PharmPill team

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اللهم طهر قلبي من النفاق وعملي من الرياء ولساني من الكذب وعيني من الخيانة فأنت تعلم خائنة الأعين وما تخفي الصدور

اللهم اهدني لأحسن الأعمال والأخلاق ..

اخواني الطلاب .. اخواتي الطالبات دفعة 426

نحن فارم بل تيم قمنا بجمع مذكرات البنات مع الأولاد في هذه المذكرة

مع إضافة نوتات هذا العام

نسأل الله أن تنفعنا واياكم ... وتعود بالنفع لغيرنا

ان اصبنا فمن الله وان اخطانا فمنا ومن الشيطان

اوجة شكر خالص الى الاخت دعاء البلوي دفعة 424 ""

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ANTI-CHOLINERGIC DRUGS

ANTICHOLINERGIC DRUGS (Cholinoreceptors Inhibitors) :

→ **Nicotinic blockers:**
- Ganglionic blocker.
- Neuromuscular blocker.

→ **Muscarinic blockers (parasympatholytics)**

Classification of antimuscarinics:

1- Naturally occurring alkaloids.
Atropine – Hyoscine
2- Synthetic atropine substitutes.

Naturally occurring alkaloids.

Atropine – Hyoscine

Pharmacokinetics:
- Tertiary amines.
- Orally absorbed
- cross BBB.
- Metabolized in liver --→ excreted in urine.
- it's well-absorbed in the gut & conjunctival membranes
- Has short duration of action on most organs except the eye.

Mechanism of action (pharmacodynamics):

- Reversible competitive blocked of all muscarinic receptors (not selective).
- Block muscarinic action Ach and other parasympathomimetics.

e.g small dose of atropine can be overcomed by a large dose of Ach or its agonist
when atropine bind to muscarinic receptors it prevents the action such as release of (Ip3) & tissues which is inhibits the action of adenylyl cyclase which is caused by muscarinic agonist
most sensitive to atropine are
salivary glands
bronchial
sweat glands
the least sensitive to atropine is gatric parital cells that secrete acid

◙ atropine does not distinguish between the M1 , M2 , M3 subgroups of muscarinic receptors however, other antimuscarinic drugs have moderate selectivity for one or another of these subgroups
◙ atropine & the other tertiary agents are widely distributed in the body e.g (it's achieved in the CNS within 30 minute to 1 hour
◙ atropine disappears rapidly from the blood after administration , with half-life of 2 hours . about 60% of the dose is excreted uncharged in the urine and most of the rest appear in urine a hydrolysi and conjuction products

◙ quaternary antimuscarinic agents
»quaternary amine antimuscarinic agents have been developed to produce more peripheral effects with reduce the CNS effects
»contrast to tertiary compounds only 10-30% of dose are absorbedfrom oral adminstration
»contrast to tertiary compounds the quaternary derivatives are poorly taken up by the brain therefore has no effect on CNS - in low doses.

Atropine : -MCQ-

Pharmacological effect:

On CNS:

1- CNS stimulation.
2- vagal nucleus (CIC) : initial bradycardia and tachycardia.
3- Antiemetic effect: block vomiting center.
4- Antiparkinsonian effect: block basal ganglia
**Toxic dose:
Hyperthermia , excitement , hallucination.

On Eye:

1- Passive mydriasis →Paralysis of circular muscle.
2- Cycloplegia (loss of accommodation) → Paralysis of ciliary muscle.
3- Loss of light reflex.
4- Increase intraoptical pressure → glaucoma.
5- Decrease lacrimal secretion → sandy eye.

On CVS:

1- Heart:
- initial bradycardia followed by tachycardia.
- increase conduction (+ve dromotropic effect)

2- Blood vessels:
- Theraputic dose: decrease vasodilatation induced by Cholinomimetics.
- Toxic dose: cutaneous VD ----→ atropine flush.

