Original Article

A comparison of haemodynamic responses between clinical assessment-guided tracheal intubation and neuromuscular block monitoring-guided tracheal intubation: A prospective, randomised study

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ABSTRACT

Background and Aims: Haemodynamic responses to laryngoscopy and endotracheal intubation and their hazards are well documented. The purpose of the study was to compare the effects of laryngoscopy and intubation on cardiovascular responses when the appropriate moment for intubation was directed by either clinical judgment or train-of-four assessment. **Methods:** A total of 68 patients, posted for laparoscopic cholecystectomy, were randomised into two groups. In Group M patients, the trachea was intubated after train of four counts became zero in adductor pollicis muscle, whereas in Group C patients, the trachea was intubated after the clinical judgment of jaw muscle relaxation. Changes in heart rate (HR) and mean arterial pressure, intubating conditions and the time between the administration of a neuromuscular blocking agent and endotracheal intubation were recorded. Results were analysed by the Analysis of variance and chi-square tests. **Results:** HR and mean arterial pressure were significantly higher in Group C as compared to Group M after laryngoscopy and tracheal intubation ($P < 0.05$). The mean time required for intubation was significantly shorter in Group C compared to Group M (175 ± 7 s vs. 385 ± 101 s). Excellent and good intubation conditions were observed in all Group M patients, whereas 24 out of 34 patients (70%) in Group C showed excellent and good intubation conditions. **Conclusion:** Haemodynamic responses to laryngoscopy and tracheal intubation can be significantly attenuated if tracheal intubation is performed following complete paralysis of laryngeal muscles, detected by neuromuscular monitoring of adductor pollicis muscle.

Key words: Haemodynamic, intubating conditions, neuromuscular monitor, tracheal intubation, vecuronium

INTRODUCTION

Laryngoscopy and endotracheal intubation during induction of general anaesthesia elicit strong nociceptive stimuli, which often lead to unintended stimulation of the sympathetic nervous system.[1] In general, cardiovascular changes accompanying intubation are transient and do not result in significant adverse effects. However, in patients with concomitant coronary artery disease, arterial hypertension or intracranial pathology, exaggerated haemodynamic parameters may lead to myocardial ischaemia or secondary brain damage. To blunt this pressor response, many drugs are successfully used.[2] However, administration of an additional drug might cause adverse haemodynamic effects or might unnecessarily increase the depth of anaesthesia. Hence, a non-pharmacological measure to reduce the response is preferred.

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The extent of circulatory responses depends on the type and depth of general anaesthesia, age of patients, concomitant diabetes mellitus, cardiovascular or any other systemic diseases and drugs used.[2] This response also depends on the duration of laryngoscopy and intubation as well as ease of the procedure.[3,4] Therefore, achievement of adequate neuromuscular block with neuromuscular blocking drugs is of utmost importance to obtund sympathetic response. Thus, the assessment of complete neuromuscular blockade appears to be necessary for proper timing of intubation. In clinical practice, however, neuromuscular monitoring and accurate timing are rarely used and many anaesthesiologists commence laryngoscopy based on the clinical assessment after a standard duration according to the onset of action of neuromuscular blocking agent used.[5] A previous study showed that if neuromuscular block monitoring technique is used to determine the moment for intubation, more time was required between muscle relaxant administration and intubation and it improved intubating conditions and minimised cardiovascular responses.[6] Another study showed that clinical judgement underestimated the time required for adequate onset of action of vecuronium, resulting in less favourable intubating conditions.[5] Literature is very limited regarding comparison of neuromuscular monitoring over clinical assessment of adequate muscle relaxation for the purpose of haemodynamic fluctuations after laryngoscopy and tracheal intubation.

We aimed at evaluation of neuromuscular block monitoring in preventing haemodynamic fluctuations following laryngoscopy and tracheal intubation after administration of vecuronium in comparison to clinical assessment of timing of laryngoscopy and tracheal intubation. We hypothesised that neuromuscular block monitoring-guided intubation would elicit lesser rise of heart rate (HR) and the mean arterial pressure compared to clinical assessment-guided intubation.

