

Indirect acting cholinomimetics

Acts like

Dr. Saed M Al-daiaen

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Mutah University

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علم فسيولوجي عن أدوية تشتمل بشكل غير مباشر نفس الآلية
"Cholinergics"

Cholinesterase enzymes

❖ CE is a protein

When A drug is given to inhibit CE which let's Ach stay in the body and increase it's activity

➤ In cholinergic synapses & RBC / plasma

➤ ^{Breaks down} Metabolizes Ach into choline & acetate

➤ Specific for Ach in cholinergic synapses

بين الخلايا العصبية + العضلة
Between the neuron & the muscle

❖ Pseudocholinesterase in plasma & liver

➤ Not specific to Ach

➤ Metabolizes other drugs (suxamethonium, procaine)

used in anesthesia
or succinylcholine

↳ local anesthetic

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Classification of indirect-acting cholinomimetics

Classified into:

- ❖ Reversible cholinesterase inhibitors
- ❖ Irreversible cholinesterase inhibitors

CE \Rightarrow is found in the body in large numbers, so when "we" inhibit these enzymes only a small part is inhibited + eventually with time, they're "numbers" will go back to normal.

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Uses of indirect-acting cholinomimetics

- ❖ Diagnosis of MG (Edrophonium)
Myasthenia gravis
- ❖ Treatment of MG (Pyridostigmine)
- ❖ Reversible NMB intoxication (Neostigmine)
Neuromuscular block *can't pass BBB*
- ❖ Alzheimer's disease (Donepezil)
- ❖ Irreversible CEI: insecticides
can pass the BBB

صدمات عصبية / دواءه عليه : - حبيقة نفسه
- تضيق البؤبؤ
- تنكس
- زيادة الإفرازات اللاعابية

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Myasthenia gravis (MG)

❖ **Autoimmune** (autoantibodies to N_M in NMJ)
لديه جسمام مضادة تحفز مستقبلات Ach / صرحه مناعي

❖ Reduction in receptor number
decrease

❖ Muscle weakness, fatigability, Ptosis, diplopia,
difficult speaking & swallowing
أارتخاء الكفة
رؤية الشيء الواحد = تشبيهاً

❖ Treatment:

➤ Reversible CEI

➤ Thymectomy → Large at Birth, gets smaller with Age
sometimes it stays large
Thymus غدة زعترية

➤ Immunosuppressant (CS, cyclosporine)

which increases the chance of
Having MG → استئصالها يقل حصة المرض

Reversible ChE inhibitors

- ❖ Inhibit reversibly CE enzyme
- ❖ Accumulation of Ach
- ❖ Electrostatic bonds (*weak Bonds Between Drug + CE*)
- ❖ Stimulate nicotinic & muscarinic receptors
- ❖ Useful in myasthenia gravis

Neostigmine

- ❖ Synthetic CEI, does not cross BBB *not useful in Alzheimer*
- ❖ Duration of action (4 hrs) *should be taken every 4 hrs*
- ❖ Mainly in MG & also in: *منه 4 ساعات*
 - Antidote to competitive NM blocker tubocurarine poisoning *used in anesthesia*
 - Paralytic ileus, urinary retention *موضوع عصبانيات*
- ❖ Given orally, SC

Adverse effects of CEI

similar to excessive activation of the parasympathetic

- ❖ Excessive salivation
ءاصموار الوجه
- ❖ Flushing and hypotension
انقباضها
- ❖ Abdominal colic and diarrhoea
- ❖ Bronchospasm → زيادة حركة الأمعاء
وزيادة إفراز السوائل
مع Stool