Non-depolarizing muscle relaxant

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objectives:

- Mechanism of action.
- Factors affecting duration of non-depolarizing muscle relaxant.
- Atracurium and cis-atracurium.
- Rocuronium bromide.
- Pancuronium bromide.
- Vecuronium bromide.
Mechanism of action:

* Non-depolarizing muscle relaxants are competitive antagonist, whereas depolarizing muscle relaxants are non competitive agonist.

* These drugs competitively block the receptors this means that you can overcome their action by increase Ach concentration by giving Ach esterase inhibitors such as pyridostigmine or neostigmine.
**Mechanism of action:**

- These drugs combine with nicotinic receptors and prevent binding of acetylcholine therefore preventing depolarization of the muscle cell membrane and inhibiting muscle contraction.
Factors affecting duration of non-depolarizing muscle relaxant:

- **PH**: changes metabolic acidosis and to a lesser extent respiratory acidosis extend the blockage duration.

- **age**: Older patients have prolonged effect also.

- **body temperature**: Hypothermia potentiate the blockage duration.

- **electrolytes changes**: Decrease in serum potassium conc. potentiate the blockage. Decrease in ionized calcium conc. also potentiate the blockage.
Suitability for Intubation

*The **ED95** is (the dose required to achieve the desired effect in 95% of the population).*
*For neuromuscular blockers one often specifies the dose that produces 95% twitch depression in 50% of individuals.*
*Muscle groups vary in their sensitivity to muscle relaxants. For example, the laryngeal muscles-whose relaxation is important during intubation-recover from blockade more quickly than the adductor pollicis.*
*In contrast to there being only a single depolarizing muscle relaxant (succinylcholine), there is a wide selection of nondepolarizing muscle relaxants:

<table>
<thead>
<tr>
<th>short acting</th>
<th>intermediate acting</th>
<th>Long acting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mivacurium</td>
<td>Atracurium</td>
<td>Pancuronium</td>
</tr>
<tr>
<td>Gantacurium</td>
<td>Cisatracurium</td>
<td>-</td>
</tr>
<tr>
<td>-</td>
<td>Vecuronium</td>
<td>-</td>
</tr>
<tr>
<td>-</td>
<td>Rocuronium</td>
<td>-</td>
</tr>
</tbody>
</table>
Atracurium
Structure:

* Has quaternary group {like all muscle relaxants}.

* Benzylisoquinoline structure {responsible for its unique method of degradation}.
*Atracurium is so extensively metabolized that its pharmacokinetics are independent of renal and hepatic function, and less than 10% is excreted unchanged by renal and biliary routes.

Two separate processes are responsible for metabolism:

A. **Ester Hydrolysis**
   This action is catalyzed by nonspecific esterases, not by acetylcholinesterase or pseudocholinesterase.

B. **Hofmann Elimination** (also known as exhaustive methylation) A spontaneous non enzymatic chemical breakdown occurs at physiological pH and temperature.
what is the physiological importance of Hofmann elimination reaction?

Atracurium lacks cardiac effects and self destruction mechanism into blood because its metabolised by hofmann elimination.
Dosage

A dose of **0.5 mg/kg** is administered intravenously for intubation.
Side Effects & Clinical Considerations

A. Hypotension and Tachycardia
Cardiovascular side effects are unusual unless doses in excess of 0.5 mg/kg are administered.

B. Bronchospasm
should be avoided in asthmatic patients.

D. Allergic Reactions
CISATRACURIUM

*Is an intermediate acting drug.
*Is one of the 10 isomers of atracurium and more potent than atracurium.
*The main advantage for this agent over atracurium is that it lacks the possibility of histamine release.
*It is the ideal choice for a patient with renal or hepatic insufficiency requiring muscle relaxation.
*eliminated by Hoffman degradation reaction.
*Dosage
Cisatracurium produces good intubating conditions following a dose of 0.1 to 0.15 mg/kg within 2 min. *Cisatracurium does not alter heart rate or blood pressure, nor does it produce autonomic effects, even at doses as high as eight times ED95.
PANCURONIUM

*It is a long acting (used for long operations longer than 6 hours ).

*Metabolism & Excretion
Excretion is primarily renal (40%), although some of the drug is cleared by the bile (10%).

*Dosage
A dose of 0.08 to 0.12 mg/kg of pancuronium provides adequate relaxation for intubation in 2 to 3 min.
Side Effects
A. Hypertension and Tachycardia: caused by the combination of vagal blockage and sympathetic stimulation.
B. Arrhythmias
C. Allergic Reactions
ROCURONIUM

*This monoquaternary steroid analogue of vecuronium was designed to provide a rapid onset of action. *It can quickly induce neuromuscular block make it suitable for rapid induction and intubation sequence.
*Dosage
Rocuronium is less potent than most other steroidal muscle relaxants (potency seems to be inversely related to speed of onset). It requires 0.45 to 0.9 mg/kg intravenously for intubation.

*Metabolism & Excretion
Rocuronium undergoes no metabolism and is eliminated primarily by the liver and slightly by the kidneys.
Other drugs:

- Mivacurium
- Alcuronium
- Tubocuratine
# Table 11-5: A Summary of the Pharmacology of Nondepolarizing Relaxants

<table>
<thead>
<tr>
<th>Relaxant</th>
<th>Chemical Structure</th>
<th>Metabolism</th>
<th>Primary Excretion</th>
<th>Onset</th>
<th>Duration</th>
<th>Histamine Release</th>
<th>Vagal Blockade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atracurium</td>
<td>B</td>
<td>+++</td>
<td>Insignificant</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>0</td>
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<tr>
<td>Cisatracurium</td>
<td>B</td>
<td>+++</td>
<td>Insignificant</td>
<td>++</td>
<td>++</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pancuronium</td>
<td>S</td>
<td>+</td>
<td>Renal</td>
<td>++</td>
<td>+++</td>
<td>0</td>
<td>+++</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>S</td>
<td>+</td>
<td>Biliary</td>
<td>++</td>
<td>++</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rocuronium</td>
<td>S</td>
<td>Insignificant</td>
<td>Biliary</td>
<td>+++</td>
<td>+</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Gantacurium</td>
<td>C</td>
<td>+++</td>
<td>Insignificant</td>
<td>+++</td>
<td>+</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

1. B, benzylisoquinoline; S, steroidal; C, chlorofumarate.
2. Onset: +, slow; ++, moderately rapid; +++; rapid.
3. Duration: +, short; ++, intermediate; +++; long.
4. Histamine release: 0, no effect; +, slight effect; ++, moderate effect; +++; marked effect.
5. Vagal blockade: 0, no effect; +, slight effect; ++, moderate effect.
The End