METHODS

This prospective, randomised trial was conducted after approval from institutional ethics committee in a tertiary care hospital. Patients of either sex, 18–60 years of age and belonging to the American Society of Anesthesiologists physical status I and II, posted for elective laparoscopic cholecystectomy were included in the study. Patient's refusal, anticipated difficult airway and patients with hepatic, renal, cardiovascular, neurological, muscular or other systemic diseases such as diabetes mellitus, hypertension and on antipsychotic medications were excluded from the study.

After pre-anaesthetic check-up, informed consent was obtained after informing the patients of the study protocol in their own language. The patients were kept fasted for 8 h and were pre-medicated with oral pantoprazole 40 mg on morning of surgery. In the operating room, monitors including 5-lead electrocardiogram, automated non-invasive blood pressure, pulse oximeter, neuromuscular monitor (train of four [TOF] watch) and bispectral (BIS) index monitor were attached, and baseline vitals were recorded. Peripheral venous access was secured. Anaesthesia was induced with intravenous fentanyl 2 μg/kg and 2.5% thiopentone till the disappearance of the eyelash reflex. After the disappearance of the eyelash reflex, a supramaximal TOF stimulus was applied to the ulnar nerve at the wrist through surface electrodes (stimulation current set at 60 mA) using acceleromyograph after automatic calibration. Baseline TOF ratio percentage was noted. After standardisation of supramaximal stimulus intravenous vecuronium 0.1 mg/kg was administered over 5 s. After the administration of the vecuronium, lungs were ventilated with sevoflurane in 100% oxygen maintaining a BIS score of 40–60 till the tracheal intubation. In the study, dosing of muscle relaxant, selection of study population, use of neuromuscular block monitor etc., were as per the Stockholm revision of good clinical research practices, 2007.[7]

The technique of tracheal intubation was as per randomised group. Totally, 68 patients were randomised into two groups (Group C and Group M) using a computer-generated block randomisation with block size varying between 6 and 8. Allocation concealment was done by sequentially numbered sealed envelope technique. In Group C, the trachea was intubated following clinical assessment of neuromuscular blockade. In Group M, the trachea was intubated following neuromuscular block monitoring by TOF Watch$_{TM}$ [Organon (Ireland) Ltd, Dublin Ireland].

In Group C, the timing of intubation was judged based on clinical assessment starting at 1 min after administration of muscle relaxant and at every 30 s thereafter by an experienced anaesthesiologist. The timing of laryngoscopy was based on ease of ventilation, jaw and upper airway tone. Jaw tone was assessed by attempting to open patient's mouth, whereas upper airway tone was determined by amount of jaw support necessary to maintain patent airway.

In Group M, anaesthesiologist performed intubation after complete loss of all 4 responses to TOF stimulation (TOF count zero), carried out every 30 s starting at 1 min after administration of vecuronium. The electrical stimulation was done with 60 mA, 2 Hz current lasting 0.2 ms.

The trachea was intubated with endotracheal tubes of appropriate sizes. The cuff of the endotracheal tube was inflated over 5 s. The time from administration of neuromuscular blocking drugs to the time of tracheal intubation and cuff inflation was noted. The patients who had oesophageal intubation were excluded from the study. Thereafter, mechanical lung ventilation was carried out using sevoflurane in oxygen: nitrous oxide (40:60) mixture and maintaining a BIS of 40–60. The ventilator parameters were adjusted to maintain end-tidal carbon dioxide ranging from 36 to 40 mm Hg.

The primary outcome was HR changes in response to tracheal intubation. HR was recorded at T0 – before shifting the patient to OT table (baseline data), T1 – immediate after vecuronium administration, T2 – 1 min after vecuronium administration, T3 – after inflation of the cuff following intubation, T4 – 1 min after intubation, T5 – 3 min after intubation, T6 – 5 min after intubation.

The secondary objectives included changes in mean arterial pressure in response to intubation and intubating conditions as graded using the Krieg's intubating score, ranging from 3 (best possible intubating conditions) to 12 (worst possible conditions).[8] The laryngoscopic views were also graded as per Cormack–Lehane (CL) grading. The time between the administration of a neuromuscular blocking agent (end of 5s infusion) and endotracheal intubation (end of 5s inflation of the sealing cuff) was also recorded.

