



Round : Anesthesia.....

Group no : A4.....

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Muscle relaxants

- There are drugs that reduce muscle contractility by blocking the transmission of nerve impulses or by decreasing the excitability of motor end plate » and result in relaxation of the muscle
- **Classification** » 1. Centrally acting (spasmolytic) » for stroke patients 2. Peripherally acting, which are further classified into » A. Depolarizing B. Non-depolarizing
- **Physiology of neuromuscular junction** » nerve impulse that reaches nerve terminal results in exocytosis of acetylcholine from its vesicles which then binds to nicotinic/cholinergic receptors of the muscle which causes its depolarization resulting in release of calcium from sarcoplasmic reticulum resulting in contraction
- The most important step in contraction cascade » binding of acetylcholine to its receptors
- **Mechanism of relaxation** » inside the synaptic cleft there's an enzyme acetylcholine esterase its function is to breakdown acetylcholine which results in repolarization of the muscle, calcium will return to its storage in sarcoplasmic reticulum which will lead to relaxation of the muscle
- The most important step in relaxation cascade » breakdown of acetylcholine by acetylcholinesterase
- **Depolarizing muscle relaxant** » agonist (succinylcholine » 2 acetylcholine molecules connected to each other) » binds to nicotinic/cholinergic receptors » depolarization of the muscle but acetylcholine esterase enzyme doesn't break it down » depolarization without repolarization » ends with muscle fatigue » muscle relaxation
- Which one of them has an **antidote**? Non-depolarizing » by increasing the concentration of acetylcholine which will reverse its action
- Inverse relationship between onset and duration of action » succinylcholine has rapid onset of action because its affinity to receptors is much higher and it has shorter duration of action of all muscle relaxants
- **Non-depolarizing muscle relaxant** » competitive antagonist » competes with acetylcholine on binding to nicotinic receptors » it blocks nerve impulse preventing depolarization of the muscle
- Factor determining which one of the 2 competitive will bind to the receptor » concentration gradient » the one with the higher concentration will bind
- **Pharmacodynamics of non-depolarizing** » hydrophilic agent (water soluble) » route of administration is IV only .. What is its effect on CNS? Zero because it doesn't cross the blood brain barrier .. effect on cardiac and smooth muscles is zero
- Most rapid onset among non depolarizing » rocuronium

- Do all skeletal muscles have the same response to muscle relaxant? No some of them are sensitive others are resistant; determinant factor is amount of receptors .. Small muscle with little neuromuscular junctions » it's sensitive which means it requires low dose .. Big muscle with large number of junctions is resistant which requires high dose
- Small muscles of the face and eyes » most sensitive muscles » they're the first muscles to be paralyzed, last muscles to recover from relaxation .. diaphragm » most resistant muscle, last muscle to be paralyzed, first muscle to recover from relaxation
- Interactions of nondepolarizing » 1. Halogenated agents » potentiation 2. Calcium channel blocker (nifedipine, diltiazem, verapamil) » potentiation 3. Antibiotics » potentiation (it binds to calcium and prevents exocytosis of acetylcholine from its vesicles) 4. Choline-esterase inhibitor » antagonization
- Classification of nondepolarizing (according to duration of action) » short, intermediate, long acting
- Short acting » Mivacurium » its metabolism by plasma cholinesterase (pseudo cholinesterase)
- Intermediate acting » Atracurium, Cisatracurium » Hoffman elimination » non enzymatic breakdown of the drug in normal pH & temperature .. Rocuronium, Vecuronium » hepatic elimination
- Breakdown of Atracurium results in laudanosine » crosses blood brain barrier and provokes seizure, it's metabolized in liver so in healthy people it doesn't provoke seizure but in people with liver impairment
- Atracurium is a potent histamine release » on skin (rash, itching, hives, redness), on RS (bronchospasm, wheezing, cyanosis, increase bronchial secretions), on CVS (tachycardia, hypotension, anaphylaxis)
- Cis-atracurium is developed version of atracurium » it doesn't have side effects of atracurium
- Long acting » Pancuronium, Picupurium » they rely on renal elimination (do not undergo metabolism they're excreted as they are by kidneys)
- What is the contraindicated drug to someone with renal impairment » pancuronium
- What is the drug of choice to patient with liver cirrhosis » cis-atracurium because it has shorter duration of action, you can use pancuronium .. not mivacurium because plasma cholinesterase is synthesized in liver
- Reversal of non depolarizing » Cholinesterase inhibitor (neostigmine) with atropine (to prevent choline crisis)
- Termination of action of depolarizing » succinylcholine moves from neuromuscular junction to plasma, plasma cholinesterase will break it down

- Onset of action for succinylcholine » 30 sec - 1 min ... Duration of action for succinylcholine » 5 - 10 min
- If a patient lacks plasma cholinesterase enzyme » succinylcholine will collect in the plasma then because of concentration gradient it will move from plasma (high concentration) to neuromuscular junction (low concentration) to bind to receptors and provoking action, it will keep going back and forth between them
- In heterozygous mutation duration of action will extend to 30 min, if homozygous duration of action will extend to 8 hours ... net result » muscle paralysis most dangerously the diaphragm » respiratory apnea » succinylcholine apnea
- The management of succinylcholine apnea » supportive (mechanical ventilation), fresh frozen plasma (indirectly give enzyme) or genetic recombinant enzyme
- Side effects of succinylcholine » 1. Trigger malignant hyperthermia 2. Succinylcholine apnea 3. Increases serum potassium 0.5 4. Transient increase in intracranial, intraocular, intragastric pressures 5. Myalgia 6. Bradycardia (direct stimulation of muscarinic receptors of the heart)
- Risky groups that could develop hyperkalemia » 1. Unexplained in pediatrics 2. Renal failure 3. Massive tissue damage (sepsis, burn, trauma) 4. Patients taking digoxin and spironolactone