WHICH MUSCLE RELAXANT TO CHOOSE FOR INDUCTION OF ANESTHESIA

R. Miller, Department of Anesthesia, University of California, San Francisco, 521 Parnassus Avenue, Box 0648, San Francisco, California 94143-0648, U.S.A.

INTRODUCTION

In the history of anesthesia, securing and maintaining a patent airway during induction and maintenance of anesthesia is one of the major reasons for the development of our specialty. Muscle relaxants are drugs that have been used extensively to facilitate endotracheal intubation. In the past 50 years, there have been hundreds of peer-reviewed articles, reviews, textbook chapters, lectures, and panels that have evaluated and discussed what the ideal approach to endotracheal intubation should be. Despite this emphasis, inability to maintain an adequate airway is still the number one cause of anesthetic-specific morbidity and mortality. Although a successful individual practitioner of anesthesia does not often experience inability to maintain an adequate airway, when it does occur it can be devastating. This summary will emphasize concepts which have evolved in the literature over the past 5 years. Examination of the reference list indicates that only references published from 1990 forward are included. References prior to 1991 can be easily identified in various textbook chapters.
It is becoming exceedingly difficult to find evaluation of literature with regard to choice of muscle relaxant to facilitate endotracheal intubation because of a frequent lack of objectivity. Recognizing that endotracheal intubation can be performed without the use of muscle relaxants in the presence of adequate anesthesia [1], it becomes difficult ascertaining the contribution of a specific muscle relaxant that may also have been given. For example, if endotracheal intubating conditions are adequate, how much of it is due to the anesthetic per se versus the muscle relaxant? Therefore, it is this author's belief that blinded studies should be conducted in articles emphasizing the contribution of one muscle relaxant vs. another to avoid investigator bias in evaluating endotracheal intubating conditions.

1. FACTORS TO BE CONSIDERED IN CHOICE OF MUSCLE RELAXANTS

Defining adequate conditions for endotracheal intubation partly depends on the clinical situation presented to the anesthesiologist. In the case of an elective surgical procedure and if the patient has had nothing to eat for an appropriate amount of time preoperatively, the rapidity with which endotracheal intubation is accomplished is less important. However, a case for which rapid induction of anesthesia and endotracheal intubation is required, the choice of muscle relaxant becomes more crucial. It will be the latter situation that will dominate this summary. Regardless of the choice of muscle relaxant, there are five conditions which should be met in all cases:

1. the lungs must be full of oxygen,
2. an adequate dose of anesthetics, inhaled or intravenously administered, should be present to ensure that the patient is adequately anesthetized. A well anesthetized patient will hasten the onset time,
3. endotracheal intubation should be accomplished within 60 seconds,
4. consideration should be given to enacting those maneuvers which would shorten the onset of action of a muscle relaxant,
5. cricoid pressure should be applied subsequent to the injection of either a muscle relaxant or anesthetic. While all experienced anesthesiologists recognize the above requirements, they have been included in this summary for sake of completeness.

1.1. PROBLEMS IN CHOOSING A MUSCLE RELAXANT

When the need arises to intubate the trachea rapidly, it seems reasonable to administer the dose of muscle relaxant which has the most rapid onset. However, there are some factors which make this assessment difficult, which is further complicated by reading the literature. First, the depth and choice of anesthetic clearly influence onset time of a muscle relaxant. Comparing one study with
another, especially with varying anesthetic techniques, is problematic. Secondly, most studies utilize the adductor pollicis muscle at the hand, although it has been well demonstrated by French investigators [2] that the laryngeal muscles are probably better indicators of adequacy for endotracheal intubation. In fact, it has been demonstrated that a drug such as rocuronium can be similar to succinylcholine in onset at the hand muscles, but slower at the laryngeal muscles [3]. Furthermore, other muscles such as the orbicularis oculi can be used to assess the onset of good intubating conditions [2]. The following considerations with regard to choice of muscle relaxant will take these monitoring factors into consideration when making our conclusions. Lastly, as indicated previously, the objectivity of this study almost demands that the investigators be blind as to which drug or dose is being given.

1.2. MANIPULATION OF AN INDIVIDUAL DRUG'S ONSET TIME

There are many methods by which the onset time (time from muscle relaxant administration to peak effect) can be shortened. The first method is by increasing the dose of a given muscle relaxant. The clinical onset time (i.e., as opposed to pharmacologic onset) can be shortened by administration of a large dose. For example, the onset time of vecuronium (0.4 mg/kg) is less than 1.5 minutes. When a large dose of rocuronium is given (e.g., 1.2 mg/kg) the onset time is comparable to that of succinylcholine. On the other hand, when the large dose of any muscle relaxant is given, duration can be markedly prolonged. One must expect a very long duration of action if a large dose of muscle relaxant is given. In the case of renal insufficiency, steroidal muscle relaxants tend to be more prolonged than those that are dependent on metabolic processes for elimination from plasma. Although not well established, one would expect a more predictable duration of action from a very large dose of cis-atracurium than from rocuronium.

