

ANTICHOLINERGIC DRUGS

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- Which block the actions of Ach on autonomic effectors and in the CNS; exerted through muscarinic receptors.
- Nicotinic antagonists are referred to as ganglion blockers and neuromuscular blockers.
- Prototype is **ATROPINE**
- Highly selective for muscarinic receptors.
- Synthetic substitutes possess nicotinic blocking prop. also.

C/F

- **Natural Alkaloids** – Atropine , Hyoscine.
- **Semisynthetic derivatives** - Homatropine, Atropine methonitrate , Hyoscine butyl bromide , ipratropium bromide
- **Synthetic Compounds** –
- **Mydriatics** – Cyclopentolate , Tropicamide.
- **Antisecretory-antispasmodics** :
 - A) **Quarternary compounds**:
Propantheline, Oxyphenonium, clidinium, Pipenzolate methyl bromide, Isopropamide, Glycopyrrolate.
 - B) **Tertiary amines** : Dicyclomine , Oxybutynin, Flevoxate, Pirenzepine, Telenzipine.

C/F

- **Antiparkinsonian** : Trihexyphenidyl, Procyclidine, Biperiden , Benztropine.
- **Other** drugs with anticholinergic properties
- Tricyclic Antidepressants
- Phenothiazines
- Antihistaminics
- Disopyramide

MUSCARINIC RECEPTORS SUBTYPES & ANTAGONISTS

- **M₁ Antagonists** –

Pirenzepine, Telenzepine, dicyclomine, trihexyphenidyl

- **M₂ Antagonists** –

Gallamine, methoctramine

- **M₃ Antagonists** –

Darifenacin, solifenacin, oxybutynin, tolterodine

Pharmacological actions

- **CNS** – Atropine has minimal stimulant effects on the CNS in clinically useful doses, esp. on parasympathetic medullary centers and a slower **longer lasting sedative effect** on the brain.
- **Scopolamine** has more marked central effects, producing drowsiness and amnesia.
- In toxic doses, scopolamine and to a lesser degree atropine can cause excitement, agitation, hallucinations and coma.

- **Parkinson's disease –**
- Relative cholinergic excess, because of deficiency of dopaminergic activity in basal ganglia – striatum system.
- A combination of an anti-muscarinic and dopamine precursor.
- **Vestibular disturbances-**
- Esp. motion sickness, involves muscarinic cholinergic transmission .
- Scopolamine (l-hyoscine) effective in preventing or reversing these disturbances.

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EYE

A) Muscarinic cholinoreceptor stimulation



- Pupillary constrictor muscle Stimulation
- Blocked by topical atropine
- Due to unopposed sympathetic dilator activity
- **mydriasis**

B) Weakening of contraction of ciliary muscle

- Cycloplegia
- Loss of accommodation
- Can't focus for near vision

C) Decrease in lacrimal secretions - Dry or sandy eyes

CVS

- Blockade of vagal slowing
- Relative tachycardia
- Low doses – Initial bradycardia before vagal block manifests
- May be due to block of presynaptic muscarinic receptors on vagal post-synaptic fibres that normally limit Ach release in sinus node & other tissues.

Respiratory System

- Smooth muscles & secretory glands of airway receive vagal innervation & contain muscarinic receptors.
- Receptor blockade leads to **Bronchodilatation & decrease in secretions.**
- For COPD or Asthma - antimuscarinic drugs are effective .

- Nonselective Antimuscarinic drugs have limited use.
- (Block of auto-inhibitory M₂ receptors on postganglionic parasympathetic nerves - Increased Ach, Opposes bronchodilatation caused by block of M₃ receptors on airway smooth muscles)
- Used prior to inhalant anesthetics, to decrease secretions in trachea.

GIT

- Marked effect on salivary secretions.
- Dry mouth.
- Gastric secretions affected less.
- Pirenzepine & Telenzepine - decrease gastric secretion with lesser side effects.
- Selective blockade of presynaptic excitatory muscarinic receptors on vagal nerve endings.
- High ratio of M1 to M3 affinity.

GIT

- Motility of git smooth muscles decreases.
- Walls of viscera relaxed.
- Tone and propulsive movements decrease.
- Gastric emptying time – Prolonged
- Diarrhoea due to overdosage of parasympathetic agents – Stopped
- Spasmolytic activity in some synthetic antimuscarinic agents.

