

SUXA

Succinylcholine (or)
Suxamethonium

- Short acting Depolarizing m/s relaxant
- Structurally contains 2 molecules of Ach.
(Dicholine ester of Succinic acid)

PRESENTATION: As a clear aqueous soln containing 50mg/ml of Suxamethonium chloride.
⇒ Preparation s/lr stored @ 4°C.
⇒ Multidose 10ml vial containing 50mg/ml.

MOA: -

Ach + Ach

↓
(Sch) + Nicotinic (R)

↓
Persistent Depolarization of end plates
↓

This mechanism results in:

- 1) Desensitization of nAChR
- 2) Inactivation of voltage gated Na^+ channels @ NM Jn.
- 3) ↑ K^+ permeability in the surrounding membrane

↓
Produce slightly prolonged action when compared to ACh b'coz its action is terminated only by diffusion out of motor end plate & subsequent metabolism by pseudocholinesterase in the plasma.

(unlike ACh which is rapidly degraded by depolarization & subsequent m/s paralysis)

↓
Sustained depolarization causes all ACh receptors to be used up, resulting in failure of depolarization & subsequent m/s relaxation. (m/s paralysis)

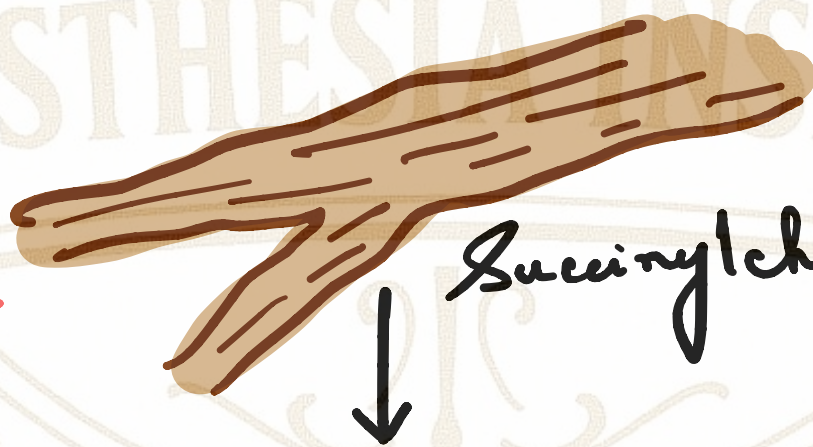
* As the depolarization is not a co-ordinated contraction, it produces FASCICULATIONS

PHARMACOKINETICS:

⇒ The ED₉₅ dose is 0.51 to 0.63 mg/kg
↓

[The dose causing on avg. 95% suppression.
of NM response]

- ⇒ ONSET: 60 Secs
- ⇒ Duration of action: 9-13 min ($? \uparrow$ min)
- ⇒ Elimination ($t_{1/2}$): 47 Secs
- ⇒ Drug is hydrolysed by plasma cholinesterase into succinic acid & choline.
- ⇒ 80% of administered dose is hydrolysed before it reaches NMJ.
- ⇒ Excretion 2-10% - excreted unchanged in Urine.



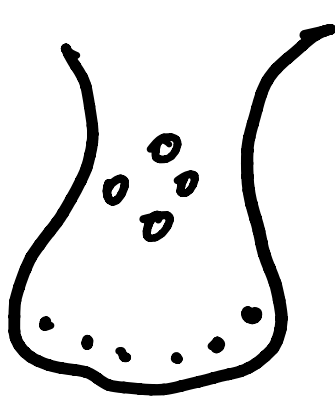
Succinylcholine.

Blood vessel

Acted rapidly upon
by enzyme PCE
Present in plasma.

Succinylmonocholine.

($1/20^{\text{th}}$ to $1/80^{\text{th}}$ potency of
parent compound)



Succinic acid + Choline.
(Inactive Metabolites)

* There is no pseudocholinesterase @ NMJ.

Termination of action occurs by diffusion of drug back into circulation.

PHARMACODYNAMICS:

CVS

- drug stimulates cholinergic autonomic (R) on both sympathetic & Parasympathetic & muscarinic (R) in sinus node of heart.

EFFECT:

Sinus Bradycardia: m/c in children & pte receiving 2nd dose of SUXA (as the hydrolysis products of SUXA may sensitize the heart to a subsequent dose)

Nodal (Junctional) Rhythm:

Mech: Greater stimulation of muscarinic (R) in the sinus node, thus suppressing the sinus

Mechanism & allowing the emergence of AV node as a pacemaker.

