

## Benefit/risk ratio of Neuromuscular blocking agents

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Muscle relaxants are widely used during anaesthesia. They provide good intubating conditions and facilitate the use of controlled ventilation. They also induce abdominal muscle paralysis and muscular relaxation that is almost mandatory for abdominal surgery. However some authors have suggested that they could induce some side effects and have suggested limiting their use during anaesthesia. The goal of this lecture will be to discuss the benefit/risk ratio of currently available NMBA in routine anaesthesia.

### 1. Complications

Some anaesthesiologists don't use routinely NMBA during intubation because of the fear of unanticipated difficult intubation. This complication can be easily prevented by checking that the patient with an empty stomach can be ventilated with a face mask prior the administration of the NMBA.

Several retrospective studies have suggested that most of the anaphylactic reactions during anaesthesia might be attributed to NMBA, latex or antibiotics.. D'Honneur et al have recently demonstrated by using prick test in volunteers that 50% and 40% of the subjects had a positive skin reaction to undiluted rocuronium and vecuronium respectively <sup>1</sup>. The risk of false-positive skin testing highlights the need for standardization of these tests and careful determination of the concentration needed for each muscle relaxant. For example if the French recommendation for prick test (undiluted NMBA) were applied in d'Honnors's study all reacting volunteers (15:30) would have fulfilled criteria of allergy <sup>2</sup>. These differences in dilution and the risk of false positive tests can explain discrepancies between countries and why in Denmark, only one patient was tested positive to a NMBA <sup>3</sup>. Due to the recent publications on the skin tests it is likely that some anaphylactic reactions attributed to muscle relaxants are due to other causes (overdosing of anaesthetic agent, hypovolemia, reactions to other agents such as chlorhexidine).

Succinylcholine can produce a number of side effects. Most of them are mild and can be easily prevented by knowledge of its clinical pharmacology.

The life threatening complications malignant hyperthermia (MH), anaphylaxis and extreme hyperkalaemia are very rare but may arise without warning. Severe hyperkalaemia, producing arrhythmias or cardiac arrest may occur in patients with burns, traumas, sepsis, neurological

and muscular disorders. The mechanism could be due to the extrajunctional spread of acetylcholine receptors. In burn patients, it has been suggested to avoid succinylcholine at least until several weeks to months after complete healing when the patient revert to a normal metabolic state. This complication can be easily avoided by the respect of the contra indications. A small proportion of patients have a genetically determined inability to metabolize succinylcholine. Neuromuscular block may be very prolonged (45-360 min) in patients homozygous for either the atypical or the silent gene. Sedation and controlled ventilation until complete recovery from neuromuscular block will prevent the risk of sequelae.

## 2. Advantages provided by NMBA

Several studies have suggested that intubation could be performed without the help of NMBA; however satisfactory intubating conditions are not reliably obtained in all patients. It was suggested that propofol in association with alfentanil and lidocaine can be an alternative to the routine use of NMBA for intubation. However such a technique in routine cannot guarantee excellent intubating conditions in most of the patients. When remifentanyl is used in association with propofol, 3 µg/kg remifentanyl is needed to obtain good intubating conditions. With lower and more usual doses of remifentanyl, (1 µg/kg) intubation conditions were not acceptable in 65% of the patients and were still not acceptable in 20% of the patients with 2 µg/kg remifentanyl. Furthermore at these doses remifentanyl cause muscle rigidity and difficulty to hand ventilate as observed in some patients. Billard et al have clearly demonstrated that when using 2 mg/kg propofol in association with the opioid dose required to intubate the patient without NMBA the mean decrease in systolic blood pressure after propofol was 50 mmHg compared to less than 30 mmHg when no opioid was given<sup>4</sup>. Such a depression can be poorly tolerated in ASA III or IV patients.

Mencke et al have recently investigated the consequence of the intubating conditions on the incidence of postoperative hoarseness and vocal cord sequelae. The most important result was that an induction technique including propofol and fentanyl but without a NMBA was associated in 44% of the patients with postoperative hoarseness, vocal cord sequelae occurred in 42%. Adding a non depolarising NMBA (atracurium) significantly reduced the incidence to 16% and 8% respectively. The authors also calculated the number needed to harm (NNH), in other words how many patients had to be intubated without a NMBA to develop postoperative hoarseness or vocal cords sequelae. The NNH to produce one patient with vocal cord sequelae by omitting atracurium compared with giving the drug was 2.9, a very significant and clinically relevant risk<sup>5</sup>.

At the present time, there is no argument to consider the association propofol–opioid agents as a routine alternative to the use of NMBA for procedures requiring tracheal intubation excepted in situations where these agents are contraindicated.

#### Peroperative surgical conditions

NMBA are used routinely for many procedures because they provide adequate abdominal muscle relaxation facilitating exposure during selected surgical procedures. They are also useful to avoid coughing, increase in intra abdominal and intra thoracic pressure or extrusion of the abdominal content during GI, urological or gynaecological surgery. They can be used to ensure patient immobility instead of higher doses of anaesthetic agents. Some authors have suggested that NMBA do not need to be used routinely for example during retroperitoneal or retropubic surgery. A prospective controlled study has clearly demonstrated that NMBA (vecuronium) decrease very significantly the rate of unacceptable operating conditions in patients undergoing retropubic surgery even if halogenated agents were used for maintenance of anaesthesia. Moreover the surgeons found that abdominal muscle relaxation, as estimated by clinical judgment, increase with increasing doses of vecuronium <sup>6</sup>

#### Other advantages

Modern non depolarizing muscle relaxants have other advantages. They present a high degree of cardiovascular stability and most of them are of intermediate duration of action. Therefore, they are well adapted to the average duration of most of the abdominal surgical procedures. They can be used in many cases, whatever the duration, because they do not show cumulation.

#### Detection and reversal of neuromuscular block

Partial neuromuscular paralysis at the end of a case can be associated with pharyngeal and oesophageal dysfunction which can induce delayed initiation of swallowing and impaired coordination of the pharyngeal muscular activity. It must be highlighted that this type of problem is not specific of the NMBA. Concerning NMBA, it is easy to avoid such type of problem by the routine use of reversal agents and monitoring in the operating room but also in the recovery room. Although minor side effects (tachycardia or increased salivation) can be induced by reversal of neuromuscular block, NMBA remain the only agents used during anaesthesia which can be easily and rapidly reversed at the end of the case without any significant risk for the patient.

Nowadays, objective monitoring of neuromuscular block is available for routine use making the management of NMBA safer. Monitors are easy to set up and can now provide useful information not only throughout the whole surgical procedure but also for detection and

treatment of residual paralysis during recovery <sup>7</sup>. The use of a nerve stimulator in association with reversal from neuromuscular block can decrease very significantly the risk of residual paralysis in the recovery room.

In conclusion, there is no evidence that morbidity and mortality are decreased when NMBA are avoided for intubation. On the contrary recent studies have clearly demonstrated the benefits of the use of NMBA for routine intubation or during surgery.

### References

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