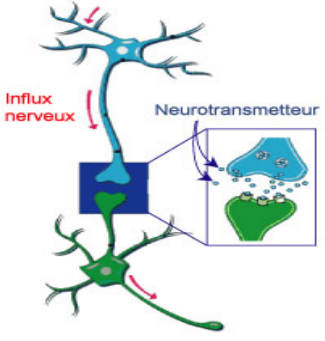
عيط بعين وذاكر بالتانية مفيش وقت.

Cholinergic Antagonist Drugs



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Cholinergic Antagonist Drugs

- **Anti-muscarinic drug:** Atropine-like drugs, Hyoscine (Scopolamine)
- **Anti-nicotinic drugs**
- **Ganglion blockers**: Used in experimental pharmacology. E.g. Nicotine, Trimethapan.
- **Neuro-muscular blockers**: Used in surgery to produce complete muscle relaxation.

1-what're the classification ?

2- what's the mechanism of action?

Anti-muscarinic anti-cholinergic drugs

a-
- Natural agents:
- Atropine, Hyoscine

→ Non-selective.

→ Tertiary amine ... pass BBB

↳ prototype.

b-
- Semi-synthetic
- Homatropine

c-
- Synthetic
- Ipratropium, Pirenzepine, Propantheline

ATropin :-
1- what's the source of it?
2- Descripe the chemical structure?
3- what's special about it?

Anti-muscarinic

- **Atropine** (Hyoscyamine)
- Alkaloids obtained from Atropa Belladona,
- Considered as prototype for parasympatolytics

Tertiary amine —N—

- **Hyoscine** (Scopolamine)
- Obtained from Hyocyamus niger plant (Datura Stramonium)

Note: Antihistamines, phenothiazides and some antidepressants have anti-muscarinic effects

Clinical pharmacology of anti-muscarinic drugs

Mechanism of action:

- **Reversible blockade** of **M** receptors
- **Exocrine glands** are most **sensitive**
- **Gastric secretion** is the **least** affected
- **Heart** is **intermediate**

Note: Atropine blocks all 3 subtypes receptors (M1,M2,M3)

Pharmacokinetics :-

- **Absorption**:
- **Natural** and most **tertiary amines**: **good** absorbation
- **Wide distribution** and **cross BBB** because it's tertiary.
- **Quaternary amines**: **poorly absorbed** and poor crossing **BBB** (Ipratropium)
- Atropine t½: 2hrs
- **Partly metabolized** and partly **excreted unchanged** ✓

Routes of administration

Oral

Parenteral

Topical (suppositories)

Some by inhalation (Ipratropium)

Pharmacodynamics :-

↳ what's the effect of Atropine?

- **Exocrine glands: at low doses reduced secretions**
- Salivary
- Bronchial
- Sweat glands

Dryness of all secretion.

1-what's the effect of Atropin and Hyoscin in CNS?

2-what's the Toxic effect?

CNS ؟!

- Central **stimulant** effects (Atropine) Cross BBB
- Some may produce **sedation** (Hyoscine) given with anesthesia
- Hyoscine blocks M receptors in vomiting centre and has **anti-emetic effect**
- **Toxic doses**: hallucination, convulsion, coma

↳ death due to inhabition of CNS.

by inhabition of excitory action of Ach.

1- what's the effect of it on eye?

Eye

- **Mydriasis** (dilatation of pupil) → indirect action → block M_3 (miosis)
  M_3 ← mydriasis ← Activation of radric
- **Cycloplegia** (relaxation of the ciliary muscle) cause: blurred vision (1) and impaired accommodation to near vision (2)
- **Decreased lacrimation** → dryness of eye.
- **Increase IOP** ⇒ Retination of iris ⇒ closure of Trapecter → aqueous humer won't drain out ← ↑ Iop

glaucoma is a contraindicator.

→ paralysis of ciliy muscle.

1- whatthe the effect of them ? what's special about them ?

