

ANTICHOLINERGIC DRUGS

MUSCARINIC RECEPTOR

ANTAGONISTS

CHEMISTRY

Tertiary amine alkaloids esters of tropic acid

Organic acid + Base $\rightarrow$ esterification

Tropic acid + tropine $\rightarrow$ Atropine

Tropic acid + scopine $\rightarrow$ Scopolamine (Hyoscine)

Mandelic acid + Tropine $\rightarrow$ Homatropine

Mechanism of action

- Antimuscarinic drugs block the muscarinic receptors, which can be reversed by increasing the concentration of muscarinic agonist.
- Antimuscarinic drugs prevents:
 - the release of inositol triphosphate (IP_3)
 - the inhibition of adenylyclase(That are caused by muscarinic agonist)

Pharmacokinetics

- Tertiary amines will absorbed from GIT
- Quaternary amines 10-30% absorbed from GIT
- Tertiary amines are widely distributed in the body
- Quaternary amines limited in their distribution
- Atropine is excreted largely as unchanged drug in urine
- Only about 1% of the oral dose of scopolamine is excreted in urine as unchanged
- Atropine effects in body remain only for a few hours but in the eye its effects persist for about 72 hours

ANTICHOLINERGIC DRUGS/MUSCARINIC RECEPTOR ANTAGONISTS

PHARMACOLOGICAL PROPERTIES OF ANTICHOLINERGICS

ATROPINE IS A COMPETITIVE ANTAGONISTS OF ACH AND OTHER MUSCARINIC AGONISTS ON MUSCARINIC RECEPTORS SELECTIVELY REDUCE OR ABOLISH THE MUSCARINIC EFFECTS OF ACH. ACTIONS MORE MARKED IN ORGANS WITH HIGH PARASYMPATHETIC INNERVATION.

EFFECTS ON CNS

- Scopolamine causes drowsiness, amnesia, fatigue, and dreamless sleep. It is effective in motion sickness.
- Both may be used to treat extrapyramidal side effects of antipsychotic drugs.
- Toxic doses of both alkaloids produces CNS excitation- restlessness irritability, disorientation, hallucination or delirium. Stimulation followed by depression, coma, medullary paralysis and death.

EFFECTS ON EYE

Mydriasis due to blockade of the cholinergic stimulation of sphincter, this will allow adrenergic Action on the radial muscle to dominate.

Photophobia – due to mydriasis. Light reflex is lost.

Cycloplegia – paralysis of ciliary muscle.

Reduction of lacrimal secretion – patient complains of dry and sandy eye when receiving large doses of anticholinergic drugs.

Intraocular pressure is increased in patients having narrow angle glaucoma.

EFFECTS ON GIT

Therapeutic dose of atropine produce a decrease in Tone, amplitude and frequency of peristalsis, and cause constipation

Large doses decrease secretion of (HCL) mucin and proteolytic enzymes in gastric juice.

EFFECTS ON RESPIRATORY & GENITOURINARY TRACT

Respiratory tract:

Inhibition of secretions of upper respiratory tract, prevent laryngospasm, induced by excessive secretions due to Certain general anaesthetic

Inhibition of bronchoconstriction produced by parasympathetic stimulation

Genitourinary Tract: No Effect on uterus.

Urinary Tract: Decrease in tone and contraction of ureter, and bladder

EFFECTS ON CVS

Heart

Small dose – bradycardia due to blockade of M_1 receptors

Larger dose – tachycardia due to blockade of M_2 receptors

Blood Vessels

Majority are not affected.

In toxic doses vasomotorparalysis occurs leading to fall in blood pressure.

Dilatation of cutaneous blood vessels may occur causing flushed skin

EXOCRINE SECRETIONS

Salivary and bronchial secretions are inhibited – dry mouth

Sweating is inhibited – hot skin.

ANTAGONIST FOR THREE TYPES OF MUSCARINIC RECEPTORS

M1. Pirenzepine, telenzepine

M2. AF-DX116, methoctramine, himbacine, tripitramine.

