NEUROMUSCULAR BLOCKING AGENTS IN DAY SURGERY 2RC2

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Neuromuscular blocking agents are key components in modern anaesthetic practice. They are mainly used to facilitate tracheal intubation and to provide adequate surgical relaxation. Even if day surgery is no exception to this, the actual number of procedures where a neuromuscular blocking agent is needed are far less in day surgery than in traditional hospital-based surgical care.

Our armamentarium consists of two major classes of neuromuscular blockingagents, the two classes being based on the molecular structure upon which the drug is built [1]. The steroid-based class of drugs are built upon a classical steroid nucleus while the benzylisoquinoliniums are ester-based drugs. Dependent on their potency, action and degradation they have different time course profiles and consequently different indications. The time course profiles are generally divided into: ultra short acting (suxamethonium), short acting (mivacurium), medium acting (rocuronium, vecuronium, cis-atracurium, atracurium) and long acting (pancuronium, d-tubocurarine). Each drug has a defined onset time and time to intubation, duration of action and recovery time [1].

TIME TO INTUBATION

Tracheal intubation is most rapidly achieved and with a minimum of tissue trauma by using a neuromuscular blocking agent in combination with an appropriate dose of an induction agent (e.g. propofol or thiopentone) [2]. Historically, suxamethonium has been the preferred agent due to its reliable onset time and ultra short duration of action.

It can be argued whether suxamethonium should be used in elective procedures. The side effects of suxamethonium (myalgia, cardiovascular instability, plasma esterase-dependent degradation and risk for arrhythmias) limit , the use of this drug. Even if suxamethonium is recommended for securing the airway in emergency situations or during a rapid sequence induction, clinicians still use this drug for intubation in day surgery. It may be argued whether this practice is ideal in the light of the above-mentioned side effects. The introduction of a rapid acting neuromuscular blocking agent, such as rocuronium, provides a suitable replacement for suxamethonium, for routine use in elective surgical cases. Clearly the use of a neuromuscular blocking agent to facilitate tracheal intubation is superior to the use of an induction technique without a neuromuscular block. Recently, it has been shown that adding a neuromuscular blocking agent (atracurium) to a propofol-opioid based induction regimen significantly improved the quality of tracheal intubation and decreased postoperative hoarseness and vocal cord sequelae [2].

Notably, in the non-fasted patient with risk factors for aspiration during induction, suxamethonium is still a preferred drug for rapid sequence induction and for securing the airway, in combination with either propofol or thiopentone [3]

An intubating dose of a neuromuscular blocking agent is generally defined as 3-4 times the ED95 of each particular drug. This has empirically been shown to shorten and optimize the onset time and limit unwanted dose-related side effects. Based on this principle, the neuromuscular blocking agents can be divided into those where intubation can be achieved under apnoea (suxamethonium and rocuronium), and those where assisted ventilation is needed until complete block is achieved (mivacuronium, atracurium, cis-atracurium, vecuronium and pancuronium). If however, a short onset time is not a priority, the intubating dose can be reduced (e.g. to 2-3 times ED95). This will lead to a prolonged time until intubation is possible, while on the other hand the duration of its action will be substantially shorter.

TIME COURSE OF ACTION

In day surgery, the time course profile of a neuromuscular blocking agent is a critical factor. Prolonged duration of action in combination with residual paralysis or problems of reversal of the neuromuscular block may introduce severe risks for the patient and substantial problems in the care process. On the other hand, correct use of a neuromuscular blocking agent may optimize the surgical conditions such that the surgical procedure can be performed under best possible conditions, shortest duration and with a minimal risk of complications.

It must be emphasized that most duration of action data presents comparable profiles after standard 3-4 times ED 95 dosages. Any of the drugs can be used in smaller dosages. Such dose adjustment will then result in substantially shorter duration of action, which may be beneficial in any day care process. For instance, the time duration of action of rocuronium can be shortened many-fold by giving 50 % less drug (e.g. rocuronium 0.30 mg/kg), whilst still providing good intubation conditions after 2-3 minutes. Similar reasoning can be applied to the other medium acting drugs. In day surgical procedures where muscle relaxation is needed due to either shared airway procedures such as ENT or for technical reasons (e.g. laparoscopic surgery) the anaesthesiologist can, based on this reasoning, titrate the correct dose of NMBA simply by giving repeated small dosages to the desired neuromuscular blocking effect. This will result in the lowest dose required for the surgical procedure and result in the shortest possible duration of action. Hence, the dose of a neuromuscular blocking agent should always be adjusted individually and not be given at a fixed recommended dose, in order to avoid unforeseen prolonged duration of block or other side effects.