On Secretion:

1- Decrease salivaly secretion.
2- Decrease Sweating → dry skin → fever.
3- Decrease Bronchial secretion → increase viscosity. (#Bronchial asthma)
4- Decrease lacrimal secretion → sandy eye.
5- Decrease gastric secretion → gastric motility. (#Peptic ulcer)

On GIT:

1- Relaxation of smooth muscle. (constipation)
2- Decrease GIT motility → antispasmodic effect.
3- increase sphincter contraction.

On Urinary tract:

1- Relaxation of the ureter smooth muscle.
2- sphincter contraction.
3- urinary retention.

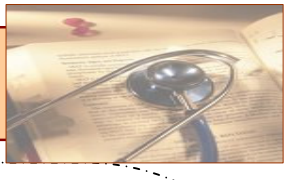
On Bronchial muscle:

1- Bronchial relaxation.
2- Decrease bronchial secretion---→ increase viscosity.

Uses:

1- Preanaesthetic medication to:
   - Decrease salivary and bronchial secretion.
   - protect the heart from excessive vagal tone.
2- Antispasmodic in renal and intestinal colics.
3- Cholinomimetics or organophosphorous poisioning.
4- Bradycardia (myocardial infarction)

MCQ :
atropine overdose may cause which of the following
a. GI smooth muscle cramping
b. increased cardiac rate
c. increased gastric secretion
d. papillary constriction
e. urinary frequency
the answer is : b



Organ System Effects:
1 - CNS :
in dose usually used , atropine has minimal stimulant effects on the CNS especially the parasympathetic medullary center specificly in vagal nucleus following slower , long-lasting sedative (مسكن)effect on the brain.

2 - eye :
effects of antimuscarinic drugs in eye are:
a- activation of the pupillary muscle constrictor muscle is blocked by local atropine & other tertiary antimuscarinic drugs , result in unopposed sympathetic dilator activity and mydriasis.
-Dilated pupils were considered cosmetically (تجميلي) desirable.
b- it is weakening of contraction of ciliary muscle , or it is called : cycloplegia > result in loss of the ability to accommodate or cannot focus for near vision.
c- reduce the lacrimal secretion.

3 - cardiovascular system:
-the SA node is very sensitive to muscarinic receptor blackade because it's heavily innervated with paraympathetic nerves
-in moderate to high dose of atropine > cause tachycardia
-in low dose of atropine > central vagal stimulation (before effect of peripheral vagal blockade) > often result in initial bradycardia follow by tachycardia (because peripheral vagal blockade become manifest).

- skeletal muscle blood vessels does not receive direct innervation from the paraympathetic nervous system , however , parasympathetic nerve stimulation dilate coronary artery and sympathetic cholinergic nerves cause vasodiltation in the skeletal muscle vessels.
- atropine can block this vasodiltation of skeletal muscle vessels.

4 - respiratory system :
- both smooth muscle and secretory gland of airway recieve vagal innervation and contain muscarinic receptors.
- atropine cause bronchodilation and reduce gland secretion.
- antimuscarinic drug are used prior to administration of general anesthetics to reduce the accumulation of secretions in trachea and reduce possibility of laryngospasm.

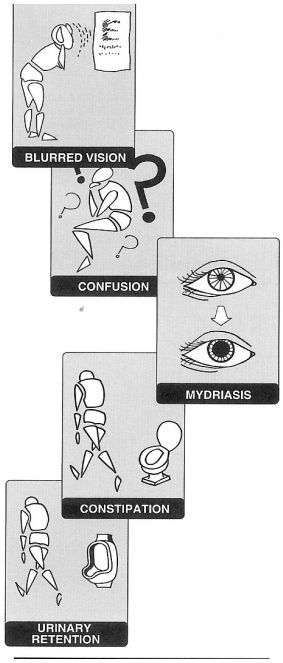
5 - GIT :
-blockade of muscarinic receptor effect the motility and secretion of the gut.
-antimuscarinic drugs have great effect on salivary secretion > dry mouth occur in pateint taking antimuscarinic drugs.
-the GIT smooth muscles motility from stomach to colon are relaxed by antimuscarinic drugs , therefore , gastric emptying is prolonged and intestinal transit time is lengthened . (used in treating diarrhea).