Tripitramine is used to block cholinergic bradycardia.

M3. Hexahydrosiladifenidol and darifenacin.
Darifenacin is used for overactive bladder

THERAPEUTIC CLASSIFICATION OF **ANTICHOLINERGICS**

MYDRIATICS

Tertiary amines: Homatropine, hydrobromide, eucatropine, cyclopentolate, tropicamide.

There advantages over atropine are: They are short acting and produce less cycloplegia.

ANTI SPASMODIC

Quaternary ammonium compounds:
Propantheline, methantheline, oxyphenonium, glycopyrrolate

Tertiary amines: Dicyclomine, oxyphencyclimine, piperidolate amprotropine, oxybutynin chloride

ANTI-PARKINSONIAN AGENT

These are tertiary amines, e.g. trihexyphenidyl, benztropine, biperidine, procyclidine, cycrimine, ethopropazine

SELECTIVE ANTI-MUSCARINIC DRUGS

Ipratropium	}	Relives bronchospasm in asthma/COPD
Oxitropium		

Oxybutynin	}	1. Relieves bladder spasm after surgery 2. Urteral spasm due to urolithiasis
Tolterodine		

CLINICAL USES OF ANTICHOLINERGICS

USE IN GIT

- Pirenzepine acts synergistically with H₂ blockers in the treatment of peptic ulcer
- Increased tone and motility of GIT
- Irritable bowel syndrome
- To reduce salivary secretion in heavy metal poisoning, Parkinsonism and Oesophageal stricture.

EYE

- Topical use of mydriatic for funduscopy examination
- Topical use of cycloplegic for iritis, iridocyclitis, choroiditis
- Alternating with miotic to prevent or break the adhesions between iris and lens

RESPIRATORY TRACT

- Ipratropium inhalation in bronchial asthma and COPD

CVS

- To antagonize reflex cardiac slowing
- In hyperactive carotid sinus reflex
- In patients with inferior or posterior wall infarction having decreased cardiac output, sinus or nodal bradycardia.
- In AV block due to digitalis toxicity.

CNS

- Benztropine for treating extrapyramidal disorder due to antipsychotic drugs.
- Scopolamine (oral transdermal) for prevention and treatment of motion sickness

GENERAL ANAESTHESIA

- To inhibit excessive salivation and secretion of respiratory tract and to prevent reflex vagal stimulation of the heart
- Atropine given with neostigmine to counter its muscarinic effect when given to end the effect of competitive type of neuromuscular blocking agent.

GENITOURINARY TRACT

- Atropine with an opioid in the treatment of renal colic
- To relieve urteral spasm and irritability of bladder (urinary urgency) and after urologic surgery (e.g, prostatectomy) and also reducing involuntary voiding in patients with neurological diseases oxybutynin is used.

ANTICHOLINESTERASES AND MUSHROOM POISONING

- Antidote for organophosphate poisoning
- To antagonize muscarinic effect of neostigmine in myasthenia gravis
- Rapid type of muscarinic (inocybe) poisoning

CONTRAINDICATIONS OF ATROPINE

- **Narrow angle glaucoma**
- **Enlarged prostate**
- **Delayed type of mushroom poisoning**
- **Pyloric stenosis**
- **Congestive heart failure with tachycardia**
- **Patients over the age of 40 years as it may precipitate an acute attack of congestive glaucoma.**

- **Chronic lung disease as this reduces respiratory tract secretions.**

Anticholinergics in Dentistry

- Atropine is a drug of choice for use as antisialogogue to control salivation
- Atropine sulphate tablets administered an hr before appointment in a dose of 0.4 mg to achieve dry field and to enhance visibility of tooth surface.
- Minimize interruption during procedure to remove pooled saliva
- As an adjunct to orthodontic bonding, prosthetics fixing impression taking to reduce moisture contamination.
- Radiographic procedure when a dry field is important
- Benztropine xerostomia may increase incidence of caries glossitis- artificial saliva may be indicated
- Atropine in the management of bradycardia.