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
الفرق بين tropicamide (6h) و Cyclopentolate (24h) :

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

4- treat bradycardia

5- Antidote for (organophosphate , physostigmine , mushrom poisning)

Atropine Adverse effect

1- blurred vission " sandy eye " 2- Constipation 3- urinary retention

4- tachycardia 5- dangerous in children causes increase in body temperature

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2 Scopolamine → - CNS depressant أقوى من atropine

- most effective anti motion sickness drug
- blocking short-term memory
- produce sedation , excitment , euphoria

- prevent motion sickness may available as topical patch last for (3 days) action
- prevent post operative nausea and vomiting

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3 ipratropium → SAMA → acute manangement of asthma + COPD

Aclidinium → LAMA → Chronic manangement of asthma + COPD

glycopyrrolate → LAMA → COPD

Aclidinium → LAMA → COPD

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

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

6 oxybutinin, Darifenancin, solifenancin, trospium, fesoterodine, tolterodine → - overactive bladder & urinary incontinence
- bind competitively blocking (M_3) receptor in bladder
- ↓ intravesical pressure
- ↓ frequency of bladder contraction
- ↑ bladder capacity
- metabolized by cyp450 except trospium
- once daily, oral dosage

① Darifenancin, solifenancin → selective M_3

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

③ trospium → - metabolized by ester Hydrolysis
- treat overactive bladder in patient with dementia

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
- Doplarizing agent
  - succinylcholine

block cholinergic transsmision between motor nerve ending and nicotinic receptor on the Skeletal musch

NON Depolarizing (Competitive) blocker

1- Cistatracurium → eleminate by (Hofmann elemination) renally excreted (renal and hepatic dysfunction)
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 inhibito to reverse the action of Neuromusclar block
- muscle doesnt respond TO the electrical stimulation

* Action → Contracting muscle:

first muscle recover: ① face and eye ② fingers, Limbs, neck ③ intercostal muscle ④ diaphragm

PK
- IM or IV
- dont cross BBB

* Drug interaction → 1.-cholinestrase inhibitor →
2- Hydrogenated Hydrocarbon anesthetic (desulfurane)
3- Aminoglycoside antibiotic (gentamicin, tobramycin)
4- Catecium channel blocker

neuromusclar blocker

* Sugamadex → Vecrounium

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Depolraizing 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.

مهم → respiratory muscle are paralyzed Last

- succinylcholine hydrolyzed by plasma pseducholinestrase.

Thraputic 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 →
  - ① * يلزم ما تأخذ ادويه الي يأخذون digoxin او diuretics
  - ② الي عنده electrolyte imbalance راح يزيد عنده افراز ال Pottasium
  - ③ الي عنده نقصان ب Cholinestrase او atypical form راح يصير عنده apnea بسبب شلل ال diaphragm
- Hypekalemia → ↑ K release: burn Patient, tissue damage, renal failure
- Hyperthermia
  - ↓ زيادة حرارة الجسم
  - malignant Hyperthermia