A previous study showed significant difference in the mean HR of 10 beats/min between the neuromuscular monitoring group and clinical assessment group in the post-intubation period with the standard deviation of 14.[6] Considering 95% of confidence interval and power of the test as 80%, sample size was calculated to be 31 in each group. To accommodate dropouts, finally, 34 patients in each group were included.

HR and mean arterial pressure are presented as mean ± standard deviation (SD). Between group comparisons of the means of HR and mean arterial pressure are done by ANOVA test. For categorical data, Chi-square test was used as a test of significance. $P \leq 0.05$ was considered as significant. Statistical analysis is done using software SPSS 16(IBM, Armonk, NY, USA).

RESULTS

A total 68 patients were recruited and all patients were included for analysis, and there were no exclusions after recruitment as none of the patients had oesophageal intubation or required more than one attempt for intubation. The demographic profile was comparable in the two groups [Table 1].

The mean HR and mean arterial pressure were higher in Group C as compared to Group M with statistical significance ($P < 0.05$) at the T3, T4, T5, T6 points of time, that means the mean HR and mean arterial pressure increased in Group C after laryngoscopy and tracheal intubation in comparison to Group M [Figures 1 and 2]. At T0, T1, T2 time points (i.e., in pre-intubation period), the mean HR and

Table 1: Demographic data of the two groups

Parameter	Group C (*n*=34)	Group M (*n*=34)	*P*
Gender (male/female)	11/23	14/20	0.451
Age (years)	44±8	47±9	0.167
Weight (kg)	57±9	60±9	0.182
Height (cm)	156±7	156±8	0.719
BMI (kg/m²)	23.6±4.3	24.8±3.5	0.189

BMI – Body mass index

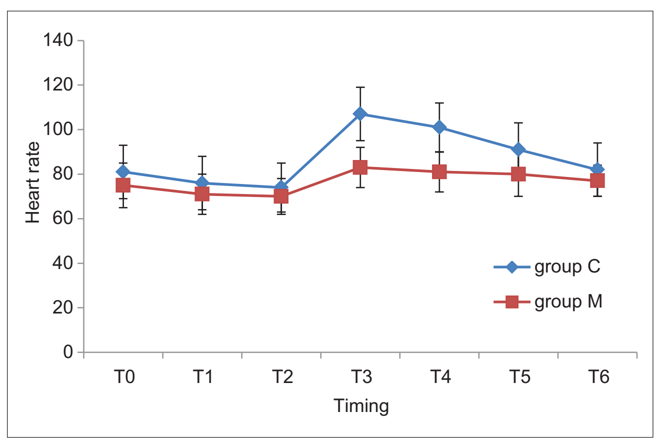

Figure 1: The mean heart rate in the two groups. T0 – Before shifting the patient to OT table (baseline data); T1 – Immediate after vecuronium administration; T2 – 1 min after vecuronium administration; T3 – After inflation of the cuff following intubation; T4 – 1 min after intubation; T5 – 3 min after intubation; T6 – 5 min after intubation. Error bars are showing standard deviations of the data

mean arterial pressure were comparable among two groups ($P > 0.05$) [Figures 1 and 2]. Intragroup analysis shows both in Group C and M, following intubation there was statistically significant rise of HR and mean arterial pressure. However, extent of rise of HR and mean arterial were significantly lower in neuromuscular monitoring group than the control group.

The mean time from administration of neuromuscular blocking agent and tracheal intubation was significantly higher in Group M as compared to Group C ($P < 0.0001$) [Table 2]. BIS values were comparable among two groups ($P > 0.05$) at different points of time. The CL grading was more favourable in Group M as compared to Group C ($P = 0.001$) [Table 2]. The intubating score was better in Group M as compared to Group C ($P = 0.002$) [Table 2].

DISCUSSION

We observed from the study that the neuromuscular monitoring-based timing for tracheal intubation causes lesser haemodynamic surge as compared to clinical-based timing for tracheal intubation. Furthermore, the intubating condition and laryngeal view was better in the group, wherein timing of laryngoscopy was guided by neuromuscular monitor as compared to conventional clinical assessment-based timing.

