Skeletal Muscle Relaxant

- Agents that reduce the tension in muscles.
- are drugs that act peripherally at neuromuscular junction/ muscle fibre itself or centrally in the cerebrospinal axis to reduce muscle tone and/ or cause paralysis.

Types

1. *Peripherally acting muscle relaxants*
2. *Centrally acting muscle relaxants*

Peripherally acting Muscle Relaxant

- block the transmission of impulses from motor nerves to skeletal muscle fibers at NMJ thus reducing motor activity.
- Used to relax voluntary muscles during surgery and are only used as an adjunct to anesthesia.

Peripherally acting Muscle Relaxant

1. Neuromuscular blocking agents

A. Nondepolarizing (Competitive) blockers

Long acting: d-Tubocurarine, Pancuronium, Doxacurium, Pipecuronium

Intermediate acting: Vecuronium, Atracurium, Cisatracurium, Rocuronium, Rapacuronium

Short acting: Mivacurium

B. Depolarizing blockers:

Succinylcholine (SCh, Suxamethonium), Decamethonium

2. Directly acting agents

Dantrolene sodium

Quinine

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Neuromuscular blocking agent

- These drugs block cholinergic (Acetylcholine) transmission between motor nerve endings and the nicotinic receptors on the neuromuscular end plate of skeletal muscle.

Types

A. *Non-depolarizing (Competitive) blockers*
B. *Depolarizing blockers*

- All neuromuscular blockers are quaternary ammonium compounds structurally similar to acetylcholine (ACh).

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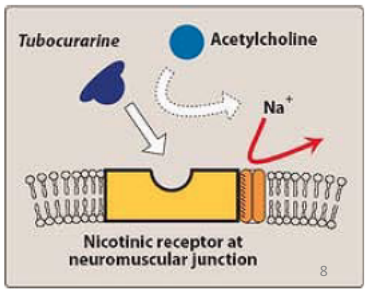
Non depolarizing blockers

- Reversible competitive ACh receptor antagonist.
- Low dose: Interact with the nicotinic receptors to prevent the binding of acetylcholine → thus prevent depolarization of the muscle cell membrane and inhibit muscular contraction.
- Anticholinesterase drugs reverse the effect these agents.
- High dose: block the ion channels; reduces the ability of anticholinesterase to reverse the action of these agents



d- Tubocurarine

Adverse effect

- Induce histamine release → cause bronchospasm, hypotension, salivary secretions

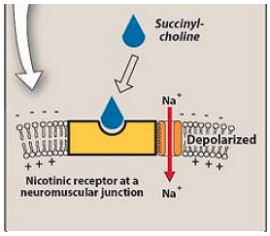
Dose: 0.2 - 0.5 mg/kg

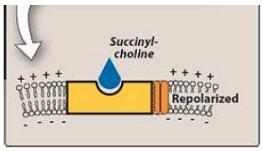
Depolarizing blockers (Succinylcholine)

- ACh agonist
- Succinylcholine is only depolarizing NMBD in clinical use.

MOA: block muscle contraction by depolarizing to such an extent that it desensitizes the receptor and it no longer initiate an action potential and cause muscle contraction.

Phase I (depolarizing phase) ***Phase II (desensitizing phase)***





Depolarizing blockers (Succinylcholine)

Adverse Effect: Bradycardia, increased intra ocular/ cranial pressure, hyperkalemia, histamine release

Uses: Endotracheal intubation, Laryngoscopy, Bronchoscopy Oesophagoscopy.

Contraindication: in persons with personal or familial history of malignant hyperthermia, skeletal muscle myopathies, and known hypersensitivity to the drug.

Dantrolene

- **Dantrolene sodium** is a postsynaptic muscle relaxant that lessens excitation-contraction coupling in muscle cells. It achieves this by inhibiting Ca^{2+} ions release from sacroplasmic reticulum stores by antagonizing ryanodine receptors.
- It is the primary drug used for the treatment and prevention of malignant hyperthermia.
- Gastrointestinal effects include bad taste, decreased appetite, nausea, vomiting, abdominal cramps and diarrhea.
- C/I : Liver disease

Centrally acting muscle relaxants

- Reduce the skeletal muscle tone causing muscles to relax.
- Selective action in the cerebrospinal axis, without altering consciousness.
- Inhibits polysynaptic reflexes in CNS
- Used to relieve skeletal muscle spasms and can musculoskeletal pain.

Centrally acting muscle relaxants

Classification

1. Mephenesin group: Mephenesin, Carisoprodol, **Chlorzoxazone**, Chlormezanone, Methocarbamol
2. Benzodiazepines: diazepam
3. GABA derivative : Baclofen
4. Central α2 agonist: Tizanidine

Chlorzoxazone

- It acts on the spinal cord by depressing reflexes.
- Adverse effect: dizziness, lightheadedness, malaise, nausea, vomiting and liver dysfunction
- Contraindication: renal impairment, CNS depression

Diazepam

- It is the prototype of benzodiazepines (BZDs) which act in the brain on specific receptors enhancing GABAergic transmission.
- Uses: spinal injury, tetanus, anxiety and tension
- Adverse effect: Drowsiness, dizziness, fatigue, constipation, blurred vision or headache.
- Contraindication: myasthenia gravis, liver disease.

Baclofen

- Baclofen is a derivative of GABA, an inhibitory CNS transmitter.
- Inhibits reflex activity mainly in the spinal cord.
- Used to treat spasticity and also for the treatment of alcoholism.
- Adverse effect: drowsiness, mental confusion, weakness and ataxia.

Tizanidine

- central alpha-2-adrenergic receptor agonist and presumably reduce spasticity by increasing presynaptic inhibition of motor neurons.
- Uses: muscle spasms
- Adverse effect: dry mouth, drowsiness, night time insomnia, hallucinations.
- Dose: 2-4 mg TID/QID per day
- Contraindication
  - ✓ Abnormally Low Blood Pressure
  - ✓ Severe Liver Disease, Kidney Disease

Skeletal Muscle Relaxant

Centrally acting	*Peripherally acting*
1. Decrease muscle tone without reducing voluntary power	Cause muscle paralysis, voluntary movements lost
2. Selectively inhibit polysynaptic reflexes in CNS	Block neuromuscular transmission
3. Cause some CNS depression	No effect on CNS
4. Given orally, sometimes parenterally	Practically always given i.v.
5. Used in chronic spastic conditions, acute muscle spasms, tetanus	Used for short-term purposes (surgical operations)