Genitourinary tract

- Smooth muscles of ureters and bladder wall – relaxed – voiding is slowed.
- Useful in treatment of spasm by mild inflammatory conditions and neurologic conditions.
- But precipitation of urinary retention in elderly men with prostatic hyperplasia, So contraindicated.

Sweat glands

- Thermoregulatory sweating suppressed.
- Sweat glands – have sympathetic cholinergic receptors – their muscarinic receptors are accessible to anti-muscarinic drugs.
- In adults body temperature increases with large doses.
- In infants and children **Atropine fever** with ordinary doses.

Mechanism Of Action

- Atropine causes **reversible(surmountable)** blockade of the cholinomimetic actions at muscarinic receptors –
- Blockade by a small dose of atropine can be overcome by a large concentration of Ach or similar drug.
- Atropine prevents actions such as release of inositol triphosphate(IP_3) and the inhibition of adenylyl cyclase that are caused by muscarinic agonists.
- Highly selective for muscarinic receptors .
. Not selective for muscarinic subtypes.

P/K

- Atropine is readily absorbed from gut and conjunctival membranes.
- Scopolamine is absorbed across the skin, (Transdermal route).
- Partially metabolised by the liver.
- Eliminated primarily in the urine.
- Half life of about 4 hours.

P/K

- **Atropine and other tertiary agents are widely distributed in the body. Reach Significant levels in the CNS , limiting the dose , when given for peripheral effects.**
- **Scopolamine is rapidly and fully distributed into the CNS, Greater effects in CNS than most other anticholinergic drugs.**
- **Quaternary derivatives are poorly taken up by the brain.**
- **Relatively free of CNS effects.**

Uses

A. For Central action-

- **Parkinson's disease –**
- Benztropine, Biperiden, Procyclidine & Trihexyphenidyl used as adjunctive therapy.
- **Motion sickness -**
- Scopolamine – one of the oldest drug for sea sickness.
- Injection, oral or transdermal (patch behind the pinna , prophylactically 4 hrs before journey, effect persists for 3 days).
- **As a lie detector.**
- **For blocking short term memory, as a useful adjunct in anesthetic procedures.**

Uses(contd.)

- **As Antisecretory-**
- **Preanesthetic medication-**
- **When irritant GA is used, before their administration anticholinergics given to decrease salivary and tracheobronchial secretion.**
- **Non-irritating GA used these days.**
- **Halothane sensitises myocardium to NAdr mediated ventricular arrhythmias which are more prone during vagal slowing . Atropine useful to prevent these.**

Uses

- **Peptic Ulcer**
- Decrease gastric acid secretion
- Selective M1 blocker, Pirenzepine, Telenzepine.
- When other drugs not effective.
- **As Antispasmodic**
- Intestinal and renal colic - abdominal cramps
- In the treatment of traveller's diarrhoea, drug induced diarrhoea.
- To relieve urinary frequency and urgency.
- Enuresis in children.
- **Oxybutinin** - to relieve bladder spasm after urologic surgery e.g. prostatectomy.
- **Tolterodine** – M3 selective for adult urinary incontinence.

Respiratory disorders –

- Hyperactive neural bronchoconstrictor reflex in asthma, mediated by vagus, acting on muscarinic receptors on bronchial smooth muscle cells.
- **Ipratropium bromide** - A synthetic analogue of atropine, used as inhalational drug in asthma. Aerosole route – Maximal conc. at bronchial targets. with reduced systemic effects.
- COPD patients – Chronic smokers, older patients.
- **Tiotropium bromide** - A long acting quaternary aerosol anti-muscarinic drug, can be given once daily.

- **Atropine depresses mucociliary clearance by bronchial epithelium. Ipratropium does not depress.**
- **Tiotropium binds tightly to muscarinic receptors , Longer acting & has high bronchial selectivity.**

- **Ophthalmological disorders-**
- Accurate measurement of refractive error in uncooperative patients, young children require ciliary paralysis (have high ciliary tone).
- **Retinal examination** - when mydriasis is required , So for complete examination, eye drops or ointment. (less systemic absorption of ointment form by passage through naso-lacrimal duct)
- Shorter acting anti-muscarinics (Cyclopentolate and tropicamide) have largely replaced atropine due to prolonged mydriasis observed with atropine (7-10 days verses 6-24 hours with other agents like tropicamide).

- For older children short acting drugs are preferred like cyclopentolate, tropicamide.
- In younger children – greater efficacy of atropine is required due to high tone.
- **For mydriasis** - never used, unless cycloplegia or prolonged action is required. Phenylephrine is used.
- **To prevent synechae formation** in uveitis and iritis, alternate with a miotic.
- Homatropine – longer acting agent used .

