

***Title of Lecture: neuromuscular blockers***

***Date of Lecture:***

***Sheet no: 17***

***Refer to slide no. : 1-19***

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Slide 2 :

Contraction of voluntary muscles

We have myelinated motor neurons with no ganglia , ach is synthesized and stored in the nerve terminals (in huge amounts) , realized into the synapse whenever needed.

This synapse is the neuromuscular junction or motor end plate.

Ach then binds to nicotinic cholinergic receptors. in response to that, depolarization of membranes of voluntary muscles will happen . opening of NA channels, NA and Ca will enter(slide3) ,generating action potential and contraction of muscles .

After that ach is quickly degraded by cholinesterase enzyme.

To have another contraction I need to have other molecules of ach binding to receptors generating new action potential and so on.

how we could achieve relaxation of muscles ?

-Blocking synthesis or release of ach is NOT a good or efficient way of relaxing muscles ,because 1.ach is synthesized in huge amounts and 2. Our respiratory muscles also use ach to contract so we need it all the time .

-ach antagonists on nicotinic receptors ( atropine will have no effect because it acts on muscarinic receptors), these antagonists we use are competitive ,so if ach concentration increased it will bind to the receptors causing contraction and reversing the effect of the antagonist.

The easiest way To increase ach concentration is by inhibiting cholinesterase enzyme . increasing ach by controlling synthesis or release is very difficult unlike with the adrenergic system ( NE,E) so we use ACHE inhibitors

-increasing the action of ACHE enzyme , toxic and not available so it is not used in relaxation of muscles.

-ach itself causes muscle relaxation if it increases , so we could use it as muscle relaxant but because it is very quickly degraded we can't give it as a drug but we can give strong agonists of ach. At first muscles will contract (first phase) but with chronic administration down regulation(desensitization ) of receptors will happen ( second phase).

-directly acting muscle relaxants

-centrally mediated relaxation , since CNS controls everything we can inhibit certain reflexes by controlling the CNS.

So eventually we have 4 effective methods of relaxing muscles :

1. Ach antagonists
2. Giving strong ach agonists
3. Directly acting muscle relaxants
4. Centrally mediated relaxation

Slide 4:

 **Pancuronium** and **Vecuronium** are widely used in surgery

slide 5:

2.depolarizing relaxants are ach agonists that cause depolarizing and contraction but after that they cause desensitizing of receptors or down regulation of them , unlike the antagonists which block the depolarization so they are non-depolarizing

succinylcholine = 2 acetylcholine

it's not widely used due to its severe side effects

3.directly acting relaxants:

Valium is orally and IV effective

Slide 7:

-muscle relaxation before major surgeries , by definition general anesthetic is a drug that causes **reversible** analgesia , muscle relaxation, amnesia and loss of consciousness

If we use the therapeutic dose we will kill the patient and if we decrease it there will be no loss of consciousness, to solve this problem we combine drugs to have useful drug-drug interaction ( anesthesia without side effect)

-muscle relaxation before intubation , before entering the bronchoscope or tracheal-scope it is wiped with LA cream to make its entrance easier and to relax muscles.

-used in the management of muscle spasm like with electro-compulsive therapy, multiple sclerosis, tetanus or malignant hyperthermia

Slide8:

They don't have direct effect on generation of AP they only inhibit AP mediated by ach.

Has short duration of action.

Flaccid =smooth paralysis

Slide9:

Their effect on respiratory muscles is not that much on therapeutic doses (which is good) , recovery occurs in reverse ; respiratory muscles are first then limbs and finally head and neck muscles.

They are given IV for these clinical uses

Slide11:

 **Isoflurane; Nitrous Oxide; Enflurane and Halothane** are anesthetics that synergies the effect of non-depolarizing muscle relaxants ( the doctor said that synergism applies more than potentiation because these anesthetics have muscle relaxation effect by their own , so using them along with the non-depolarizing relaxants will have enhanced effect of both of them "synergism" )

Slides13,14:

Depolarizing agents are not widely used , only in minor procedures

They act as strong agonists of ach

Muscle relaxation by these drugs is achieved by 2 phases :

1. Initial depolarization and fasciculation leading to inactivation of NA channels and hence inhibition of generation of action potential. but later on depolarization of the membrane occurs
2. Paralysis is maintained by the phenomena of desensitization or down regulation of the receptors.

Slide 16:

Prolonged action of these drugs could be due to liver disease, since cholinesterase enzyme is synthesized in the liver its concentration will decrease leading to prolonged action of these agonists.

 Slide17:

Apnea: difficulty in breathing , this is more noted with the depolarizing drugs compared to the non-depolarizing

Apnea is the major and most dangerous side effect of succinylcholine

Both hypo and hyper kalemia cause cardiac arrhythmias

Malignant hyperthermia : severe elevation in body temperature and severe muscle spasm , one must have the gene defect to have it(it is hereditary ) but the condition is initiated by this drug. If the patient develops malignant hyperthermia the chance of his death is 90 to 95%

Slide18:

Diazepam = valium , it is also an anti-anxiety or sedative drug , leads to addiction. It is also widely used as anti-convulsing drug

Slide19:

These drugs have analgesic effect along with the muscle relaxation

Anti-inflammatory drugs have no muscle relaxation effect but good analgesic effects

Could lead to addiction especially carisoprodol.