Ideally, the neuromuscular blocking agents used in day surgery should have a very rapid and reliable recovery which results in prompt and complete return to full muscle strength. Unfortunately this is not the case and there is no drug that can be preferred in this context. The variation in recovery time is wide and the effect of reversal agent not necessarily reliable. Consequently, day care patients cannot be guaranteed to have returned to an adequate level of neuromuscular recovery unless the neuromuscular function is monitored correctly (see below).

Residual effects of neuromuscular blocking agents may put patients at risk of postoperative complications and seriously interfere with the day care process . The residual effects of neuromuscular blocking agents are associated with impaired airway protection, regulation of breathing and the risk of pharyngeal dysfunction [4-6]. In some cases of prolonged neuromuscular block, patients may develop postoperative pulmonary complications due to incomplete reversal of the block [6]. This risk is increased in the elderly patient population and those with a long acting neuromuscular block [6]. Residual neuromuscular block is very common when reversal is omitted or ignored [7]. Interestingly, up to 45 % of patients receiving a medium acting drug can be anticipated to have residual effects in the recovery room if reversal is not given. On the other hand, if reversal is routinely administered, the risk is reduced but unfortunately not eliminated, i.e. about 5-10 % of patients receiving medium acting drugs followed by a reversal agent have a significant residual block when admitted to the recovery room [8,9].

Residual paralysis can be eliminated by regular use of an objective neuromuscular monitoring device [10,11]. Such devices are easy to handle and commercially available at a reasonable cost. It must be stressed that manual evaluation of the contractions in response to peripheral ulnar nerve stimulation cannot be used to adequately detect residual neuromuscular block, i.e. to detect residual fade in the response to train-of-four stimulation. Such small but significant levels of residual block can only be detected with objective techniques, which include accelomyography, mechanomyography or electromyography.

Monitoring the neuromuscular block in day surgery means that the dose can be adjusted more accurately according to both the patient's and surgical needs [10,11]. Ideally, an objective monitor should be used whenever a neuromuscular blocking agent is administered. Objective neuromuscular monitoring provides a correct estimate of the block level at all times, even when the block is profound. Deep neuromuscular block is assessed by using the post-tetanic-count (PTC)mode. Using this stimulus mode, the administration of a neuromuscular blocking agent can be adjusted to a complete paralysis of the diaphragm (PTC 1-2) which is sometimes necessary during surgical procedures on the airway. Even more important, during recovery, objective recording of the train-of-four ratio can be performed until adequate return of muscle function. At a TOF ratio of 0.90 or more the recovery of neuromuscular function is associated with safe extubation and the return of normal airway protection and regulation of breathing [10]. This level of recovery can only be detected with an objective neuromuscular monitoring device. Finally, the device will provide key information as to whether a reversal agent is needed.

Manual detection of the train-of-four response with a peripheral nerve stimulator provides limited information about how to adjust the dose of drug and the number of contractions detected in the train-of-four response can serve as an indicator of when reversal agent may be given. As mentioned above, manual evaluation of the train-of-for response cannot be used for detection of more superficial levels of block.

The recovery time after a non-depolarizing neuromuscular blocking agent is shortened by the use of a reversal agent, e.g. neostigmine. The dose should be adjusted to the actual level of block by the time the drug is given,i.e. 30-70 µg/kg body weight, the lower dose range being used for lesser levels of block. In general terms, the recovery time will be half as long when reversal agents are used when compared to spontaneous recovery without reversal. There is a relationship between the timing of reversal and the most pronounced effect on recovery time. Ideally, the reversal agent should be administered at the return of the first or second contraction in response to TOF nerve stimulation, i.e. between 10-15 % twitch recovery [12]. The duration of effect of neostigmine is approximately 45 minutes. Therefore, administration of neostigmine whilst there is a profound block should be avoided since such practice results in an increased risk of incomplete reversal and a risk for recurarisation when spontaneous recovery outweighs the effect of the reversal agent. At present, it is not fully understood as to whether the administration of an anticholinesterase drug such as neostigmine will produce more postoperative nausea and vomiting than if such an agent not was given.

In summary, day care surgery may require the use of neuromuscular blocking agents for tracheal intubation or surgical relaxation. The use of reduced doses of a non-depolarizing neuromuscular blocking agent is a feasible alternative to suxamethonium. For optimal intraoperative muscle relaxation in day surgery, the recommended approach is to use small repeated doses of muscle relaxant adjusted according to information from neuromuscular monitoring. Safe return to normal neuromuscular function at the end of the procedure can only be achieved by dose adjustments, the routine use of reversal agents or even better by routine use of objective neuromuscular monitoring.

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