Chapter 5

Anticholinergic Drug

1- Antimuscarinic Drug (parasympatholytics)

muscarine agonist

① Atropine
② scoplamine
③ Buscopan
④ Homatropine
⑤ Tropicamide
⑥ Ipratropium
⑦ oXybutinin

2- Antinicotinic Drug

1- Ganglion blocker

2- NMJ blocker

Cholinergic agonist * parasympathetic ↓ ACh ↓

Cholinergic antagonist * ACh ↓

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① Antimuscarinic agent

Atropine → tertiary belladona alkaloid — CNS ↓

- Act centrally and peripherally
- action 4 hours (except topical to the eye 7-14 days)

action →

- eye → mydriasis, cycloplegia (inability to focus for near vision) ↑ intraocular pressure, ↓ closure angle glucoma
- GIT → antispasmodic, reduced gastric motility without affect HCl acid production ↓ saliva ↓ urination
- Cardiovascular → Low dose → M_1 inhibitory to presynatic neuron cause increase Ach secretion (decrease heart rate)

  2- High dose → blocking M_2 (SA) Cause (increase heart rate)
- Secretion → dryness of the mouth (xerostomia)

atropine Theraputic use

1- Opthalmic → Topical to eye for measurment of refractive error
& لتستبدله بـ Cyclopentolate (24 h) , tropicamide (6 h) لأن فترتهم اقل

2- antispasmodic

3- Antisecretory (block secretion of upper and lower respiratory tract prior surger)

4- treat bradycardia

5- Antidote for (organophosphate , Physostigmine , mushrom poising)

Atropine Adverse effect

1- blurred vission " sandy eye " 2- Constipation 3- urinary retention
4- tachy cardia 5- dangerous in children causes increase in body temperature

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2 Scoplamine →
- CNS بحت
  وتأثيره عليه أكثر من تأثير ال atropine
- most effective antimotion sickness drug
- blocking short -term memory
- produce sedation , excitment , euphoria
  [redacted]
- مهم كتير — prevent motion sickness may available as topical patch last for (3 days) action
- prevent post operative nausea and [redacted] vomiting

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3 ipratonium → SAMA → acute manangement of asthma + COPD
Atiotropium → LAMA → Chronic manangement of asthma + COPD
glycopyrrolate → LAMA → COPD
Aclidinium → LAMA → COPD

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4 Cyclopentolate (24 h) & tropicamide (6 h) → mydriasis & cycloplegia

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5 Benzatropine & trihexyliphenidyl → parkinsons disease including antipsychotic-induced extrapyramidal symptoms.

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6 — مجاعة المثانة

- Oxybutinin
- Darifenancin
- Solifenancin
- trospium
- fesoterodine
- tolterodine

→

- overactive bladder & urinary incontinence
- bind competitively blocking (M_3) receptor in bladder
- ↓ intravescral pressure
- ↓ frequency of bladder contraction
- ↑ bladder capacity
- metabolized by CYP450 except trospium
- once daily, oral dosage

ملاحظات مهمة على هالمجموعة

1. Darifenancin, solifenancin → selective M_3
   adverse effects فيه تكون قليلة و يامن

2. Oxybutinin → neurogenic bladder, its present topical gel, transdermal patch, oral

3. trospium → هذا يميز عن البقية
   - metabolized by ester Hydrolysis
   - treat overactive bladder in patient with dementia — مهمة كلش كلش
   يعالج المثانة النشطة بحالة اللي عدهم خرف لان يعبر للـ CNS بشكل قليل

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Ganglionic blockers

- act on nicotinic receptor of
  1. parasymphathetic autonomic ganglia
  2. sympathetic autonomic ganglia
- block ion channels of the autonomic ganglia
- show no selectivity toward the parasymphathetic or symphathetic ganglia, not effective as neuromuscular antagonists

* rarely used therapeutically, but serve as a tool in expermintal pharmacology

- Nicotine (ganglionic blocker)
  - * Component of cigarrate smoke, no Theraputic benifet, deleterios to health
  - * nicotine depolarize autonomic ganglia resulting first in stimulation and then paralysis in all ganglia
  - * Stimulatory effect cause increase release of neurotransmitter
    - Ach → increase perstalisis and secretion
    - NE → ↑BP, ↑ cardiac output
  - * Nicotine at higher Dose causes fall in blood pressur due To ganglionic blockade.

Non depolarizing Competitive blockers

- NonDepolarizing (competitive)
  - Pancoronium
  - Mivacoronium
  - rocorunium
  - Cistarcornium
  - Vancoronium

  → block cholinergic transsmision between motor nerve ending and nicotinic receptor on the Skeletal musch
- Doplarizing agent
  - succinylcholine

NON Depolarizing (competitive) blocker

1- Cistatracurium → eleminate by (Hofmann elemination) renally excreted (renal and hepatic dysfunction) أفضلية للمريض
2- mivacurium → plasma cholinestrase elimination
3- pancuronium → eleminated in urine
4- rocronium → eleminated in bile
5- vecuronium

action

* AT Low Dose → - block Ach at nicotinic receptor
  - it can overcome the block by use of cholinestrase inhibitor (edrophonium, physostigmine, Neostigmine
  - The muscle respond to direct electrical stimulation from a peripheral nerve stimulator

* AT high Dose → - block the ion channel of The motor endplate
  - reducing The ability of cholinestrase inhibitor to reverse The action of Neuromusclar block
  - muscle dosent respond to The electrical stimulation

* Action → contracting muscle :
  - حفظ بالتسلسل اذا { ① face and eye ② fingers, Limbs, neck ③ intercostal muscle ④ diaphragm
  - حال first muscle recover فهي بالتسلسل بالعكس

PK - IM or IV
- dont cross BBB

* Drug interaction → 1.- cholinestrase inhibitor → يثبط فعاله وبس بحالة اذا دخل وسد ال ion channel ع راح يكون اله تأثير
  2- Hydrogenated Hydrocarbon anesthetic (desulfurane)
  3- Aminoglycoside antibiotic (gentamicin, tobramycin)
  4- Calcium channel blocker
  - [2–4] تزيد تأثير ال neuromusclar blocker

* Sugammadex → Vecrounium يوقف تأثير ال

Depolarizing agent (succinylcholine)

- Depolarizing the plasma membrane of the muscle fiber, similar to Ach.
- Succinylcholine attach to nicotinic receptor.

Action

Phase I: depolarizing agent cause opening of sodium channel result in Depolarization of the receptor.

Phase II: Continous Depolarization gives way to gradual repolarization as the sodium channel closses or is blocked, this cause flaccid paralysis.

- respiratory muscle are paralyzed Last
- Succinylcholine hydrolyzed by plasma pseducholinestrase.

Theraputic use

1- useful when rapid endotracheal intubation is required during the induction of anesthesia
2- used during electroconvulsive shock treatment

Adverse effect

H_2A

- Apnea
  - diuretics أو digoxin
  - electrolyte imbalance
  - Potassium
  - Cholinestrase
  - atypical form
  - diaphragm
- Hypekalemia
  - ↑ K release
  - burn Patient
  - tissue damage
  - renal failure
- Hyperthermia
  - malignant Hyperthermia