Comparison of Effect of Ephedrine and Priming on the Onset Time of Vecuronium

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Abstract

Background: Succinylcholine has been the neuromuscular blocking drug of choice for laryngoscopy and intubation, but it has several adverse effects. Nondepolarizing neuromuscular blocking drugs are good alternative provided their onset of action is hastened. Priming technique and use of ephedrine or MgSO\textsubscript{4} pretreatment is good options. Aims: To compare the effects of priming and ephedrine pretreatment on the onset time of intubating dose of vecuronium. Settings and Design: A prospective, randomized comparative study was done at a state-owned tertiary care teaching hospital. Materials and Methods: After obtaining the Institutional Ethical Committee approval and written informed consent, sixty patients of either gender aged 18–60 years, the American Society of Anesthesiologists physical status Class I/II, weighing 40–70 kg, were randomly divided into two groups of thirty each. Group E received 70 µg/kg ephedrine, and Group P received 0.01 mg/kg of vecuronium 3 min before intubating dose of vecuronium. Intubation was done after getting a train of four zero. Intubation time, clinical intubation grade using Cooper’s scale, and hemodynamic parameters were noted. Statistical Analysis Used: Chi-square test and independent t-test were done with PASW statistics 18 to analyze data. Results: The mean time for intubation in ephedrine group (E) was 104 ± 23.282 s and in the priming group (P), it was 142 ± 55.671 s (P = 0.001). All patients had clinically acceptable intubating conditions, and the grades were comparable among groups (P = 0.791). Hemodynamic parameters were comparable between groups at all time frames (P > 0.05). Conclusion: Pretreatment with ephedrine 70 µg/kg shortens the onset time of vecuronium for intubation and is superior to the priming technique. Low-dose ephedrine, when used along with propofol induction, provides hemodynamic stability during induction and intubation.

Keywords: Endotracheal intubation, ephedrine, intubating conditions, priming, vecuronium

Introduction

Traditionally, succinylcholine has been the neuromuscular blocking drug of choice for laryngoscopy and tracheal intubation. It is the gold standard in the rapid sequence induction and intubation, but it is not without adverse effects.\textsuperscript{11} Succinylcholine can produce bradycardia, myalgia, hyperkalemia, raised intracranial, intraocular, and intragastric pressures among others. Nondepolarizing neuromuscular blocking drugs are without many of these side effects. However, these drugs have a slow onset of action making the patient vulnerable to regurgitation and aspiration between induction and intubation. Various methods have been used to shorten the onset time of nondepolarizing neuromuscular blocking drugs which include use of higher dose, priming, improving cardiac output and thereby muscle blood flow, use of magnesium sulfate, etc. Use of higher doses of neuromuscular blocking drugs and MgSO\textsubscript{4} hastens the onset of neuromuscular blockade at the risk of prolonged duration of action and delayed recovery.\textsuperscript{[2]} Priming is a popular technique to facilitate the faster onset of neuromuscular blockade for endotracheal intubation.\textsuperscript{[3-5]} Ephedrine, a synthetic noncatecholamine sympathomimetic, increases the cardiac output and muscle blood flow and hence shortens the onset of action.\textsuperscript{[6]}

In a meta-analysis of pharmacological interventions for acceleration of the onset time of rocuronium, it was found priming technique and pretreatment with MgSO\textsubscript{4} or ephedrine was found to be effective.\textsuperscript{[7]} However, similar studies on vecuronium, one of the most commonly used nondepolarizing

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**Materials and Methods**

After obtaining the Institutional Ethical Committee approval and written informed consent, sixty patients of either gender, aged 18–60 years, the American Society of Anesthesiologists (ASA) physical status Class I/II, weighing 40–70 kg, scheduled for elective surgery under general anesthesia, were recruited for the study. They were randomly allocated into two groups of thirty each based on group assigned by a random number generating software. Sample size selection was done from a previous study by power analysis. Patients with difficult airway or having history of any drug intake, which are likely to interfere with the action of neuromuscular blocking agents were excluded from the study. Patients were warned of possible symptoms of muscle weakness, after priming doses of vecuronium, which includes difficulty in breathing and swallowing, double vision, and decreased hand grip strength.

