Skeletal Muscle Relaxant:

– Given in GA to Provide Muscle Relaxation in surgery

They ↓ skeletal Muscle tone by peripheral or central Action at NMJ.

Motor nerve impulse
↓
Release of Ach
↓
Bind with Nm Receptor at NMJ
↓
Depolarization
↓
contraction
↓
Ach inactivated by cholinesterase
↓
Muscle Ready for fresh nerve Impulse

SMR

Centrally Acting (depress polysynaptic pathways in spinal cord/supraspinal site)

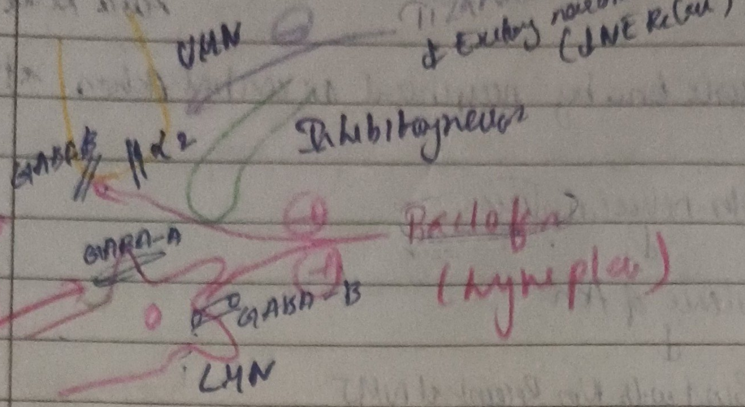
- Diazepam
- Methocarbamol
- Chlorzoxazone
- Baclofen

Peripherally Acting

- NM Blocking Agent
  - Depolarizing blocker
    - Succinyl choline
    - Decamethonium
  - Nondepolarizing blocker
    - T. D-Tubocurarine
    - Pancuronium
    - Doxacurium
    - } long Acting
    - Vecuronium
    - Rocuronium
    - Atracurium
    - } Intermediate Acting
  - Other
    - Botulinum Toxin A
- Directly Acting
  - Dantrolene
  - Quinine

Spasticity

Basics



Receptor:
GABA A → present on LMN only

When there is AP from cortex, there will be Release of Excitatory NT like glutamate or norepinephrine which will act on LMN, then Release Ach at NMJ → contract skeletal muscle

Both GABA A & B act on by Release Inhibitory neuron GABA release Releasing GABA into synaptic cleft

↓

this will Inhibit GABA-B Receptor on the UMN to stop Excitatory NT

& Also on LMN (GABA-B) cause hyperpolarized (↑Cl⁻ influx)

↓

& no conduction of AP → no contraction

These drugs ↑ GABA within synaptic cleft

Diazepam: They act in the brain on specific BZP (Benzodiazepines) Receptor enhancing GABAnergic transmission.

→ Muscle tone Reduced by supra spinal action.
→ given in spinal injury & tetanus.
→ combined form in Rheumatic disorder.

Baclofen: ↑ Cl⁻ conductance & ↓ exciting transmission. Act on GABA B Receptor. Produce → Muscle weakness, less sedation, → used in sclerosis

GABB - G protein coupled Receptor. hyperpolarize by ↑ K^+ channel

Tizanidine → α_2 Adenergic Agonist

Inhibit Release of excitatory AA in CNS

Polysynaptic Reflex Inhibited → ↓ Muscle tone

but Muscle strength remains same

Uses:

→ Acute Muscle spasms → Overstretching of Muscle, sprain, tearing of ligament or tendon, dislocation. combined with NSAIDs given.

→ Torticollis, backache → is painful spasm.

→ Spastic neurological disease → ↑ in Muscle tone conditions such as Hemiplegia, paraplegia, ALS, Cerebral palsy.

→ Tetanus → Diazepam. is infused IV.

Pharmacology:

NMB.

Depolarizing blocker

Unlike central skeletal Muscle Relaxants these drug interfere with NM Transmission do not affect CNS. ← Depolarizing / Non depolarizing.

MOA:

phase I block

I → depolarizing phase. → Ach Acts on NM Receptor on Skeletal Muscle cell membrane

phase II block

II → Desensitization. → Continuous exposure of drug to the Receptor → Receptor get desensitized do not respond to drug lead to Relaxation

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Succinylcholine:

→ It cause muscle fasciculation (Muscle twitch), soreness, changes BP & HR, ↑K+ → arrhythmias & many complications.

→ Sch is most commonly used in tracheal tube passing (As Muscle Relaxant)
cause,
Excellent Intubating condition.
Relaxed jaw
Vocal cords, immobile patient.
obtained within 1-1.5 min.

→ Avoided in children as lead to cardiac Arrhythmia can occur.

Competitive Blockers (Non depolarizing)

MOA: Curare is a mixture of Alkaloids & was used as an Arrow poison.

→ Among them, d-TC is most imp. which has Nm blocking Activity.

MOA → Ach is Agonist → Nm Receptor NMJ ⇌ d-TC Antagonist

→ They produce flaccid Paralysis.
Order of Muscle affected → eye muscle, neck, face, hand, feet finally Intercostal M. & diaphragm – so breathing stop.
But Recovers in Reverse order. 1st Resp Ms.

Blockers are Reversed by the use of Anticholinesterase (neostigmine)

1) Histamine Release:
d-Tc - Release them from mast cell.
→ Histamine contributes to hypotension, bronchospasm, ↑ Respiration.

2) CVS
→ ↓ B.P due to
- ganglionic blockage
histamine release
- ↓ Venous Return.

3. CNS → All NMJ blockers do not cross compound - do not cross BBB.

All NMJ are given IV

→ Pancuronium: ~5 times more potent than d-Tc
lower histamine Release.
longer duration of Action, need Reversal
so not used now a days.

→ Pipecuronium: Slow onset long Action.

→ Vecuronium: Shorter duration of Action due to
Rapid distribution.
commonly used as Muscle Relaxants for routine surgery
of intensive care units

→ Atracurium/ → Require elimination through Hofman elimination.
cisatracurium.

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Rocuronium: most Rapid onset.
Alternate of SCh for tracheal Intubation.
attained with 90sec.
duration of paralysis is dose dependent.

-used to facilitate mechanical ventilation.

Drug interaction

→ With non depolarizing blockers:

Ether has curimimetic effect on skeletal Muscle → enhance the effect of non depolarizing blockers.

→ Non depolarizing blocker & Antibiotics.

Aminoglycoside Inhibit the Release of Ach from motor nerve & potentiate effect of non depolarizing blockers → Hence ↓ Amount is therapeutic