Table 2: Study parameters in the two groups

Parameters	Group C	Group M	*P*
Mean time from administration of neuromuscular blocking agent and tracheal intubation (s)	175±7 s	385±101	<0.0001
CL grading (1:2:3:4) (*n*)	24:10:0:0	32:2:0:0	0.001
Intubating condition (score 3:4:5) (*n*)	19:5:10	29:5:0	0.002

Intubation condition score 3 and 4 are considered as favourable intubation condition. CL – Cormack–Lehane

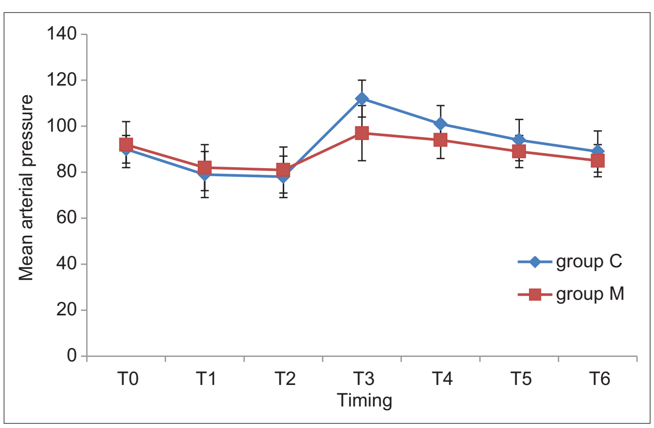

Figure 2: The mean arterial pressure in the two groups. T0 – Before shifting the patient to OT table (baseline data); T1 – Immediate after vecuronium administration; T2 – 1 min after vecuronium administration; T3 – After inflation of the cuff following intubation; T4 – 1 min after intubation; T5 – 3 min after intubation; T6 – 5 min after intubation. Error bars are showing standard deviations of the data

Laryngoscopy and endotracheal intubation can cause striking changes in haemodynamics and intracranial pressure, probably as a result of intense sympathetic nervous system stimulation. Various techniques using various pharmacological agents are reported to attenuate these cardiovascular responses.[9,10] The effect of these drugs may persist even after the stimulus of laryngoscopy and tracheal intubation ceases, and thus, causes subsequent haemodynamic fluctuation. Here lies the importance of a non-pharmacological measure to prevent this surge. Many studies have already shown that this haemodynamic response also depends on the duration of laryngoscopy and intubation as well as ease of the procedure.[3,4] Therefore, achievement of adequate neuromuscular blockade with a muscle relaxant is of utmost importance to avoid undue stimulation of sympathoadrenergic system. Thus, assessment of complete neuromuscular blockade appears to be necessary for proper timing of intubation. Assessment of complete paralysis was done by observing the response to TOF stimulation. When the TOF count becomes zero it can be said that the laryngeal muscles are completely paralysed. In this study, in the neuromuscular monitoring group (M), intubation was performed when the TOF watch showed "zero count" following TOF electrical stimulation.

The laryngoscopy and subsequent endotracheal intubation induce strong nociceptive stimuli resulting numerous responses for example, motor response, characteristic electroencephalographic evidence of central nervous system stimulation or stimulation of the sympathetic nervous system manifested by increased arterial pressure and accelerated HR.[11,12] In our study, patients intubated by clinical judgment showed higher mean values of mean arterial pressure and HR during and after intubation in comparison to the patients who were intubated under guidance of neuromuscular monitoring ($P < 0.05$). It seems that in patients with incomplete neuromuscular block, laryngoscopy and intubation cause stronger nociceptive stimulation, hence a stronger reflex cardiovascular reaction. The previous studies showed that if neuromuscular block monitoring technique is used to find out the timing for tracheal intubation, more time gap would be available between neuromuscular blockade administration and tracheal intubation. It also improves intubation conditions and minimises cardiovascular responses.[6] In a study, the two techniques of tracheal intubation using clinical assessment and neuromuscular monitor-based timing with cisatracurium was assessed.[6] They concluded that neuromuscular block monitoring following neuromuscular blockade administration prolongs the endotracheal intubation time, improves intubation conditions and minimises cardiovascular reactions in comparison to clinical assessment. In that study, the mean time for intubation was 162.3 ± 35 s (mean ± SD) in patients under clinical monitoring group and 339.3 ± 73.7 s (mean ± SD) in patients under neuromuscular monitoring group.[6] In our study, we used vecuronium as muscle relaxant and the result was found in the same direction like the previous study. Another study showed that clinical judgment underestimated the time required for adequate onset of action of vecuronium, resulting in less favourable intubating condition.[5] In that study,[5] the trachea was intubated after either vecuronium or rocuronium administration on the basis of clinical judgement of jaw and airway tone and the ease of the ventilation. At the same time, twitch height in comparison to baseline value was measured. Patients who received vecuronium showed median twitch height value of 8% when laryngoscopy was attempted, whereas the patients who received rocuronium showed median twitch height of 0% when laryngoscopy was attempted. That means after vecuronium administration, on the basis of clinical assessment, anaesthesiologists attempt laryngoscopy when complete relaxation was not achieved. However, in case of rocuronium, complete relaxation is usually achieved when laryngoscopy was attempted on the basis of clinical judgment. In our study, we also found that monitoring of neuromuscular block substantially prolonged the time between vecuronium administration and intubation. Furthermore, there was a wide variation of intubation time in neuromuscular monitoring group as compared to conventional clinical-based group. As in the control group, anaesthesiologist intubate following clinical judgment, this similarity in intubation time in this group may be due to their habits in day-to-day practice.[13,14]