CVS

- To counteract bradycardia and partial heart block in selected patients where increased vagal tone is responsible.
- digitalis toxicity .
- Reflex vagal discharge sometimes accompanies the pain of myocardial infarction (vaso-vagal attack), which may depress SA node or AV node function.
- Vagal discharge due to pressure on the neck for example ; tight collar.
- Atropine is useful.

POISONINGS

- **OPC poisoning** : 1-2 mg i.v. atropine sulfate every 5-15 min until signs of dry mouth, reversal of miosis occurs.
- **Some type of mushroom poisoning-**
- Massive doses of antagonist may be required over a long period of time to counteract the poisons.
- Also blocks the effects of excess Ach resulting from cholinesterase inhibitors, such as **physostigmine.**

Adverse effects

Dry mouth, mydriasis, blurred vision tachycardia, dry eyes, hot & flushed skin, Body temp. increases, constipation, hallucinations, agitation, delirium which may progress to depression, collapse of circulatory and respiratory system, coma and death.

Atropine Poisoning – Attempt of suicide.

Dry as a bone, Blind as a bat

Red as a beet, Mad as a hatter.

Children are very sensitive to hyperthermic effects of atropine. Death can occur even with 2 mg .

Treatment

- Temperature control with cooling blankets and seizure control with diazepam .
- Physostigmine – small doses given slowly i.v.
- To manage ganglionic blockade with marked orthostatic hypotension, give symatho-mimetic agents –phenylephrine,

C/Is

- Glaucoma patients esp. angle closure.
- Systemic use of moderate doses may ppt. angle closure.
- In elderly men with caution. Avoided in those with a history of prostatic hyperplasia.
- Slow gastric emptying may increase symptoms in patients with gastric ulcer.
- Nonselective anti-muscarinic agents should never be used to treat acid-peptic disease.

GANGLIONIC STIMULANTS

- **SELECTIVE NICOTINIC AGONISTS –**
- **NICOTINE**
- **LOBELINE**
- **DIMETHYL PHENYL PIPERAZONIUM IODIDE (DMPP)**

- **NONSELECTIVE MUSCARINIC AGONISTS-**
- **ACETYLCHOLINE**
- **CARBACHOL**
- **PILOCARPINE**
- **ANTI-CHOLINESTERASES**

GANGLIONIC BLOCKING AGENTS

A. COMPETITIVE BLOCKERS (NON-DEPOLARISING)

QUARTERNARY AMMONIUM COMPOUNDS

HEXAMETHONIUM

PENTOLINIUM

AMINES

MECAMYLAMINE

PEMPIDINE

MONOSULFONIUM COMP.

TRIMETHAPHAN

B. PERSISTENT DEPOLARISING BLOCKERS

NICOTINE }

ANTICHOLINESTERASE } DOSES

LARGE

MOA

- **Specifically act on the nicotinic receptors of both parasympathetic or sympathetic ganglia.**
- **Some also block the ion channels of autonomic ganglia.**
- **No selectivity toward the parasympathetic or sympathetic ganglia and are not effective as neuromuscular antagonists.**
- **Responses observed are complex and unpredictable.**
- **Rarely used therapeutically.**
- **Tools in experimental pharmacology**

Nicotine

- **Imp. In the context of smoking or chewing tobacco.**
- **Nicotinic patches, gums, lozenges for nicotinic dependence as an aid to stop smoking.**
- **Depending on the dose ,it depolarises autonomic ganglia , resulting first in stimulation then in paralysis of all ganglia.**
- **First increased blood pressure and HR, increased peristalsis and secretions.**
- **At higher doses, the BP falls because of ganglionic blockade,**
- **Activity in GI tract and bladder ceases.**

• TRIMETHAPHAN-

- BLOCKS nicotinic receptors**
- It is an ultra-short acting ganglion blocker, has been occasionally used to produce controlled hypotension and in hypertensive emergency due to aortic dissection.**

QUIZ

1. In very young children most dangerous effect of belladonna alkaloids is –

- Dehydration
- Hallucinations
- Hypertension
- hyperthermia

2. All of the following may cause cycloplegia (paralysis of accommodation) when used topically in the eye except –

- Atropine
- Cyclopentolate
- Physostigmine
- Scopolamine
- Tropicamide

3. You have been asked to give consultation in the treatment of an 80 yr old female patient. An antimuscarinic drug is being considered. Atropine therapy in your patient may be hazardous because-