The second method by which the onset can be manipulated is via the "priming principle". Usually the priming principle hastens the onset of most non-depolarizing muscle relaxants by 30-60 seconds. If the priming dose of a non-depolarizing muscle relaxant is given 3-6 minutes before the intubating dose, tracheal intubation can be achieved approximately 90 seconds after injection of a second dose of muscle relaxant. In the case of vecuronium, the ideal situation seems to be administering a priming dose of 0.01 mg/kg with a subsequent wait of 4 minutes, and then intravenously administering an intubating dose of 0.07 - 0.15 mg/kg. Nevertheless, even though a larger dose and the priming principle clearly shorten the onset time of non-depolarizing muscle relaxants, the shortest time is still achieved with succinylcholine. Also, one will have a frequent incidence of diplopia without weakness when the priming dose of a muscle relaxant is given. In some instances, drugs have been given in divided doses in order to minimize the cardiovascular effects and still take advantage of a shortened duration of action. This has certainly been the case with mivacurium. However, it is this author's opinion that while the divided dose approach is successful experimentally, clinically it does not work well [4]. Furthermore, there are too many muscle relaxants
available in which the initial doses do not need to be divided in order to achieve a rapid onset of neuromuscular blockade.

The last approach to hastening the "clinical" onset is to give the non-depolarizing muscle relaxant first, wait a short period of time and then give the intravenous induction dose of anesthetic. In theory, the peak effect of the muscle relaxant and the anesthetic occur at the same time. This author has never utilized this technique, but rather views it with considerable caution [5].

1.3. ACTUAL IMPORTANT CLINICAL FACTORS IN THE CHOICE OF A MUSCLE RELAXANT

While there are many secondary factors that should be considered, as indicated above, the three most important are:
1. duration of action,
2. cardiovascular effects,
3. onset.

1.3.1. DURATION OF ACTION

The second most common anesthetic induced cause of morbidity and mortality is due to inadequate dissipation or inadequate reversal of the anesthetic state. Inadequate reversal of the neuromuscular blockade for muscle relaxants is partly responsible. It has been demonstrated that residual neuromuscular blockade is less likely with intermediate- or short-acting muscle relaxants. This author wonders why long-acting muscle relaxants are given to facilitate endotracheal intubation when intermediate-acting muscle relaxants, and the upcoming shorter acting muscle relaxants, have an extremely short onset time. Part of the justification for using these long-acting drugs is that the surgical procedure itself will be long. Alternatively, this author fails to understand why intermediate-acting drugs are not given on a repetitive basis rather than long-acting drugs for long cases if the expectation is tracheal extubation and spontaneous ventilation in the recovery room. Nevertheless, studies have been conducted that justify the use of long-acting muscle relaxants to facilitate endotracheal intubation [6].

Most clinicians would probably select the duration of action that is related to the duration of the surgical procedure for which it is being given. In out-patient anesthesia, succinylcholine would probably be the preferred muscle relaxant, the neuromuscular blockade of which can be maintained with a succinylcholine drip or mivacurium infusion. Nevertheless, there are studies advocating the use of an intermediate-acting drug, such as rocuronium [7]. While there are many concerns about the continued use of succinylcholine, perhaps the development of a very ultra-short acting, rapid onset, non-depolarizing neuromuscular blockade will eventually eliminate the use of succinylcholine. An example of this is ORG 9487 [8].

In essence, the duration of action of a muscle relaxant is extremely important. Regardless of what muscle relaxation combination the clinician chooses, complete dissipation of neuromuscular blockade in a spontaneously breathing patient in the recovery room must be guaranteed. Monitoring the adductor pollicis has been a
common method of monitoring adequacy of reversal, but clearly laryngeal muscles can still be weak in the presence of a block that appears to be completely reversed [9, 10].