Ventricular Dysrhythmia: ↓ threshold of ventricle to catecholamine induced dysrhythmias

RS: Apnoea occurs after subsequent m/s relaxation
Hyperkalemia

⇒ ↑ plasma K^+ levels by approx. 0.5 mEq/dl
dlt sustained opening of receptor ion channels
↑ IOP dlt generalized depolarisation

⇒ ↑ in IOP develops within 1 min, peaks @ 2-4 min & subsides by 6 min.

Action on Eye:- Contraction of tonic myofibrils & transient dilatation of choroidal blood vessels.

↑ Intra Gastric Pressure - due to fasciculations of abdominal
↑ by 7-12 cm H₂O of skl m/s & vagomimetic action of Sch.
- Salivation & Gastric secretions ↑

↑ ICP - can be prevented by pre-Rx with NDMR.
dlt ↑ cerebral activity dlt stimulation of m/s stretch

Myalgia - Incidence 0.2 to 89%
dlt unsynchronized skl m/s contractions dlt generalized depolarisation. Myoglobinuria. results dlt m/s

Masseter m/e - ↑ in Masseter tone of up to 500g lasting 1 to 2 mins
Rigidity
dlt exaggerated response of Succa @ NMJ.

Malignant Hyperthermia.. Esp. in children & myopathies & squint

Anaphylaxis:- 0.06%

Mech: Succa cross links with IgE
↓
Degranulation & release of histamine.
neutrophil chemotactic factor &
platelet activating factor occur.
↓
Cardiovascular collapse
Bronchospasm
Skin reactions.

USES & DOSES:

⇒ Endotracheal Intubation: 1 - 1.5 mg/kg
(RSI)

⇒ Treatment of laryngospasm: (0.25 - 0.5 mg/kg)
Dose reqd to Rx laryngospasm: - 0.1 - 0.3 mg/kg.

⇒ Used in ECT to minimize the S.E of violent m/c contractions (0.5 mg/kg)

IV :- $0.5 - 2 \text{ mg/kg}$

IM :- 2.5 mg/kg

Infants req. higher dose (2 mg/kg) due to their greater body water.

CONTRAINDICATIONS:

- 1) Open globe injury
- 2) Burns pt. after first 24 hrs
- 3) Hyper K^+
- 4) Congenital Myopathies
- 5) Spinal cord Injury
- 6) Raised ICP / IOP
- 7) Malignant hyperthermia.

SPECIAL POINTS:

- ① The incidence of m/c pain can be ↓ by pre-treatment with:

- low (0.2 mg/kg) of SuxA
- Small dose of NDMR
- Diazepam
- Dantrolene
- Aspirin
- Vit C.

② SuxA is photosensitive & hence comes in amber coloured vial. On long duration exposure to light, it can breakdown to Ach molecule & this might produce severe bradycardia when injected.

③ **FASCICULATIONS:-** are unco-ordinated m/c twitching that occur aft action of Sch on pre-synaptic Ach receptors.

can be $\ominus$ by using subparalyzing dose of NDMR (Atrac. 0.03 mg/kg , Vec 0.007 mg/kg , Pancuronium 0.01 mg/kg ,] given 3 mins before SuxA.

PHASE I BLOCK

a) End Plate Depolarization

Presynaptic ACh receptors (NICOTINIC)

Action of Sch on presynaptic (R)