- Can elevate intraocular pressure in pts with glaucoma
- Can cause ventricular arrhythmias
- Urinary retention pptd by atropine in women
- Elderly prone to get dangerous hyperthermia with atropine

4. A 35 year old man has been treated with several autonomic drugs for 4 weeks. He is admitted to emergency with signs of drug toxicity .Which of foll. Sign would distinguish between an overdose of a ganglion blocker verses a muscarinic blocker –

- Mydriasis
- Tachycardia
- Postural Hypotension
- Blurred vision
- Dry mouth, constipation

5. Accepted therapeutic indications for the use of antimuscarinic drugs include all except –

- Hypertension
- Motion sickness
- Parkinson's disease
- Postop bladder spasm
- Traveller's diarrhoea

6. Atropine overdose may cause which one of following –

- Gi sm. muscle cramping
- Increased heart rate
- Pupillary constriction
- Increased gastric secretions
- Urinary frequency

NEUROMUSCULAR BLOCKERS

- These drugs block cholinergic transmission between motor nerve endings and the nicotinic receptors on the neuromuscular end plate of skeletal muscle.
- These NM blockers are structural analogs of acetylcholine, and act either as
- **Antagonists (non- depolarising type) or Agonists (depolarising type)** , at the receptors on the end plate of the NM junction.

- Clinically useful during surgery to produce muscle paralysis –
- to facilitate surgery or artificial ventilation by endotracheal intubation, without cardio-respiratory depressant effects produced by deep anesthesia.
- **Spasmolytic drugs** - To reduce abnormally increased tone caused by neurologic or muscle end plate disease.

C/F

- **Non-depolarizing**

- **Tubocurarine**

- **Atracurium**

- **Mivacurium**

- **Pancuronium**

Depolarizing

- **Succinylcholine(suxamethonium)**

- **Decamethonium**

Spasmolytic Drugs

- **For Chronic Conditions -**
- **CENTRALLY ACTING**
- Baclofen
- Diazepam
- Tizanidine
- **DIRECTLY ACTING**
- Dantrolene

- **FOR ACUTE CONDITIONS –**

- Carisoprodol
- Chlorzoxazone
- Methocarbamol
- Cyclobenzaprine

Non-depolarizing blockers

- NM blockers have increased the safety of anesthesia because less anesthetic is required to produce muscle relaxation, patient can recover quickly and completely.

MOA

- At low doses these interact with nicotinic receptors to prevent the binding of Ach .
- Prevent the depolarization of muscle cell membrane and inhibit muscle contraction .

. **Competitive blockers**, because they compete with Ach at the receptor without stimulating the receptors.

Their action can be overcome by increasing the conc. of Ach in the synaptic gap -

By giving neostigmine , pyridostigmine or edrophonium . They are used to shorten the duration of NM blockade.

Pharmacological Actions

- Small rapidly contracting muscles of face and neck are most susceptible and are paralysed first followed by the fingers .
- Thereafter the limbs, neck and trunk muscles.
- Lastly the diaphragm muscles.
- Recovery in reverse order, diaphragm regaining function first.
- Tubocurarine , Mivacurium, Atracurium release histamine , Produce fall in BP, flushing , bronchoconstriction .

- D-TC produces significant fall in BP due to-
- Ganglionic blockade
- Histamine release
- Decreased Venous Return due to paralysis of limbs and respiratory muscles.

CNS-

- No central effects on i.v. administration.

Therapeutic uses

- As adjuvant drugs in anesthesia during surgery to relax skeletal muscle.
- These agents are also used to facilitate intubation as well as during orthopedic surgery. (d-TC may induce histamine release and promote ganglionic blockade, rarely used as a therapeutic agent).

- **Mivacurium** has quick onset and recovery is rapid, useful for short surgical procedures.
- **Cis-atracurium** useful in mechanical ventilation of critically ill patients.
- **Rocuronium** has most rapid onset of action, useful for tracheal intubation in patients with gastric contents.

Pharmacokinetics

- Injected intravenously, as oral absorption is minimal.
- Possess two or more quaternary amines in their bulky ring structure, making them **orally ineffective**.
- Penetrate the membrane very poorly.
- Do not enter cells or cross the BBB.

