# Skeletal muscle relaxants

drugs that act peripherally at NMJ/ muscle fiber itself or centrally in the cerebrospinal axis to ↓ muscle tone and/or cause paralysis

- occur from interruption of function at several sites ⇓
  - The motor end plate
  - CNS
  - contractile apparatus

## Neuromascular blocking drugs IV

peripherally

- interfere with cholinergic transmission at neuromascular end plate.
- highly polar
- inactive when administered by mouth.
- Therapubric uses ⇓
  - provide muscle relaxation during surgery (adjuvant to anasthesia)
  - they relax vocal cords & facilitate tracheal intubation
  - Intensive care units (ICU) they may paralyse muscle required for breathing, mechanical ventilation

### Competitive (non depolarising blocking drugs)

slower onset of action than suxamethonium

- constitute the majority of clinically relevant neuromascular blocks.
- competitive antagonist of Ach., prevent depolarisation.

↳ result ⇒ Flaccid Paralysis.

#### Isoquinoline derivatives

→ all except cisatracurium) ⇒ associated with His release.

Flushing ← release → bronchospasm, hypotension, brachycardia

- Atracurium
  - start → intermediate acting (30-40) min
  - undergo → non-enzymatic metabolism independent on liver & kidney.
    - ↳ used in patient with hepatic or renal failure.
  - contraindicated in epilepsy, MG, bronchial asthma
- Tubocurarine
- Cisatracurium
- Mivacurium short acting (15-30) min.

#### Steroid derivatives

not associated with His release.

- Pancuronium long acting (60-120) min.
- Vecuronium
- Pipecuronium
- Rocuronium.

used in patients receiving long-term mechanical ventilation in ICU.

# Reversal of non-depolarizing blocking drugs

↓ cholinestrase inhibitors ⇒ e.g.: Neostigmine IV

4 minutes, lasts 30 minutes

### Depolarising blocking drugs

- Succinyl choline (Suxamethonium)
  - the only drug used clinically
  - depolarising the end plate, similar to Ach except it produces a longer effect.
    - most rapid onset ⇒ 30 seconds
    - shortest duration of action ⇒ 5-10 minutes
  - is destroyed by plasma cholinestrase.
  - repeated injection → bradycardia / ventricular arrest

↑prevented by atropine

#### Phase I (Depolarising phase)

It reacts with nicotinic receptor & causes depolarisation of end plate.

- This in turn spreads & depolarises adjacent membranes causing generalised disorganised contractions of muscle motor unit (transient muscle fasciculations)
  - It is not metabolised effectively at synapses
    - ↳ the membrane remains depolarised & unresponsive to additional impulses.

#### Phase II (Desensitising phase)

with continued exposure to suxamethonium, initial end plate depolarisation ↓ & membrane becomes repolarised.

- cause flaccid paralysis → cardiac arrest

# side effects ⇒ • Hyperkalemia • Muscle pain • apnea
• should be given after anasthesia.

## Baclofen

- It acts as GABA agonist at $GABA_BR$
- activation of R in brain ⇒ hyperpolarisation

↓ Ca influx → ↓ reduce release of excitatory neurotransmitters in brain & spinal cord.

this serves a presynaptic inhibitory function.

it does not ↓ general muscle strength as much as ↓ tone

rapidly/completely absorbed after oral use bt ⇒ 3-4 hours

dose ⇒ 15 mg daily. ↑ to 100 mg

## Dantrolene.

by interfering with excitation-contraction coupling in muscle fibers.

- Binds to ryanodine receptor & ↓ intracellular [Ca]

$t_{1/2}$ ⇒ 8 hrs

treatment begun ⇒ 25 mg daily ↑ ⇒ 100 mg 4 times daily.

# Major side effects ⇒ generalized muscle weakness & sedation.

# Spasmolytics

centrally. ↓ spasticity

how

- ↑ level of inhibition
- ↓ level of excitation.
- interfering directly with skeletal muscle excitation contraction coupling.

disorder of motor system especially CNS, certain muscles are continuously contracted.

- cerebral palsy
- multiple sclerosis
- stroke

## Diazepam.

Benzodiazepines facilitate action of γ-aminobutyric acid (GABA) in CNS

- it can be used in patient with muscle spasm of any origin including local muscle trauma.
- It produces sedation in most patients at doses required to ↓ muscle tone.

## Tizanidine.

newly introduced $\alpha_2$-adrenoceptor agonist.

- indicates for spasticity ↓BP associated with multiple sclerosis or spinal cord injury.

Drugs used for acute local muscle spasm.

- Orphenadrin
- Metaxalone
- Cyclobenzabine.

# NSAIDs

## Weak or no clinically useful anti-inflammatory action.

- **Paracetamol** (Acetaminophen) (Panadol)
  - 0.5-1 g / 3/d
  - max. → 4 g
  - ← antipyretic, analgesic, mild to moderate pain
  - ← child with viral infection..
  - ← patient with peptic ulcer

## Mild to moderate anti-inflammatory action.

- **Aspirin** (Acebelylsalicalic acid)
  - 325-650 mg 3/d
  - ↳ analgesic & antipyretic.
  - 4-6 g/d in 3 devided doses.
  - ↳ anti-inflammatory
  - irreversible.
  - 80-100 mg ↳ prophylactically → TIA / stroke
- **Propionic acid derivatives** — less GI effects than aspirin.
  - Ibuprofen
  - Ketoprofen
  - Naproxen
- **Fenamates** (mefenamic acid) (ponstan)

## Marked anti-inflammatory action.

- **Arylacetic acid derivatives** → **Diclofenac** (voltaren)
- **Acetic acid derivatives**
  - **Indomethacin** (indocin) — IV/within 72 hrs ⇒ closes PDA.
  - **Sulindac**.
    - pro-drug
    - less side effect
- **Oxicam derivatives** — once daily
  - **Piroxicam** (Feldene) — more GI side effects
  - **Meloxicam** (Mobic)
    - preferential Cox-2 selectivity
    - less GI side effects.
- **Selective Cox-2 inhibitors (coxib)** — once daily
  - ↓ $PGE_2$ / PGI2
  - Rofecoxib *
  - Celecoxib
  - Valdecoxib *
  - Etoricoxib.
  - → was withdrawn from market.
  - *sulphonamide hypersensitivity

~~Sulindac~~.

Diclofenac > Naproxen / Indomethacin > aspirin > Sulindac.