# Skeletal Muscle Relaxants

SMR

Centrally acting → only local spasms

peripherally acting → block all action of muscle → Complete relaxation

- when spasms → centrally acting

Central MR

MOA → by CNS depression.

① $GABA_A$ ↑ ⇒ diazepam.
$GABA_B$ ↑ ⇒ Baclofen.

- GABA → Inhibitory NT.
- GAB ↑ → CNS depression

② $\alpha_2$ - Brain receptors.
↓
agonist
↓
Tizanidine.
↓
muscle relaxation.

③ polysynaptic reflex ⊖.
↓
Thiocholchicoside.
Chlorzoxazone.

For muscle spasms!

peripheral MR

centrally acting

NM blocker

$Ca^{2+}$ Ryanodine R

Dantrolene → directly acting MR
↓
Block Ryanodine receptors
↓
no $Ca^{2+}$ release from SR
↓
no contraction
↓
muscle relaxation

Dantrolene.
↓
Drug of choice.
↓
- malignant hyperthermia
- Neuroleptic malignant Syndrome.

malignant hyperthermia:

Reynaudin ruptors are overactive
↓
$Ca^{2+}$ release ↑↑↑.

Nm Blockers

Nm ⊖ → Competitive Non-depolarizing

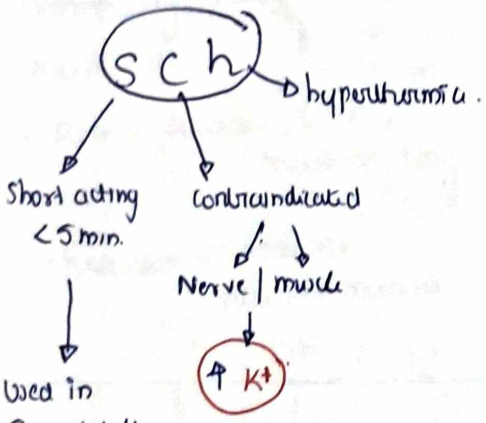
Nm overstimulation → depolarizing

Nm → needs optimal stimulation, Not high nor low

## Non-depolarizing

- Succinyl choline.

like choline, but long ie, depolarize / overstimulate




Succiny choline.

↓ pseudocholinesterase.

metabolism.

if a person has atypical pseudocholinesterase.

↓

Prolonged Apnea

Contraindicated in

- Nerve / muscle injury. (e.g. crush injury)

↓

will lead to

severe hyperKalemia.

Sch → cause hyperthermia.

Dantrolene → treat hyperthermia

Sch.

↓

Nm - overstimulation.

↓ initial contraction.

→ fasciculation

↓ some fibres break.

↓

post operative muscle pain.

- post operative muscle pain → Sch.
- post operative muscle rigidity
- → fentanyl.

Why do we need to contract first? can't we just not depolarize?

↓

if we don't depolarize / overstimulate just → there won't be muscle contraction. ✗

↓

there won't be post op muscle pain

So we use, Non-depolarizing muscle relaxants.

NDMR

↓

Tubocurarine.

They don't cause post op muscle pain

- Disadvantage.

lot of.

- Cause Histamine release

↓

vasodilation — BP ↓

patient can die.

So we need.

NDMR that doesn't release Histamine

low Histamine production

→ CURIUM

Atracurium.

Cisatracurium.

Mivacurium.

(Short acting (30 min))

No histamine.

CURONIUM

Pancuronium.

Pipecuronium.

Rapacuronium

↓

DOC in asthma patients (as histamine can cause Bronchoconstriction)

Atracurium

Cis-atracurium

↓

Hoffman's elimination

- spontaneous - non enzymatic.
molecular rearrangement to make a drug inactive.
↓
Hoffmann's elimination.

- doesn't require liver / kidney for elimination

Atra / Cis ] DOC in kidney & liver failure patients.

Reversal of action of MR

MR
- depolarizing (Sch. short)
- Non-dep. (long acting.)

MR → during surgery.

- but we need to reverse after surgery!
- For short acting, Sch, mevacurium → don't need.
- Others → need

Reversal agent.
- Neostigmine.
- Suggamadex.

Neostigmine.
⊖ AchE.
↓
Ach ↑
- Nm ⊕ (☺)
- $m_1$ $m_2$ $m_3$ Side effects. (☹)

give atropine.

Atra
no Histamine at all

- Hoffman.
  - 80%
  - 20%
- 20% - liver.
- Laudanosine.
- Seizures can occur.

Cis-atra
negligible.

100% hoffman

No seizures.

Suggamadex.
- SRBA → Selective relaxant binding agent.

→ they bind to MR & ⊖ action
→ advantage: no cholinergic side effects
→ Dis → allergy

# Skeletal Muscle Relaxant

## Succinyl Choline.

- depolarizing blocker, ~~Competetive~~ Noncompetitive.

MOA

peak - 3 min.
duration < 5 min.

### phase I depolarizing block

Succinyl choline.
↓
Binds to Nicotinic receptors at NMJ
↓
mimics Ach
↓
Opens Ion channels
$Na^+$ - influx
$K^+$ - efflux
↓
Sustained depolarization of membrane.
↓
Initial fasciculation
↓
Anti-cholinesterase worsen phase 1 block.

### P. Baxe-II Block – Desensitization block

prolonged Succinyl cholxe binding to receptor.
↓
Continuous stimulation of receptor
↓
eventual repolarization (since $Na^+$ channels close eventually)
↓
receptor become desensitized.
↓
receptor is unable to respond.
↓
Ion channel remain closed
↓
Flaccid paralysis.
↓
Anticholinesterase can reverse phase 2 block.

probable diagnosis →

Succinyl choline apnea due to
Abnormal pseudocholinesterase.

↓

prolonged phase II block.

↓

prolonged muscle paralysis
and apnea.

## Line of treatment

- Discontinuation of Succinylcholine.
- Mechanical ventilation
- Antidote → not that effective.

↓

Neostigmine.
Edrophonium

alternatives

— Rocuronium
— Vecuronium.

## Atracurium

- Unique dual metabolism
  - short duration of action

(1) Hofmann elimination.

- Spontaneous non-enzymatic rearrangement.

(2) plasma cholinesterase.

DOA → not altered in hepatic / renal disease.

preferred

- liver } disease.
- renal }
- Elderly
- Neonates.

optional

- Laudanosine - metabolite

↓

CNS toxicity

## Dantrolene in malignant hyperthermia

- Dantrole – chemically different. Effect resembles to centrally acting agents.

MOA

- Block Ryanodine receptors.
- depolarization is uncoupled from contraction.

## pharmacokinetics

- Oral / IV
- Good GIT absorption.
- Cross CNS
- metabolism - liver
- Excretion - urine.
- $T_{1/2}$ - 10 hours.

## Uses

- malignant hyperthermia → muscle rigidity, ↑ Body temp, tachycardia, metabolic acidosis,
- Spasticity in UMN disorders.
- hemiplegia
- paraplegia.

## ADR

- muscle weakness.
- sedation.
- malaise.

## d-Tubocurarine

It has very prominent

→ Histamine release

→ Ganglion block

→ Cardiovascular side effects.

not used now.

## → pancuronium

is a non-depolarizing muscle relaxant that blocks action of acetylcholine at NMJ leading to muscle paralysis.

- effect can be reversed by AchE ⊖