- Muscles with higher blood flow receive more drug and are affected earlier.
- **Redistribution** – termination of action
e.g. tubocurarine , pancuronium , mivacurium are excreted in urine unchanged .
- Atracurium is degraded spontaneously in plasma non-enzymatically (Hoffmann degradation) in addition to hydrolysis by esterase.

P/K

- Atracurium releases histamine and is metabolised to laudanosine, which can provoke seizures.
- Replaced by its isomer cis-atracurium.
- Vecuronium, Rocuronium de-acetylated in liver, clearance may be prolonged in patients with hepatic disease.

Drug Interactions

- **Anesthetics(halothane)** - augment NM blockade.
- **Antibiotics** – Enhance their action (esp. Aminoglycosides)
- **Local Anesthetics & Antiarrhythmic Drugs** - Enhance NMB.
- **Calcium-channel blockers** – may increase the NM block of tubocurarine and other competitive blockers as well as depolarising blockers.
- **Other NM blocking drugs-**
 - Depolarising muscle relaxants are antagonised by non-depolarising blockers.
 - **Neostigmine & Pyridostigmine** antagonise non-depolarising NM blockade by increasing Ach availability at muscle end plate.

Depolarising Agents

- Succinyl choline – 2 Ach molecules linked end to end.
- **Mechanism Of Action-**
- Succinylcholine attaches to the nicotinic receptors and acts like Ach to depolarise the junction.
- Unlike acetylcholine, which is instantly destroyed by acetyl-cholinesterase, **this depolarising agent persists at high conc. in the synaptic cleft, remaining attached to the receptor for a relatively longer time and providing a constant stimulation of the receptor.**

MOA

- **Phase I -**
- Opening of sodium channel associated with the nicotinic receptors,
- Depolarization of the receptor,
- An initial discharge that produces transient fasciculations,
- Continued binding of the depolarising agent renders the receptors incapable of transmitting further impulses.

- **Phase II-**
- With time continuous depolarization gives way to gradual repolarization as sodium channel closes.
- Receptor is desensitised to the effect of acetylcholine and there is flaccid paralysis.

Actions

- Respiratory muscles are paralysed fast.
- Succinylcholine initially produces short-lasting muscle fasciculations, followed within a few minutes by paralysis.
- The drug does not produce ganglionic block except at high doses.
- Weak histamine - releasing action.

- Succinylcholine that gets to NM junction is not metabolised fast by acetyl-cholinesterase
- allowing the agent to bind to nicotinic receptors and
- redistribution to plasma is necessary for metabolism (therapeutic benefit lasts only for a few min)

Succinyl choline induced Apnea-

Genetic variants in which plasma cholinesterase levels are low or absent, or an atypical form of enzyme, lead to prolonged NM paralysis leading to prolonged apnea.

Uses

- Rapid onset & Short duration of action,
- So, useful when **rapid endotracheal intubation is required during the induction of anesthesia.** (a rapid action is essential if aspiration of gastric contents is to be avoided during intubation).
- Other short procedures like laryngoscopy, bronchoscopy, esophagoscopy, reduction of fractures and dislocations.
- During electro-convulsive shock treatment.
- Treatment of convulsions - Status epilepticus or local anesthetic toxicity.

P/K

- Sch injected i.v.
- Brief duration of action results from redistribution and rapid hydrolysis by plasma cholinesterase.
- **Usually given by continuous infusion.**

Adverse effects

- **Malignant Hyperthermia-** when halothane used as anesthetic, Sch can lead to hyperthermia, caused by abnormal release of calcium from stores in skeletal muscle,
- With muscular rigidity and hyperpyrexia in genetically susceptible people.
- Treated by Rapid cooling of the patient and Dantrolene (blocks release of Ca^{++} from the sarcoplasmic reticulum , reducing heat production and relaxing muscle tone)

- **Apnea**
- **Hyperkalemia-**
- Increases potassium release from intracellular stores.
- Dangerous in burn patients with massive tissue damage, in which potassium is rapidly lost from within cells.
- **Increased Intra gastric pressure –**
- Due to fasciculations associated with Sch -
- Increasing the risk of regurgitation and aspiration of gastric contents.
- **Increased Intraocular pressure –**
- May be due to tonic contraction of myofibrils or
- transient dilatation of ocular choroidal blood vessels.
- **Muscle Pain.**

Spasmolytic Drugs

- For Chronic Conditions -
- **CENTRALLY ACTING**
- Baclofen(GABA derivative)
- Diazepam (Benzodiazepine)
- Tizanidine
- **DIRECTLY ACTING**
- Dantrolene

- **FOR ACUTE CONDITIONS –**

- Carisoprodol
- Chlorzoxazone
- Methocarbamol
- Cyclobenzaprine
- Mephenasin

Spasmolytic Drugs

- Spasticity – Increase in tonic stretch reflexes and flexor muscle spasm along with muscle weakness.
- **A/W-** Cerebral Palsy, Multiple Sclerosis, stroke.
- Spasticity involves stretch reflex arch and higher centers in CNS, with damage to descending pathways in s.cord resulting in hyperexcitability of alpha motor neurons in the cord.