All patients were premedicated with intravenous glycopyrrolate 5 μg/kg, midazolam 50 μg/kg, morphine 0.1 mg/kg, and ondansetron 10 μg/kg. Standard monitoring included heart rate (HR), electrocardiogram, noninvasive blood pressure mean arterial pressure (MAP), pulse oxymetry, end-tidal carbon dioxide, and neuromuscular transmission monitor. For elicitation of train of four (TOF), the ulnar nerve contralateral to the intravenous fluid administration was selected. After adequate preparation of the area, surface electrodes were applied over the volar aspect of the wrist along the course of ulnar nerve. The negative electrode was placed about one centimeter proximal to the proximal wrist crease, and the positive electrode was placed about three to four cm proximal to the first one. Control TOF was recorded with a supramaximal stimulus of 0.2 ms duration administered at a frequency of 2 Hz. Baseline HR and MAP were recorded before the induction of anesthesia.

After preoxygenation with 100% oxygen, patients received either 70 μg/kg of ephedrine or priming dose of vecuronium (0.01 mg/kg), prepared by an anesthesiologist who was not involved in the further assessment of patient. Induction of anesthesia was done with intravenous propofol 2 mg/kg over 20 s. The depth of anesthesia was maintained using oxygen and isoflurane (0.6%–1%). Three minutes after ephedrine or priming dose, intubating dose of vecuronium (0.09 mg/kg) was given. The response of adductor pollicis (AP) stimulation using TOF was recorded every 30 s until the response to the same became zero. Patients were then intubated.

The time taken to obtain zero response to TOF stimulation after intubating dose of vecuronium was taken as the duration of onset of vecuronium. Intubation was done with 7–7.5 mm internal diameter (ID) endotracheal tube for females and 8–8.5 mm ID endotracheal tube for males. The clinical intubating condition was assessed by Cooper’s criteria using three parameters, namely, jaw relaxation, vocal cord movement, and gross response of the patient to laryngoscopy and intubation [Table 1]. Patient’s HR and MAP were recorded immediately before intubation, and then after intubation, at 1 min interval up to 5 min for any hemodynamic disturbances. A variation of 20% from the baseline was considered as statistically significant.

Statistical analysis was done using PASW Statistics 18 (Chicago, SPSS Inc.). Pearson’s Chi-square test was used for the comparison of demographic data. Independent t-test was used for comparing age, weight, time to intubation, HR, and MAP at various time intervals between the groups.

**Results**

The two groups were comparable with respect to age, sex, ASA status, and weight [Table 2]. The mean time to intubation in ephedrine group (E) was 104 ± 23.282 s and in the priming group (P), it was 142 ± 55.671 s (P = 0.001). In the Group E (n = 30), 13 patients (43%) attained TOF ratio zero within 90 s, and 29 patients (97%) had TOF zero by 120 s. In the Group P (n = 30), only five patients (17%) had a TOF zero at 90 s, 14 patients (47%) at 120 s, and five patients (17%) took 180 s or more to attain a TOF zero [Figure 1]. In Group E, the intubating conditions were excellent in 11 patients (37%) and good in 19 patients (63%). In Group P, the intubating conditions were excellent in 12 patients (40%) and good in 19 patients (60%), and the intubation grades were comparable between groups (P = 0.791).

There were no significant changes in HR and MAP in either group and were comparable between groups at all time frames (P > 0.05) [Figures 2 and 3]. No patient had desaturation, arrhythmia, or any symptoms related to muscle weakness.

