Muscle Relaxants

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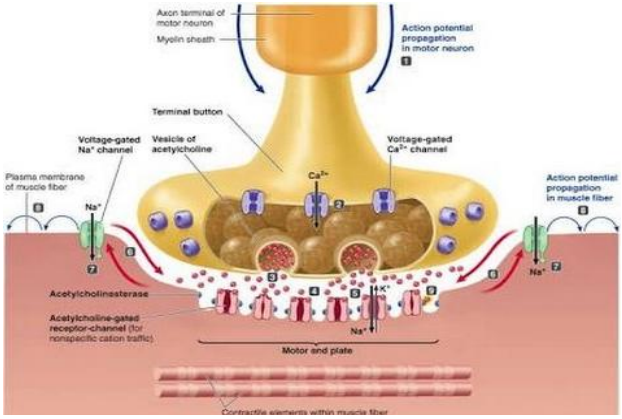
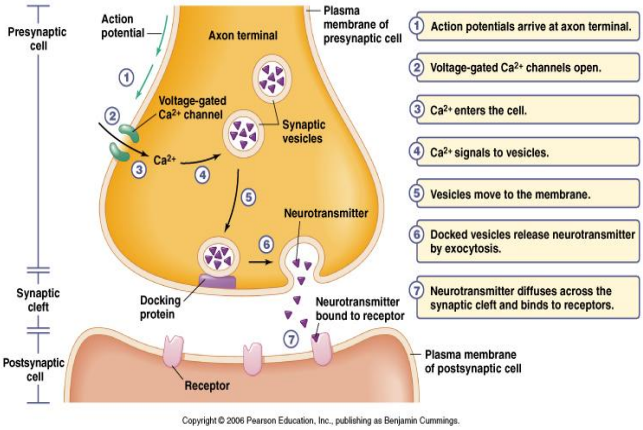
Neuromuscular Junction



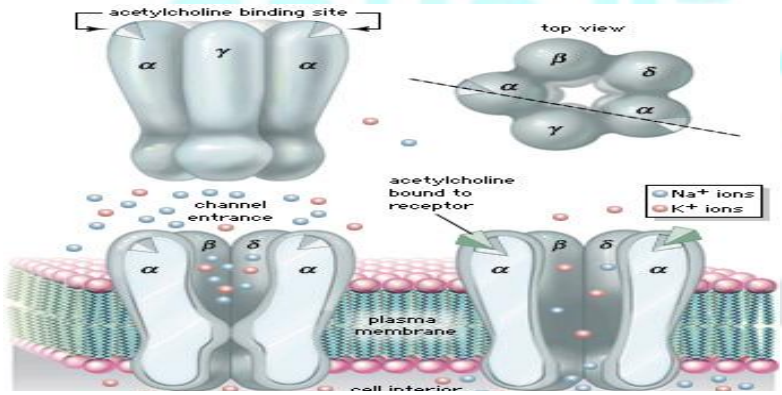
Action Potential



The structure of ACH receptors consists of **five protein subunits** , two α sub unit , and single β ,δ ,ε .

Only the two α subunits are capable of binding ACH molecules .

- the NTMs should bind to both α proteins to function, one α isn't enough



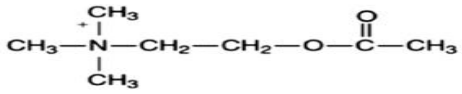
- ACH is rapidly hydrolyzed into acetate and choline by **acetylcholinesterase** .

Also this enzyme called true cholinestrease

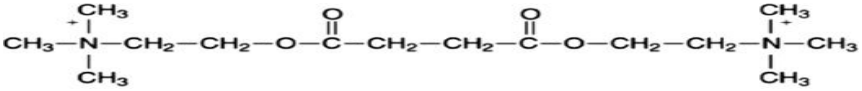
* Neuromuscler blocking agents are divided into two classes ; **depolarizing** and **nondepolarizing** .

By the mechanism of action , reversal of block .

All neuromuscler blocking agent are quaternary ammonium compound



Acetylcholine



Succinylcholine

irreversible muscle relaxation in non depolarizing way >> organophosphourous and botulinum toxin : may lead to respiratory failure and death due to diaphragmatic paralysis

Mechanism for depolarizing and nondepolarizing ???

Reversal for dep and non-dep….

- For non-dep.the effect reverse by high concentration of ACH

usually in 30-60 min 25% remains & within 1:15 hr it returns to normal

Tidal volume : 5-7 ml\kg

SUCCINYLCHOLINE (agonist for ACH)

- Dose: 1-1.5 mg/kg

- Stored under refrigeration 2-8 c

- More molecular weight and more potent

- mechanisum of action:

Continuous muscle cotnraction >>>all k out of cell >>> flaccid paralysis for 10m ,

- after 10 m release from receptor to blood stream and metabolized by **pseudocholinesterase**

- The onset of action 30-60 s , duration of action less than 10 min = useful for rapid induction patients + used for full stomach .non fasting patient

- Metabolized by pseudocholinestrease (in bloodstream) into succinylmonocholine

- Low pseudocholinestrease level >> **prolongation** which seen in:

Pregnancy , liver disease , renal failure , genetics

- Low pseudocholinesterase >> SCOLINE APNEA

(genetics cause) Homozygous(two genes mutation) 8hrs.

Heterozygous(one gene mutation) 20-30 mins.

Phase I >> same as ACh cause contraction

Phase II >> continues muscle contraction cause flaccid paralysis

* Why we consider pregnant women a full stomach ?

