MUSCLE RELAXANTS AND ANABOLIC STEROIDS

MUSCLE RELAXANTS

Skeletal muscle relaxants are drugs that act to reduce muscle tones/or cause paralysis, they act peripherally at the neuromuscular junction or on muscle fibre itself or centrally in the cerebro spinal axis to reduce muscle tone and/or cause paralysis.

PHERIPHERALLY ACTING MUSCLE RELAXANTS

There are two types:Non depolarizing and depolarizing blockers

Non-depolarizing is divided into3;-(l) long acting. (2) intermediate and (3) short acting

1. NEUROMUSCULAR BLOCKING AGENT:-

(A) Non-depolarizing (competitive) Blockers.

(1) Long actinge.g. d-Tubocurarine, Gallamine triethiodide, Pancuronium, Doxacurium, Pipecuronium.

(2) Intermediate-Acting :- e.g. Vecuronium, Atracurium, Rocuronium

(3) Short-Acting:- e.g. Mivacurium

(B) Depolarizing Blockers

Snccinylcholine (Suxamethonium), Decameth Onium (c-10).

II DIRECTLY ACTING AGENTS:-

Dantrolene Sodium

Quinine

Note: Aminoghycosides, tetracycline, polypeptide antibiotics interfere with neuromuscular transmission at high doses, but are not employed as muscle relaxants.

Several drugs employed clinically as neuromuscular drugs have as their major action, the interruption of transmission on of the nerve impulse at the skeletal neuromuscular function.

On the basis of the primary mechanism by which they produce these effects, they are classified either as competitive non-depolarizing or depolarizing.

NON-DEPOLARIZING NEUROMUSCULAR

The cellular locus and mechanism of action of D-Tubocurarine and Dimethy tubo curarine and Gallamine is explained by the combination of the drug with cholmoceptive sites at the post functional membrane and thereby blocks the transmitter action of acetylcholine, thus leading to flaccidity or paralysis of the muscle.

Depolarizing agents**:** e.g. Succinylchiline and Decamethonium:- Prior to causing paralysis the depolarizing agent evoke transient muscular fasciculation observed especially over the chest and abdomen.

Relaxation occurs within one minute after a single intravenous dose of 10-30mg of sucking/choline.

Q: Discuss briefly D-TC and School

1. d-Tubocurarine:- Because of its prominent histamine releasing, ganglion blocking and cardio vascular actions as well as long duration and need for pharmacological reversal, d-TC practically is not used now.
2. Succiny/choline; Despite its propensity to cause muscle fasciculation and soreness, changes in BP and HR, arrhythmias, histamine release and K+ efflux from muscle, SCh is the most commonly used muscle relaxant for passing tactual tube. It induces repaid, complete and predictable paralysis with spontaneous recovery in 5 minutes. Excellent incubating condition via relaxed jaw, vocal cord apart and immobile with no diaphragmatic movement is obtained within 1-1.5 minutes. Occasionally, it is used by continuous I.V. infusion for producing controlled muscle relaxation of longer duration.
3. Vecuronium: A close congener of pamcuronium with a shorter duration of action due to rapid distribution and metabolism. Recovery is generally spontaneous not needing neostigmine reversal unless repeated doses are given. Cardiovascular stability is still better due to lack of histamine releasing and gangionic action; tachycardia sometimes occurs.
4. Mivacurium:- This is the shortest acting curyzchtine blocker does not need reversal. Transient dose and speed of injection related cutaneous flushing can occur due to histamine release. Fall in BP or change in HR is rare. It is metabolized/orily by plasma cholinesterase: prolonged paralysis can occur in pseudochrolinest erase deficiency.

USES

1. The most important use of neuromuscular blocker s.h as adjuvant to general anesthesia; adequate muscle relaxation can be achieved at lighter planes. Many surgical procedures are performed more safely and rapidly by employing muscle relaxants. They also reduce

reflux muscle contraction in the region undergoing surgery, and assist maintenance of controlled ventilation during anesthesia. They are particularly helpful in abdominal and thoracic surgery, intubations and endoscopies, orthopedic manipulations etc. succury/choline is employed for brief procedures e.g. endotracheal intubations, laryngoscope, bronchoscope, esophagoscopy, reduction of fractures and dislocations etc. for ocular surgery competitive blockers are preferred as they paralyze extraocular muscles at doses which have little effects in larger muscles.

Other factors which should be considered in selecting the relaxant are – onset of action, duration of blockade required, cardiovascular effects of the drug as well as patients hepatic, renal and haemodynamic status.

2. Convulsions and trauma from electro convulsive therapy can be avoided by the use of muscle relaxants without decreasing the therapeutic benefit. Sch is most commonly used for this purpose.
3. Server cases of tetanus and status epilepticus which are not controlled by diazepam or other drugs may be paralyzed by a neuromuscular blocker (repeated doses of a competitive blocker) and maintained on intermittent positive pressine respiration.