1.3.2. CARDIOVASCULAR EFFECTS

The cardiovascular effects of muscle relaxants have been studied extensively. Because there are multiple choices available, it seems reasonable to choose a muscle relaxant that either has no cardiovascular effects or produces a slight increase in heart rate. The increase in heart rate may be beneficial because of the tendency of some opioids to produce a decrease in heart rate. Of prime importance is avoiding a cardiac arrhythmia or hypotension, which could be detrimental. In this respect, it seems as if either rocuronium or cis-atracurium should be the drugs of choice. Rocuronium clearly has the quickest onset time of any currently available muscle relaxant, other than succinylcholine. Cis-atracurium and vecuronium can be given in larger doses to affect a more rapid onset. The lack of dependence on the liver or kidney for the termination of a cis-atracurium neuromuscular block, may determine the preference of this drug over extremely large doses of vecuronium. Clearly, muscle relaxants should be chosen in order to avoid disastrous cardiovascular results [11, 12].

1.3.3. ONSET TIME

We are fortunate to have access to drugs that have a quick onset time. As indicated above, rocuronium (0.6 - 1.2mg/kg) and very large doses of cis-atracurium have a short onset time. Hopefully the development of ultra-short acting muscle relaxants with rapid onset times will eliminate the use of rocuronium and cis-atracurium, and will produce effect similar to succinylcholine [8].

2. SPECIAL SITUATIONS - BASED ON THE LITERATURE

2.1. OPIOIDS AND LARGE DOSES OF VECURONIUM

There has been frequent debate as to whether bradycardia during induction of anesthesia with drugs such as sufentanil and vecuronium was more likely to occur with this particular combination. Sharp et al. [13] recently demonstrated in patients undergoing coronary bypass surgery that vecuronium does not affect the heart rate or the incidence of bradycardia following sufentanil administration. More importantly, their study showed that patients who took beta-adrenergic blockers were more likely to have bradycardia during sufentanil administration.

2.2. CAESAREAN SECTION

Baraka et al. [14] found that pregnant women had a more rapid onset of neuromuscular blockade from vecuronium than women who were not pregnant. Abdulatif et al. [15] in a similar study, utilized a surgeon-controlled mivacurium administration during Caesarean section and found that the total dose given was less.
than that required for continuous infusion. This author has considerable reservations about this approach, however one should be aware of this trend.

2.3. ASTHMA AND DECREASED VENTILATION COMPLIANCE

There are two issues regarding this topic. First, do muscle relaxants which release histamine result in an increased incidence of bronchospasm versus muscle relaxants which do not release histamine? Caldwell et al. [16] compared atracurium with vecuronium and concluded that indeed atracurium was associated with more adverse cardiovascular effects. However the incidence between patients with regard to adverse respiratory events was not different. It seems, however, in asthmatic patients, non-histamine releasing drugs should be used.

One must also worry about the "stiff chest" with administration of opioids. Horrow et al. [17] found that pretreatment with a small dose of pancuronium did not prevent difficulty in ventilation associated with moderate doses of sufentanil. However, if a combinant infusion of sufentanil and pancuronium were given, compliance did improve, measured both subjectively and objectively, without causing early paralysis in suitably medicated patients.

2.4. EMERGENCY AIRWAY MANAGEMENT

In many academic hospitals, more than 30% of the anesthetics are given outside the operating room. Furthermore, at institutions with a large number of critical care beds, emergency endotracheal intubation is often necessary. The outcome of these emergent intubations are now being studied. For example, Schwartz et al. [18] show that emergency tracheal intubation is associated with frequency of major complications. These complications will be analyzed.

The use of muscle relaxants for induction of anesthesia in emergency airway management has become incredibly reliable. Nevertheless, a close examination of muscle relaxant choice is warranted because there have been sufficient numbers of adverse effects resulting in morbidity and mortality. We, as anesthesiologists, should make the best choice possible, although proving that our choice improves outcome is, indeed, difficult.

CONCLUSION

Administration of anesthesia has become incredibly safe. The incidence of serious adverse morbidity and mortality, solely due to anesthesia, is becoming extremely rare. However, when a case of morbidity or mortality does occur, it is frequently disastrous. For over 40 years, inability to obtain a patent airway is the most common cause of serious anesthetic induced morbidity and mortality. Some examples include inadequate examination of the airway preoperatively, unusual reactions to drugs, such as bronchospasm, technical difficulties, and so on. It has always been assumed that decreasing the time between administration of anesthetic
drugs and intubation will reduce the incidence of vomiting and aspiration of gastric contents. Therefore, it seems as if the ideal drug would be that which has no cardiovascular effects and has a rapid onset. Furthermore, having a predictable duration of action is desirable if the expectation is to have the patient tracheally extubated and spontaneous ventilation ensuing postoperatively. It seems that the two ideal choices would be rocuronium and/or cis-atracurium. To make these drugs maximally effective, the proper dose and adequate anesthesia must be delivered. Hopefully, a non-depolarizing equivalent of succinylcholine will soon be available.
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