6 - Genitourinary tract :
-the antimuscarinic drugs relaxes smooth muscle of the ureter and bladder wall , and slow voiding.
-the antimuscarinic drugs have no significant effect on the uterus

7 - sweat gland :
-atropine supprese thermoregulatory sweating.
-in adult , body temperature is elevated by this effect only if large dose is administered , but in infants & children even ordinary does may cause " atropine fever"

Adverse effects and toxicity:

- Blurred vision.
- Mydriasis.
- Tachycardia
- Atropine flush.
- Urinary retention
- Constipation.
- Dryness of mouth
- Sandy eye.
- Malegnant hyperthermia (due to decrease sweating)
- Hallucination
- Excitation (toxic dose)



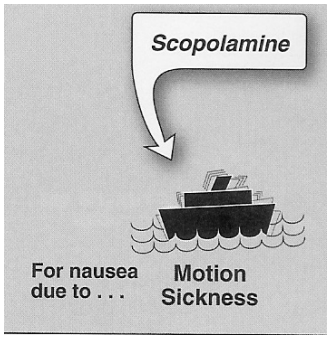
Ttreatment (of atropine toxicity):

- Gastric lavage.
- Abticonvulsant.
- Cooling blanket.
- **Antidote**: Physostigmine. (IV slowly)

Contraindication of Atropine:

1- Glucoma
2- Bronchial asthma
3- prostate hypertrophy in old patient.
4- Tachycardia.
5- Peptic Ulcer.
6- Constipation and paralytic ileus.

Hyoscine (Scopolamine):



What is difference between atropine and hyosine ?

- Rapid onset of action.
- Short duration .
- Less mydratic action (2-4 days)
- CNS depressant:
  Sedation , Inhibit of vomiting center , Has amnesic action.
- Less CNS effects.

Uses:

- Preanaesthetic medication.
- Antiemetic action (motion sickness)

MCQ :
which of the following best describes the mechanism of action of scopolamine
a. irreversible antagonist at nicotinic receptors
b. irreversible antagonist at muscarinic receptors
c. physiology antagonist at muscarinic receptors
d. reversible antagonist at muscarinic receptors
e. reversible antagonist at nicotinic receptors
the answer is : c

MCQ :
the drug of choice for treating decreased salivation accompanying head and neck irradiation :
a. physostigmine
b. scopolamine
c. carbacol
d. acetylcholine
e. pilocarpine
the answer is : e

Synthetic Atropin substitutes: -V.MCQ-

(اسم الدواء و استخدامه)

* **Eye:** - for fundus examination of the eye

Atropine	7 days
Homatropine	24 h
Cyclopentolate	12 h
Tropicamide	6 h

***GIT:**

- peptic ulcer

Pirenzepine (selective M1 blocker)

***Antispasmodic**

1- Hyoscine butyl bromide.
2- Oxyphenonium

***Parkinsonism**

Benztropine.

***Bronchial asthma:**

Ipratropium bromide:

- Quaternary compound
- Taken by inhalation (bronchodilator)
- Little effect on viscosity.

Uses of antimascarinic (muscarinic receptor blocker)

- AS mydratics.
- Bronchial asthma.
- Antispasmodic in renal and intestinal colics.
- Traveller's Diarrhea.
- Peptic Ulcer (# Atropine)
- Antiparkinosonian
- Antiemetic. motion sickness (Hyoscine)
- Preanaesthetic medication.
- Cholinomimetics intoxication .

	Drug	Therapeutic uses
Muscarinic blockers	*Atropine**	In ophthalmology, to produce mydriasis and cycloplegia prior to refraction
		To treat spastic disorders of the GI and lower urinary tract
		To treat organophosphate poisoning
		To suppress respiratory secretions prior to surgery
	Scopolamine	In obstetrics, with morphine to produce amnesia and sedation
		To prevent motion sickness
	Ipratropium	Treatment of asthma