CVS

Depending in the doses

- **Central** effect:
- **Decrease heart rate** ⇒ in case of IV → initial bradycardia.
- **Peripheral** effect:
- Blockade of vagus nerve and **increase heart rate**
- **ABP**:
- **No** change

→ blockage of M_2 → decrease the cAMP.

→ because M_3 is non-innervated , so blockage of it result No thing.

↓

1- what's the effect of Atropine?

Respiratory system

- ① **Bronchodilatation** ⇨ Indirect effect of Atropine → blockage of M_3 → B_2 dilation.
- ② **Reduced** bronchial **secretion**
- Ipratropium (quaternary amine derivate of Atropine) inhalation:
- Useful in asthma and chronic obstructive pulmonary disease (COPD), also in patient who are unable to take adrenergic agonists.

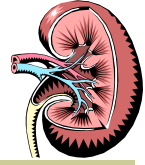
GIT

block M_1 & M_3

- Decrease salivation
- Decrease acid secretion
- Decrease motility
- Delay gastric emptying
- Prolong intestinal transit time
- Anti-diarrhoeal and anti-spasmodic effects

genitourinal tract

GUT M3



- **Relaxation of bladder** wall + open sphincter.
- Useful in **inflammatory spasm** and **pains** of the urinary tract
- **Risky** in patients with **BPH** (Benign Prostatic Hypertrophy)

⇨ used in patient with constipation.

Therapeutic uses

CNS disorders:

- **Parkinson's** disease → "excessive stimulation of cholinergic receptors"
- Drug-induced parkinsonism as Phenothiazine (induced acute dystonias)
- Benztropine, Benzhexol: useful
- **Motion sickness**: Hyoscine oral, injection, trans-dermal patches

Therapeutic uses

Ocular uses:

- In **eye examination** (Tropicamide) produce mydriasis and cycloplegia
- In **iritis** (Atropine eye drop) prevent synechia (adhesion of the iris to the lens)

Note:

- Atropine eye drops effects: 7 days
- Tropicamide eye drops effects: 4-12hrs

Therapeutic uses

- **Premedication**: Hyoscine and Atropine (use as **adjunct in anaesthetic** procedure)
- **Bronchial asthma**: Ipratropium inh. (produce bronchodilatation)

Cardiovascular:

- **Bradycardia and heart block following AMI**: Atropine

Therapeutic uses

GI disorders:

- **Anti-diarrhoeal**
  - Lomotil= atropine + diphenoxylate synthetic from morphin.
- **Anti-spasmodics** (in intestinal colic, IBS)
  - Atropine, hyoscine, clidinium, prifinium

"Buscopan" "Librauxam" "Riabal"

→ more selective in secretion and movement of intestine.

Urinary disorders:

- **Urinary urgency** with UTI
- Renal **colic**

→ spasm of bladder → uncomfortable feeling

Therapeutic uses

- **Cholinergic poisoning** as:
  - Irreversible CEI insecticide poisoning
  - Chemical warfare intoxication
- To **counteract muscarinic effects**
- (nicotinic effects can not be reversed)
- Atropine IV

Adverse effects of anti-muscarinic agents

- Dry mouth / Dryness of secretion → ATropin fever of children.
- Blurred vision
- Tachycardia
- Constipation
- Hot flushed dry skin & hyperthermia may occur with high doses

→ Toxic VD → Direct effect unrelated to its effect on receptor.

Contraindications

- **Glaucoma**
- Increase IOP
- **BPH**
- Bladder wall relaxation & sphincter contraction → urine retention

Atropine poisoning

- Hot flushed dry skin & hyperthermia,
- Agitation, delirium, hallucination,
- Convulsions & coma
- Treatment is symptomatic

Individual drugs

- **Atropine**
- **Hyoscine**
  - Buscopan
- **Clidinium**
  - Libraxam
- **Prifinium**
  - Riabal