Muscle relaxants in current practice

Dr. Ashok Badhe
Prof. & Head
Dept. of Anesthesiology & Critical Care
JIPMER
PUDUCHERRY

Muscle relaxation is an essential component of balance anaesthesia. D-tubocurarine is probably the first neuromuscular blocking drug (NMB) to be used in anaesthesia. The development in understanding of neuromuscular physiology and pharmacokinetics and pharmacodynamics of the drugs has led to the development of newer muscle relaxants. The muscle relaxants in current anaesthesia practice in India are as follows - succinylcholine, atracurium, cisatracurium, vecuronium, rocuronium, & pancuronium.

Depolarizing muscle relaxants

Succinylcholine

Succinylcholine is the only depolarizing drug that is used in current practice. It gives the best muscle relaxation required with a rapid onset and short duration of action. It has got a unique method of metabolism that is hydrolysis by plasma cholinesterase. The present use of succinylcholine is limited to rapid sequence induction intubation, to overcome laryngospasm and potentially difficult airway where mask ventilation is possible. This is because of the various side effects of succinylcholine.

Side effects of succinylcholine:

1) Sinus bradycardia - is more common in children & with repeat doses
2) Fasciculation’s & muscle pain
3) Raised intracranial, intraocular & intra gastric pressure
4) Rise in serum potassium- normally there is rise of ~0.5 meq/l, but the rise can be to a dangerous level in certain clinical conditions like
   a) Burns, strokes
   b) Major denervation injuries
   c) Prolonged immobilization
d) Septicaemia &
e) Major trauma
5) Prolonged duration of action due to abnormal plasma cholinesterase
6) Masseter muscle spasm and malignant hyperthermia
7) Phase 2 blockade

Repeated use, infusion for prolonged duration or intramuscular use of succinylcholine can lead to phase 2 blockade, which means the NM blockade characteristics now resembles that of non-depolarizing blocker. Phase 2 blockade occurs in 5 stages as follows:

1) Stage of depolarizing blockade
2) Stage of tachyphylaxis
3) Stage of Wedensky inhibition
4) Stage of post-tetanic potentiation &
5) Stage of non-depolarizing blockade

Management options for phase 2 blockade are:

1) Assisted ventilation till the patient recovers (safest option)
2) Cholase (a purificed plasma choline esterase)
3) FFPs, fresh whole blood transfusion
4) Reversal with cholinesterase inhibitors

Among these various options, most commonly practised, consistent & safest is to support ventilation with positive pressure assist ventilation until patient has spontaneous recovery of neuromuscular function.

**Succinyl choline** - In neonate and infants the dose required may be more because of higher ECF volume, leading to larger volume of distribution. The onset time is also shorter and the incidence of vagal mediated bradycardia is higher compared to adults.

**OBESITY** - The dose required may be calculated according to lean body mass rather than actual body weight. The dose should be 20% more than lean body mass. Obese patient recover more slowly from vecuronium and rocuronium probably because of diminished elimination of these drugs. The recovery of
Atracurium is not affected by obesity because of lack of dependence on the end organ function for elimination.

**Non-depolarizing muscle relaxants**

**Atracurium & cis-atracurium**

These are the drugs belonging to benzylisoquinoline group with intermediate duration of action. Both have dual mode of metabolism which makes them more useful and safer drugs to be used in renal and liver failure. They have a unique mode of metabolism that is by Hoffman elimination in addition to ester hydrolysis. The duration of action may be prolonged in the presence of hypothermia.

Cis-atracurium is four times more potent than atracurium because of which the onset time is longer (bowman’s postulate). The increase potency of cis-atracurium results in less production of toxic metabolite laudanosine. This is of special concern when these drugs have to be used for prolonged duration in intensive care units. Cis-atracurium has also the benefit of less histamine release.

**Atracurium** may cause release of histamine & produce Laudanosine hence it is not used for prolong use in intensive care. Both the drugs can be reversed very easily by acetyl cholinesterase inhibitors, like neostigmine.

**Vecuronium & Rocuronium**

These are the drugs belonging to steroidal muscle relaxants of intermediate duration of action without having any hormonal action. They do not produce histamine release and are more cardio stable. Vecuronium produces bradycardia due to less Para sympathetic action on heart, especially when it is used in combination with fentanyl.

Vecuronium is metabolised in liver and has biliary excretion of metabolites, and renal elimination because of which dose adjustments is required in cases with hepatic and renal failure.

Rocuronium has shorter onset of action among its class of drugs, because of which it can be used for rapid sequence intubation in cases where succinylcholine is contraindicated. Reversal of neuromuscular blockade with
rocuronium and vecuronium can be done with sugammadex (a cyclo gamma dextrin) anytime during the blockade irrespective of the presence or absence of any neuromuscular recovery.

Prolonged use of these agents in critically ill patients can lead on to the development of critical illness myopathy. So they should be used only sparingly in such setting.

**Pancuronium**

This drug belongs to steroidal neuromuscular blocker with long duration of action. Its use is associated with tachycardia & hypertension, which is advantageous in certain cases like congenital cyanotic heart disease where maintenance of systemic blood pressure is of utmost importance to prevent reversal of shunt.

Dose adjustments is required in hepatic failure & reversal is possible with acetyl cholinesterase inhibitors once partial recovery of neuromuscular blockade is ascertained clinically and/or by NM monitoring.

**Classification according to duration of action**

<table>
<thead>
<tr>
<th>Muscle relaxants</th>
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<tbody>
<tr>
<td><strong>Agent</strong></td>
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<tr>
<td>Ultras short acting Scaline</td>
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<tr>
<td>Short acting</td>
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<tr>
<td>Mivacurium</td>
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<tr>
<td>Intermediate acting</td>
</tr>
<tr>
<td>a) Atracurium</td>
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<tr>
<td>b) Cisatracurium</td>
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<tr>
<td>c) Rocuronium</td>
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<tr>
<td>d) Vecuronium</td>
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<tr>
<td>Long duration</td>
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<tr>
<td>Pancuronium</td>
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Neonates and infants-they have large volume of distribution and are more sensitive to non-depolarising muscle relaxants .These two effects balance each other, hence the same dose may be required as adults .The on-going maturation may delay the excretion of drugs , hence the duration of action is
unpredictable. In case of vecuronium, the duration of action is prolonged because of liver immaturity.

Muscle relaxants are the drugs most commonly used drugs in anaesthesia practice. Their judicious use, keeping in mind their pharmacokinetics & pharmacodynamics will result in safe anaesthesia & in avoiding delayed recovery.

References:

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8. Miller anaesthesia 7th edition. Ronald miller vol 1