In our study, the values of BIS index found in both groups of patients were comparable. Hence, the impact of awareness or sedation status on the intergroup haemodynamic differences appears to be comparable. Adductor pollicis muscle was chosen to monitor the neuromuscular block in our study. It is reported that in the orbicularis oculi muscle, TOF count becomes zero more faster than the adductor pollicis muscle after administration of neuromuscular blocking drugs.[15,16] As a result, early intubation can be performed if orbicularis oculi muscle was chosen for monitoring. However, in some patients, unsatisfactory intubation conditions were found. It has also been reported that when adductor pollicis monitored for tracheal intubation, more favourable intubation condition is observed in all patients.[6,17,18] As the favourable intubation condition helps to reduce the haemodynamic surge, adductor pollicis muscle was chosen for monitoring in this study. Furthermore, being a peripheral muscle it is easier to monitor.

We observed more satisfactory intubating conditions in neuromuscular monitoring guidance as compared to clinical judgment. In the monitoring group, anaesthesiologist found intubation score 3 or 4 (excellent or good intubation conditions) in all the 34 patients. However, in the control group, only 24 patients (70%) among 34 patients had good or excellent intubation condition. Hence, excellent intubation conditions were observed in all patients when the moment of intubation was chosen after complete loss of the reaction to TOF stimulation, assessed visually and also by acceleromyography. Literature reports, 95% to 100% of patients were provided with excellent intubation conditions using the same assessment of the reaction to supramaximal TOF stimulation of the ulnar nerve.[6,17] Thus, this method seems suitable to ensure optimal conditions for intubation in the majority of cases.

In a recent study,[19] endotracheal intubation was performed after TOF count became zero in orbicularis oculi muscle after vecuronium administration. They found the mean for onset of action of vecuronium to be 116.66 ± 55.37 s but in only 70% of patients they found favourable intubation condition. In our study, in the clinical group, intubation was tried after an average of 175 s after vecuronium administration and favourable intubation conditions were found in 70% of patients. However, in the neuromuscular monitoring group, where intubation was tried after an average of 385 s of vecuronium administration, favourable intubation condition was found in 100% of patients. Neuromuscular monitoring of adductor pollicis muscle is one of the important reasons for getting longer time gap between vecuronium administration and intubation attempt in the neuromuscular monitoring group in our study.

Using neuromuscular monitor during endotracheal intubation is not a common practice among anaesthesiologists. It is mainly used for muscle relaxation monitoring during operative procedure and to diagnose any residual paralysis at the end of the procedure. Hence, more research in neuromuscular monitoring during intubation is required. A limitation of the study is that the time gap between fentanyl administration and endotracheal intubation is different in two groups. This may have contributed to the difference in haemodynamic response in the above-mentioned groups.

CONCLUSION

The haemodynamic responses to laryngoscopy and tracheal intubation can be significantly attenuated if tracheal intubation is done following complete paralysis of laryngeal muscles, detected by neuromuscular block monitoring of adductor pollicis muscle as compared to conventional time-based clinical assessment. Furthermore, intubating conditions are improved when endotracheal intubations were attempted following neuromuscular monitoring.

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Conflicts of interest

There are no conflicts of interest.

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