Because the uterus pressure on the gastric contents which delay the emptying

Side effects

- CVS effects are found most common in children , bradycardia following administration first dose and 2nd in adult

- Fasciculation : continuous muscle contraction leads to :

Hyperkalemia & Muscle pain

- Fasiculations are mostly seen in facial muscle

- Intragastric pressure elevation and increase lower esophageal sphincter tone (so don't affect the intubation)

- Intraocular pressure elevation

- Masster muscle rigidity (early sign of malignant hyperthermia)

- Malignant hyperthermia

- ICP elevation

Non-depolarizing muscle relaxant (competitive antagonist)

Chemically they are either benzylisoquinolines(B) or steroidal compound (S) ,

(B)tends to **release histamine** : (V.D , skin rash, itching , tachycardia and hypotension)

(S) rends to be **vagolytic** (decrease vagal effect : tachycardia, hypotension, bronchoconstriction)

- The more potent one is the longer its speed of onset.

- In general the diaphragm , jaw , larynx , fascial muscles respond to and recover from muscle relaxation sooner than the thumb , but glottic musculature is quite resistant to blockade

- Water soluble

Atracurium :

- Benzylisoquinoline structure

- Metabolism by **nonspecific estrease** , or by **hofman elimination** (nonenzymatic chemical breakdown into laudanosine)

Laudanosine >> its accumulation leads to renal failure & seizures

- Dose 0.5 mg/kg ,onset of action 1-2mins for intubation .

- Stored at room temp

Side effect : B tend to release histamine, so:

1- Hypotension and tachycardia

2- Bronchospasm

3- laudanosine toxicity

4- Allergic reaction

Cisatracurium :

- Is a stereoisomer of atracurium that is four times more potent .

- **Hofmann elimination** > laudanosine

- Dose 0.1 – 0.15 mg/kg

- Stored under refrigeration

- Side effects not significant

Mivacurium :

- Metabolized by **pseudocholinesterase** (the only one)

- Side effects histamine release

- Other muscle relaxant doxacurium

Pancuronium

- Steroidal compound

- Metabolized by **the liver** and exerted renaly

- Dose 0.08-0.12

Side effect:

- Hypertension and tachycardia (vagal blockade = sympathetic stimulation)

- Arrhythmias

- Allergic reaction (because of bromide hypersensitivity , NOT histamine release)

Pipecuronium : more potent but lack cvs side effects

Vecuronium

Rocuronium : rapid onset

Cholinestrease Inhibitors:

- Acetylcholine is hydrolyzed by acetylcholinesterase into acetate and choline

- Two types of receptors for acetylcholine : **nicotinic receptors** and **muscarinic receptors**.

- Cholinestrease inhibtors cause increase acetylcholine which acts on several organ ; cvs , pulmonary , GI

Neostigmine:

- Lipid insoluble , so can't cross BBB .

- Dose 0.04 mg / kg

- It is reported that It can cross the placenta and cause fetal bradycardia

Side effects: bradycardia , nausea , vomiting , fecal incontinence

- It is used to treat mystenia graves

Pyridostigmine ; slower onset and less potent

Edrophonium : less potent but the most rapid onset of action and shortest duration .

Physostigmine ; lipid soluble so can cross BBB

Anti-Cholinergic Drugs:

- Ester linkage for an aromatic acid with organic base .

- Competitively blocks acetylcholine receptors (muscarinic receptors)

Cardiovascular : blockade of MU receptors in SA node resulting in tachycardia , this effect is useful in reversing bradycardia due to vagal reflexes : eg , baroreceptor reflex , perperitoneal stimulation , oculocardiac reflex .

Respirtory : inhibit the secretions of the respirtory mucosa and relaxation of bronchial smooth muscle

Gastrointestinal ; reduce GI secretion

Ophthalmic ; mydrasis

Genitourinary ; urinary retention

Thermoregulation : inhibition of sweat gland rise temp (Atropine fever)

Antagonist for M receptor : atropine

Antagonist for N receptor : non-dep.

Atropine:

-Anatgonist of muscarinic receptor

- Dose 0.4 – 0.06 mg / kg

- Cross BBB

- useful management for patient with SVT

- **Scopolamine**

- **Glycopyrolate** : can't cross BBB

Archive Questions:

MCQs :

1)Anticholinergic HAS the following effects except :

a. No sedative effect

b. Parkinson

c. affect Muscarinic receptors

d. mydriasis

e. inhibit secretions

Ans: a

2)Succinylcholine is contraindicated in a patient with?

a. Chronic renal failure

b. Duchene muscular dystrophy

c. Myasthenia gravis

d. Patient with full stomach

e. Patient with potassium 5.0 mEq/L.

Ans: a

3) Wrong about atracurium? Dose 0.1-0.15

4))All the following is steroidal non depolarizing muscle relaxant except : doxacorium.

5) Wrong regarding succinylcholine : metabolized by acetyl cholinesterase.

Written:

1)Mention the benzylisoquinolone muscle relaxants.

2)Adverse effect of cistacurioum.

3)Drug that inhibit cholinesterase.

4)Side effects of succinylcholine.

5)Uses of muscle relaxant

" من طلبَ العلم ليُحيي بهِ الاسلامَ فَهوَ مِنَ الصديقينَ وَ دَرَجتُهُ بعدَ دَرجةِ النُبوّة "

- ابنُ القيّم