**Discussion**

The airway of the anesthetized patient is unprotected and very vulnerable to aspiration. Hence, securing the airway at the

### Table 1: Cooper’s scoring for grading intubation

| Score | 0          | 1                | 2                | 3                |
|-------|------------|------------------|------------------|------------------|
| Jaw relaxation | Poor | Minimal | Moderate | Good |
| Vocal cords position | Closed | Closing | Moving | Open |
| Response to intubation | Severe coughing, bucking | Mild coughing | Light diaphragm movements | No movement |

Total score of 8–9 was considered excellent, 6–7 good, 3–5 poor and 0–2 bad; good and excellent were taken as clinically acceptable.
The rate of onset of neuromuscular blockade in any one individual is influenced by several factors, such as the potency of the drug, the dose administered, and the cardiovascular status, including cardiac output and muscle blood flow. Thus, an increase in cardiac output and muscle blood flow at the moment of induction could lead to faster onset of neuromuscular blockade. Ephedrine is a weak, indirect, and direct-acting sympathomimetic agent that produces vasoconstriction to a greater degree than arteriolar constriction, which improves venous return and increases cardiac output.

The present study supports the effect of ephedrine in shortening the onset time of neuromuscular blocker vecuronium. The use of ephedrine did not produce tachycardia or hypertension in our study, probably due to the obtunding effect of induction dose of propofol on the sympathetic nervous system. This finding is consistent with earlier studies where ephedrine 70 μg/kg shortened the onset time of vecuronium and...
Atracurium without hemodynamic effects.\cite{8,12} Higher doses of ephedrine caused tachycardia and hypertension.\cite{12-14} Hypotension and bradycardia that may occur with propofol induction were also not found in the current study. Ephedrine pretreatment may effectively counter the hypotensive effect of propofol induction.\cite{15,16} However, in another study of 100 patients, pretreatment with ephedrine, either 75 or 100 μg/kg improved the intubating conditions during rapid tracheal intubation using propofol and rocuronium, but contrary to the above-mentioned studies, it was not effective in preventing the hypotension which follows induction of anesthesia with propofol.\cite{13}

All the patients in the current study had clinically acceptable intubating conditions. In a previous study, clinically acceptable intubating conditions were produced in 100% of cases with low-dose ephedrine along with priming when attempted 1 min after loading dose of atracurium, whereas it was only in 52% when ephedrine or priming technique was used alone.\cite{17} The fact that we monitored TOF at AP, which has a slower onset time compared to central muscles orbicularis oculi (OO) or corrugator supercilii (CS), might have contributed to 100% of cases giving the clinically acceptable intubation grades.

TOF at AP, OO, and CS do have variability with respect to clinical intubating conditions.\cite{18,19} The laryngeal muscles have a faster onset and early recovery compared to AP with neuromuscular blocking drugs.\cite{20} Monitoring the onset of neuromuscular block in the CS can predict the presence of good or excellent intubating conditions earlier than the use of AP. Though OO monitoring showed the shortest onset time, it was not clinically useful as there was an unacceptable incidence of inadequate intubating conditions. CS provide the best balance by shortening the onset time as well as maintaining the 100% incidence of good or excellent intubating conditions.\cite{21} The CS and not the OO has a sensitivity similar to that of the laryngeal adductor muscles because of the similarity in their muscle fiber types.\cite{21,22} Another study also found OO monitoring predicting good intubating conditions when compared with AP after vecuronium in children.\cite{19}

Cardiac output monitoring was not done in our study to correlate the faster onset rendered by ephedrine compared to the priming technique. It was demonstrated that the increase in cardiac output with ephedrine facilitated the faster onset of rocuronium when compared with esmolol.\cite{23} However, in another study, the improved cardiac output by ephedrine failed to demonstrate a faster onset of intubation time of vecuronium.\cite{24} The authors have even concluded that the onset of the vecuronium-induced neuromuscular block is primarily determined by factors other than cardiac output. This may be because of their method, administration of vecuronium after 11 min of stable propofol anesthesia to standardize the duration of ulnar nerve stimulation, which might have caused depressed hemodynamic conditions. Further studies may be done with cardiac output monitoring and our findings, the effect of ephedrine pretreatment on the onset time of vecuronium, may be reestablished.

**Conclusion**

Pretreatment with ephedrine 70 μg/kg shortens the onset time of vecuronium for endotracheal intubation and is superior to the priming technique. Low-dose ephedrine, when used along with propofol induction, provides hemodynamic stability during induction and intubation.
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Conflicts of interest
There are no conflicts of interest.

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