine.
4. Tricyclic antidepressants (TCA).
5. Typical antipsychotics.

These drugs have adverse effects & contraindications similar to other anticholinergic drugs.