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Editorial

EDITORIAL

Optimising conditions for tracheal intubation: should neuromuscular blocking agents always be used?

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'Striving to be better, oft we mar what's well.'

Shakespeare, 1605–6. King Lear

Over the last 20 years, Cochrane systematic reviews of health care research have become internationally recognised to represent the highest standard of evidence-based research. These reviews are designed to address clearly formulated questions using complex meta-analysis and are most helpful when the clinical question proves vexing and difficult to answer accurately. In this respect, they are particularly useful in anaesthesia when addressing clinical questions where, for instance, various anaesthetic techniques have been used in many cohort studies investigating the same conundrum. However, the results of some Cochrane reviews such as the recent report comparing the clinical pharmacology of sugammadex with neostigmine are neither surprising nor especially enlightening.[1] But in this instance they do confirm clinical impressions with hard data, which is in itself a very important function. Similarly, the report by Lundstrom and colleagues[2] in this issue of the *British Journal of Anaesthesia*, based on a recent Cochrane review[3] of the effects of avoiding the use of neuromuscular blocking agents (NMBAs) on perceived intubating conditions, possible adverse effects, and postoperative discomfort, confirms much of what many experienced clinicians already recognise. But it does provide the factual proof of our clinical opinion. Tracheal intubation is easier and less traumatic if a NMBA has been administered. Hopefully, this report will also serve to convince the sceptics of the need always to use NMBAs unless they are specifically contraindicated to assist in tracheal intubation.

Meta-analyses define a primary outcome variable, in this report whether NMBAs reduce difficulty with tracheal intubation,[2] and secondary outcomes. They then consider subgroup analyses of the primary outcome variable, in this instance whether the use of i.v. opioids or topical local anaesthesia affected the ease of tracheal intubation when NMBAs were not used or whether excluding patients who were expected to be a difficult intubation altered the results (they did not). Indeed, none of the subgroup analyses altered the findings of the primary outcome variable in this study.

The findings in a meta-analysis are regularly graded as of low, moderate, or high risk. The Cochrane Grade system assesses the quality of the evidence associated with specific outcomes in an attempt to clarify how confident we should be that any effect, such as being a known difficult intubation, has on the variable being studied. It takes into account the risk of bias, the heterogeneity or diversity of the data, the precision of the estimates, and the risk of publication bias. Bias is also assessed according to standard Cochrane criteria including whether participants and investigators were blinded to the study findings (which is not always easy to achieve in intubation studies), whether only incomplete data were obtained in any of the cohort studies, and if bias was induced by commercial sponsorship.

In classic Cochrane fashion, Lundstrom and colleagues[2] have gone to great lengths to eliminate bias from their findings, and their analyses are exhaustive. They included 34 trials of 3565 patients aged >14 yr in their meta-analysis, which is impressive, and found a significantly increased risk of difficulty with tracheal intubation if NMBAs were not used, both in four trials with a low bias and when all the studies were included. There was also a significantly increased risk of upper airway discomfort or injury after operation if NMBAs were avoided in all the analyses, and these complications were significantly associated with difficult laryngoscopy.

Disappointingly, however, the authors' conclusion lacks conviction: 'one must balance arguments for using or not using neuromuscular blocking drugs when performing tracheal intubation'.[2]

Inevitably, challenges arose with their approach. In particular, the question of how a 'difficult intubation' should be defined and how it should be classified is very apparent: it is such a subjective assessment. Various scoring systems were used to assess the ease of tracheal intubation between studies, which contribute to the heterogeneity of this data. These scoring systems have been designed for other purposes as the authors acknowledge. Scoring systems for assessing the ease of tracheal intubation were introduced in the 1980s. The highly respected Cormack and Lehane score[4] became established and was subsequently modified for more general use.[5] The original score was designed for use in obstetric anaesthesia to assess the degree of difficulty with tracheal intubation which was known to then be a major cause of maternal mortality. But Cormack and Lehane[4] gave no consideration as to whether NMBAs were being used: they presumed that they were. Yentis and Lee[5] modified this score, increasing the detail and number of subgroups in the classification to make it suitable for use before a wide range of surgical procedures. It was not until 1996, under the leadership of Viby-Mogensen in Denmark, that it was fully appreciated that intubating conditions when a NMBA is being used must also be standardised. The Good Clinical Research Practice Guidelines which he and his colleagues introduced in this respect are now widely accepted and oft quoted.[6] They were subsequently updated by the same group in 2007.[7] Although they were designed for different purposes, these very different types of scoring systems are all used in the cohort studies under investigation by Lundstrom and colleagues,[2] potentially limiting the accuracy of the findings. The time to initiation of intubation after induction of anaesthesia also varied between studies; this tended to be longer in groups not receiving a NMBA, which is again a cause of heterogeneity. However, these dichotomies exemplify the benefits of using meta-analysis to understand such data optimally.