Depolarization of Nerve terminal

Backward propagation of action potential to all branches of that motor unit

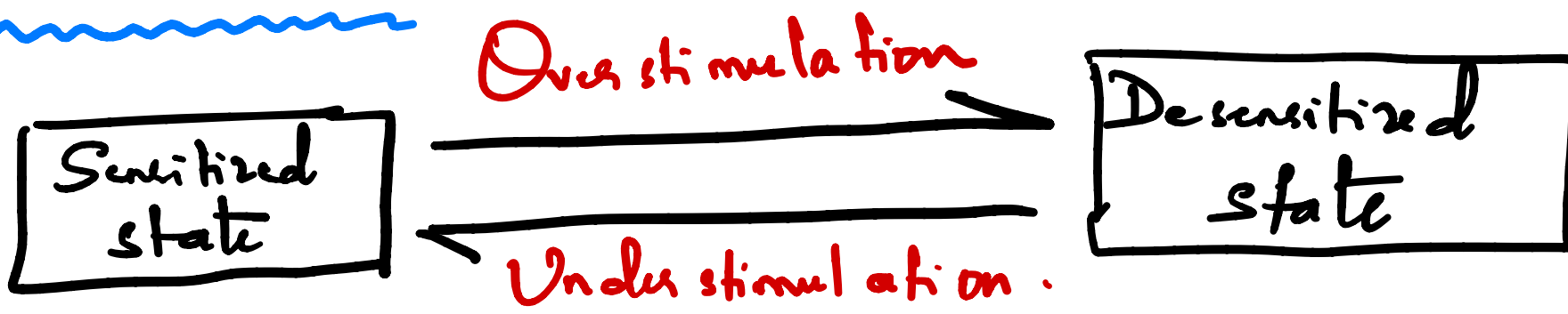
m/s pain in post-op

Unco-ordinated m/s twitching

Increased ICP

↑ Intra-gastric pressure.

b) Desensitization:



Clinical Significance: Total no. of channels available for Impulse transmission is ↓ if more receptors remain desensitized.

⇒ Patients become more sensitive to NMJ after Sch use.

PHASE II BLOCK

Repeated dose, Infusion. Single bolus dose (5-7 mg/kg)

↓
Duration of block is prolonged.

↓
Phase II Block.

Mechanism:

- ① Repeated end plate depolarization causing ionic imbalance of NMJ & altered membrane fn.
 - ② Desensitization d/t cont. presence of agonist @ the site of action.
- Pts with atypical plasma cholinesterase may develop

Phase II Block even τ usual dose of succA.

Clinical Significance :-

In c/o phase II Block; one must ventilate the pt till spontaneous recovery occurs.

→ Reversal with anticholinesterase - not seqd.

Characteristics of Phase I & Phase II Block

Phase I

1) Well sustained tetanus during stimulation @ 50-100 Hz

2) Absence of post tetanic facilitation.

3) TOF ≥ 0.7

4) Potentiation of anti-cholinesterase

Phase II

1) Poorly sustained tetanus

2) Post tetanic facilitation.

3) TOF < 0.3

4) Tachyphylaxis

Enzyme Pseudocholinesterase

- Pseudocholinesterase is a lipoprotein synthesised in the liver.

Reduced Sch Metabolism.



CAUSES



low conc. of
Pseudochoolinesterase
in the blood.



Conditions also.

Liver df
Pregnancy
Renal failure
Heart failure
Hypoproteinemia.
Burns
Thyrotoxicosis
Carcinomatosis

low activity of
Pseudochoolinesterase.



Presence of ATypical
Pseudochoolinesterase



Drugs that depress
Pseudochoolinesterase

Bambuterol

OCPs

Lithium

Cytotoxic drugs

Lignocaine

Neostigmine

Metoprolamide.

Pseudochoolinesterase for is measured in terms of
DIBUCAINE NUMBER.

DIBUCAINE NUMBER

- Congenital pseudocholinesterase deficiency or % of $\ominus$ of pseudocholinesterase is k/a Dibucaine no.
- Directly proportional to Pseudo cholinesterase fr.
- Dibucaine Number is the % inhibition of hydrolysis of benzyl choline by dibucaine added to the plasma sample
- $\textcircled{N} - > 70$: This means $\textcircled{N}$ pseudocholinesterase is $\geq 70\%$ $\ominus$ by dibucaine.
- 50-60 - Individual is heterozygous for atypical pseudocholinesterase
- 20-30 - Homozygous " "

Fluoride Number

- Number derived from % $\ominus$ of hydrolysis of benzyl choline by fluoride.
- $\geq 60 - \textcircled{N}$

→ < 36 - Homozygous for atyp. PCES.

Scoline Apnoea

→ Apnoea > 20 min after Suxa 1-1.5 mg/kg administration d/t deficiency of Pseudo-cholinesterase. — Qualitative or Quantitative

→ Quantitative

↓
Physiological

Pregnancy & women
on OCPs

↓
Pathological

Liver d/t
Hypoproteinaemia.
Malignancies
Aft^r Radiotherapy.

Drugs that compete for Pseudocholine esterase

IV Induction - Propofol

LA - Ester like Cocaine, Procaine

Antiarrhythmic :- Procainamide

Non-Depolariser :- Mivacurium

Anti-HA :- Σ mol
of compounds - Σ cothiophate
Other drugs:- Hexafluorine.

Hysteresis

Soon after IV administration of NDMR, the plasma concentration of the drug will be much higher than its concentration @ NM Junction.

→ However, subsequently with passage of time conc. @ NM Junction falls below the plasma concentration.

This is k/a Hysteresis.