- **Pharmacotherapy** may decrease some of the symptoms of spasticity by -
 - modifying the stretch reflex arc or
 - by interfering directly with skeletal-muscle (excitation-contraction coupling).
- Centrally acting drugs do have some sedative property

BACLOFEN

- Analogue of GABA
- Orally Active
- Acts as GABA agonist at **GABA_B** receptors
- Stimulation of receptors in the brain -
 - Hyperpolarization by increased K⁺ conductance & Presynaptic Inhibitory function .
- Can also decrease pain in patients of spasticity
 - by inhibiting the release of **substance P** in the spinal cord.

Uses

- Decreases spasticity in patients of –
- Multiple Sclerosis
- Amyotrophic Lateral Sclerosis
- Spinal injuries
- Flexor spasms

S/Es

- Drowsiness
- Mental confusion
- Weakness
- Ataxia
- Increased serum transaminases
- Sudden withdrawal-
Hallucinations, Tachycardia, Seizures.

Diazepam

- Facilitates GABA action in the CNS
- Useful anti-spastic activity
- Used in muscle spasm of any origin, including local muscle trauma
- Sedation in most patients at doses required to significantly decrease muscle tone.
- Initial dose 4 mg, Increased gradually to 60 mg.

Tizanidine

- Congener of clonidine
- Significant α_2 agonist effect- inhibits release of excitatory aminoacids in spinal interneurons.
- Absorbed orally
- Used in spasticity due to neurological disorders and in painful muscle spasm of spinal origin.

S/Es

- Dry mouth
- Drowsiness
- Night time insomnia
- Hallucinations

Dantrolene

- Effect resembles that of centrally acting muscle relaxants.
- Reduces skeletal muscle strength by interfering with excitation-contraction coupling in muscle fibre.
- Interferes with the release of activator calcium via sarcoplasmic reticulum calcium channels called the ryanodine receptor channel.
- Rapidly contracting motor units are more sensitive to the drug than are slow units.

P/K

- One third of an oral dose of dantrolene is absorbed.
- Half life – 8 hours.
- 25 mg/day – 100 mg ,4 times if necessary

Adverse Effects

- Generalized muscle weakness
- Sedation
- Hepatitis

Use

- Special use in the treatment of **Malignant Hyperthermia** - Heritable disorder
- Triggered by a variety of stimuli – GA , SCh
- Hereditary impairment in the ability of sarcoplasmic reticulum to sequester calcium.
- After giving triggering agent, Sudden & prolonged release of calcium with massive muscle contraction, Lactic acid production, increased body temperature.
- I/v dantrolene 1mg/kg I/V , max. 10 mg/kg.

Drugs for acute local muscle spasm

- Spasm by local tissue trauma or muscle strain.
- Act primarily at the level of the brainstem.
- Cyclobenzaprine is the prototype
- It has strong anti-muscarinic actions, may cause significant sedation ,Confusion, transient visual hallucinations.

Botulinium toxin

- Local facial injections of botulinium toxin for short term treatment of wrinkles around the eyes and mouth.
- Local injection useful treatment for generalized spastic disorders (Cerebral palsy).
- Benefit persists for weeks to several months after a single treatment .
- Type A botulinium toxin is used .

Uses of Centrally Acting

- Acute muscle spasms –
- Sprain
- Ligament and tendon injuries
- Dislocation
- Bursitis
- Fibrositis
- Rheumatic disorders
- Spasm- pain – spasm –To break this cycle

Uses

Spastic neurological diseases –

Hemiplegia , paraplegia, spinal injured, multiple sclerosis, amyotrophic lateral sclerosis, cerebral palsy.

Tetanus – Dizepam i.v.

ECT- convulsions. Succinylcholine.

Orthopedic manipulations – done under the influence of diazepam or methocarbamol i.v.