Disconcertingly, as clinicians may well consider this question of relevance especially to the incidence of side-effects, only minor consideration is given in Lundstrom and colleagues' study[2] to any differences between the effect of using depolarising rather than nondepolarising NMBAs on the incidence of difficulty with tracheal intubation. This subgroup analysis is only reported in the supplementary material and the findings are the same. In the subgroup of trials where succinylcholine was the muscle relaxant used, there was, not surprisingly, an increased risk of difficulty with intubation in the group that did not receive this drug. Similar findings are reported when only nondepolarising NMBAs are compared with no muscle relaxant. Viby-Mogensen and colleagues[6] recommended that patients receiving succinylcholine should always be used as a control group in intubation studies to compare with patients only receiving nondepolarising NMBAs.

Are the side-effects of neuromuscular blocking drugs really so significant that they should impair their routine use? Anaphylaxis to these drugs is rare, in the order of 1 in 6000–20,000 administrations,[8] and anaesthetists should now be well able to manage this life-threatening response successfully. The transient cardiovascular effects of NMBAs are usually dealt with easily. Although well recognised, the evidence for clinically significant side-effects occurring frequently and sufficiently to deter the clinician from the use of intermediate-acting NMBAs is unimpressive.[9] Only one study considered in this meta-analysis[2] reported a serious adverse event from a NMBA (out of 3565 patients), and that was bronchospasm after administration of rapacuronium, a drug with an ephemeral history that was never available for clinical use in the UK and is no longer commercially available. I would suggest that NMBAs will be ubiquitous in anaesthetic practice for many years to come.

Tracheal intubation became more sophisticated in an attempt to save lives during the First World War.[10] Severe injuries to the head and neck from armed conflict were causing death during anaesthesia from loss of the airway and hypoxia. Metal tracheal tubes replaced tracheal catheters, and the introduction of red rubber tubes over the following decade improved the ease of intubation and reduced airway trauma. Over the next 20 years, it became increasingly apparent that muscle relaxation would ease tracheal intubation especially if it was difficult and the introduction of NMBAs into clinical practice in 1942 was a major step forward in this respect.[11]

By the 1970s, deaths during general anaesthesia were decreasing.[12] In Australia, Bodlander[12] reported a decrease in the incidence of anaesthetic deaths to 3.7% in the decade from 1963–72, and a reduction from 20.9% in the previous 10 yr. Respiratory complications were responsible for >50% of these deaths. With that trend came the increasing realisation that anaesthetists were now duty bound to improve the quality of their anaesthetic technique to reduce postoperative morbidity and mortality. In 1975, Riding[13] (the fifth Editor of the *BJA*) stressed the need for anaesthetists to take great care to prevent morbidity after general anaesthesia. One of his main messages was to stress the need for gentle and careful tracheal intubation only when the patient was fully relaxed to reduce the incidence of airway trauma and in particular of postoperative sore throat. The highest standards of clinical practice require such an approach. Indeed, it could be argued that the need to adhere at all times to an excellent anaesthetic technique is paramount; this maxim should not be lost in idiosyncratic practice.

Introduction of the i.v. induction agent propofol in 1980 undoubtedly led to improved intubating conditions.[14] Compared with the i.v. barbiturates and etomidate,[15] relaxation of the pharynx and larynx was increased by propofol such that clinicians started to consider omitting the use of NMBAs putatively to avoid their side-effects. Introduction of the short-acting opioids fentanyl, alfentanil, and, subsequently, remifentanil[16] potentiated the effect of propofol in this respect. Perhaps it became tempting to avoid the use of NMBAs not primarily because of concern over their side-effects, but simply to try something new and to add another gimmick to one's anaesthetic armamentarium.

Many studies of avoiding the use of NMBAs before tracheal intubation have been carried out in patients who were not considered to be difficult to intubate, but with failure rates of up to 20%, which is unacceptable even in patients in whom intubating conditions are difficult.[17] Woods and Allam[17] thoroughly reviewed the then existing literature on tracheal intubation without use of NMBAs in 2004. It was very apparent that the acceptable (not ideal) intubating conditions that could be achieved in these studies depended very much on using a pre-selected dose of opioid, which varied between studies. The higher the dose of propofol and opioid, the better the intubating conditions, but large doses of propofol and opioid also have side-effects, especially of a cardiovascular nature