DIRECTLY ACTING MUSCLE RELAXANTS

1. Dantrolene: This MR is chemically and pharmacologically entirely different from neuromuscular blockers. It effect superficially resembles that of centrally acting muscle relaxants. It does not affect neuromuscular transmission or MAP but uncouples contraction from depolarization of the muscle membrane; depolarization friggened release of Ca^{2+} from sarcoplasmic reticulum is reduced. Fast contracting "Twitch" muscles are affected more than slow contracting "antigravity" muscles.
2. Quinine: - It increases the refractory period and decreases the excitability of motor end-plates. Thus responses to repetitive nerve stimulation are reduced. It decreases muscle tone in myotonia congent and taken at bed time (200-300mg). it may abolish nocturnal leg cramps in some patients.

CENTRALLY ACTING MUSCLE RELAXANT

There are drugs which reduces skeletal muscle tone by a selective action in the cerebrospinal axis without altering consciousness. They selectively depress spinal and supraspinal

polysynaptic reflexes involved in the regulation of muscle tone without significantly affecting monosynaptically mediate stretch reflex. All centrally acting muscle relaxants do have some sedative property. They have no effect on neuromuscular transmission and on muscle fibres, but reduce upper motor neurone splasticity hyperreflexia.

CLASSFICATION

i. Mephenesin group:- mephenesin, Carisoprodol
ii. Benozodiazepines:- Diazepam and other
iii. GABA derivation:- Baclofen.

i. Mephenesin:- It was the 1^{st} drug found to cause muscle relaxant in animals without producing unconsciousness and was called internuncial neurone blocking agent because its primary site of action is the spinal internuncial neurone which modulate reflexes maintaining muscle tone. Injected i.v., it is effective in tetanus but it has been superseded by diazepam; because it causes thrombiflebitis, heamohysis and marked fall in BP.

ii. Diazapam: Is the prototype of benzodiazepines (BZDs) which act in the brain on specific
   (a) Receptors enhancing GABAergic transmission
   (b) It reduces muscle tone by supraspinal rather than spinal action, muscle relaxant; sedative activity ration is low.
   (c) It does not cause gastric Irritation and is very well tolerated though sedation limits the dose which can be used for reducing muscle tone. It is particularly valuable in spinal injuries and tetanus.

iii. Baclofen:- It is an analogue of the inhibitory transmitter GABA; acts as selective $GABA_B$ receptor agonist. The 1^0 site of action baclofen is considered to be in the spinal cord where it depresses both polysynaptic and monosynaptic reflexes.

USES OF CENTRALLY ACTING MUSCLE RELAXANT

1. **ACNTE MUSCLE SPASIN:-** Overstretching of a muscle, sprain, tearing of hgaments and tendons dislocation, fibroitis, bursitis, rheumatic disorders etc. cause pain of muscles. Muscle Spasm produces pain which in turn reinforce Spasm. The mepheorsin like and BZD

muscle relaxants, often combined with analgesics, are aimed at interrupting this vicious cycle.

2. **TORTICOLLIS, INMBAGO, BACKACHE, NEUALGIAS:-** These are other conditions in which painful spasms of certain muscles is a prominent feature, and respond in the same way as acnte muscle spasms.
3. **ANXIETY AND TENSION: -** These states are often associated within cresed tone of muscles. Diazepam group of drugs and chlormezanone, benefit by their anti-anxiety as well as muscle relaxant actions.
4. **TETANUS: -** Most commonly Diazepam is infused i.v. and the dose is titrated by the response
5. **ORTHOPEDIC MAINPULATIONS: -** These may be undertaken under the influence diazepam or methocarbamol given i.v.

COMPARATIVE FEATUES OF CENTRAL AND PHERIPHERAL MUSCLE RELAXANTS

	Centrally Acting	Pheripherically Acting
1.	Decrease muscle tone without reducing voluntary power	Cause muscle physis, and voluntary movement is lost.
2.	Selectively inhibit polysynaptic reflexes in CNS	Block Neuromuscular transmission
3.	Given orally, sometimes paventerally	Practically always given I.V.
4.	Cause some C.N.S. depression	No effect on CNS
5.	Used inchronic spastic conditions, Acute muscle spiny tetanus	Used for short tem purposes (surgical operations) as premedicants

SYNTHETIC ANABOLIC STEROIDS

These are synthetic androgens (substances) which are devoid of the virilizing effect of testosterone and are used for stimulating constructive metabolism as occur in

1. Senilitiy or animals recovering from debilitating diseases, e.g. in carine distemper, heavy parasitism, malnutrition and after major surgery. (take care of –ve N balance)
2. To counteract gluecorticoid overdose: here they induce catabolism and osteoporosis
3. Renal insufficiency: - Anabolic steroids reduce area production – frequency of dralysn needed in acute renal failure can decrease. However this effect is short lasting, so, only transient improvement is seen in chronic renal failure.
4. Stimulating erythropoesis:- e.g. in a plastic amaeania or myoproliferative disorders and regenerative anaemia in cats and dogs.
5. Suboptimal growth in Young ones:- Use is controversial. Brief spurts in linear growth can be induced by anabolic steroids, but this probably does not make a difference in the final stature. Use for more than 6 months is not recommended – premature chorine of epiphyses and shortening of ultimate stature may result.

To enhance physical ability in athletes: - When administered during the period of training, anabolic steroids can increase the strength of exercised muscles. However, effects are transient and contrary to popular belief, there is no scientific evidence that performance is enhanced. (it basically increase vigor