ORIGINAL ARTICLE

The Effect of Bolus Dose of Ephedrine on the Onset Time of Vecuronium

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ABSTRACT

Objective: To evaluate the effect of ephedrine on the onset time of vecuronium
Study design: Interventional experimental study.
Setting: Department of Anesthesiology, Bhatti International Hospital attached to Central Park Medical College, Lahore
Duration of study: Study was carried out over a period of six months from 22-1-2012 to 21-7-2012.
Materials and methods: Sixty adult male patients presenting for general surgical procedures under general anesthesia in the operation theatre of Bhatti international hospital were allocated into two groups using random number table. 30 patients each group (ephedrine group and saline group).
Results: Mean age was observed 35.5±4.3 and 35.9±5.2, in group A and B, respectively. Excellent intubating conditions were in 15 patients (50.0%) in group-A, and 10 patients (33.33%) in group B while good intubating conditions found in 15 patients (50%) in group A and 17 patients (56.7%) in group B. poor conditions were found in 3 patients (10%) in group B. ASA classification showed 20 patients (66.7%) in group A and 18 patients (60%) in group B belong to ASA-I, while 10 patients (33.33%) in group A and 12 patients (40%) in group B were ASA-II. Mean values of onset time 120.0±9.6 and 170±27.1 in group A and B, respectively. The difference between two groups was statistically significant (P<0.001).
Conclusion: Ephedrine 70ug/kg given before the induction of anesthesia improved intubating conditions at 2 min after vecuronium by increasing cardiac output without significant adverse hemodynamic effects.
Key words: Intubation, bolus dose, ephidrine

INTRODUCTION

Circulatory factors including muscle blood flow and cardiac output affect the onset of action of muscle relaxants. The onset of neuromuscular blockade usually determines the period from the neuromuscular blocker induction to tracheal intubation. Routinely we use suxamethonium for rapid induction but it causes many side effects such as myalgias etc[1]. Various strategies have been developed to shorten the onset time of muscle relaxation by non-depolarizing muscle relaxants, including increasing the dose, priming and combination of drugs. Ephedrine may also reduce the onset time of muscle relaxants (NMBs)[2]. However ephedrine might be associated with adverse hemodynamic effects. The appropriate dose of ephedrine has not been determined[3].

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Although the mechanism of the response to vecuronium may be controversial[4] ephedrine in combination of propofol significantly improved clinical intubating conditions at 30 seconds following priming with vecuronium compared without priming[5]. Use of priming dose, however, has produced condition suitable for intubation within 90 seconds following vecuronium. It is important to keep in mind that muscle groups vary in their sensitivity to muscle relaxants. The onset of action is influenced among other factors by the rapidity with which neuromuscular blockers are delivered to the synaptic cleft. Szmuk[6] reported a significant reduction or prolongation of the onset time of vecuronium in patients pretreated respectively, with ephedrine esmolol whereas Ezri et al[7] demonstrated that comparable reductions or prolongations of onset time were coupled respectively following administration of ephedrine or esmolol. Vecuronium is a monoquatemary relaxant, the intubating dosee is 0.08-0.12mg/kg[8].

Shah reported a series of hundred cases of children in whom tracheal intubation without neuromuscular blockade was possible[9].

This study was carried out to evaluate the effect of a bolus dose of ephedrine on the onset time of vecuronium. By increasing cardiac output and muscle blood flow, a bolus of ephedrine accelerated the onset of non-polarizing neuromuscular blocker vecuronium by promoting its delivery to its site of action. Enhancing the onset of action of vecuronium in this way, we tried to find an alternative of suxamethonium for rapid sequence endotracheal intubation in emergency procedure to prevent the side effects of suxamethonium.

MATERIALS AND METHODS

This interventional experimental study was carried out in the Department of Anesthesiology, Bhatti International Hospital attached to Central Park Medical College, Lahore from 22-1-2012 to 21-7-2012. Sixty adult patients presenting for general surgical procedures under general surgical anesthesia in the operation theatre of Bhatti International Hospital were allocated into two groups using random numbers table. 30 patients each group (ephedrine and saline group). Sampling echnique was non-probability convenience sampling. ASA I and II male patients between 20-44 years of age were included in the study. Patients with cardiovascular disease and cardiovascular medications, chronic obstructive pulmonary disease and respiratory tract infections, neuromuscular disease, metabolic and endocrine diseases were excluded.

Data collection procedure: Sixty adult patients undergoing general procedures fulfilling the inclusion and exclusion criteria were included. An informed consent was taken explaining the merits and demerits of the study. Patients were randomly allocated into two groups, Group A (ephedrine and vecuronium) and Group B (vecuronium and saline) using random numbers table- thirty patients in each group were selected. During preoperative visits, their detailed history, physical examination (general physical examination, cardiovascular system examination, respiratory tract examination) and laboratory investigation (blood complete examination, urine complete examination and serum electrolytes) were reviewed. On the day of operation patients were premedicated with midazolam 0.05mg/kg and nalbuphine 0.1mg/kg intravenous about 10 minutes before induction. Monitoring equipment (NIPB, $ETCO_2$, SpO_2, ECG) were applied. ASA-I and ASA-II patients were induced with propofol 2.5mg/kg who received either ephedrine (70ug/kg prepared in volume of 2ml) along with vecuronium 0.1mg/kg or equal volume of 2ml saline along with vecuronium 0.1mg/kg just after propofol injection. Airway was maintained by bag and mask ventilation with 50% O2 in N2O. The anesthesiologist performing the induction of anesthesia was blinded to the study doses of the drug (ephedrine).Tracheal intubation after vecuronium injection was performed by a skilled anesthesiologist blinded to group assignment. Intubating conditions were treated by the intubator as excellent (jaw relaxed, vocal cords immobile and no diaphragmatic movements), good (jaw relaxed, vocal cords immobile and some diaphragmatic movements), poor (jaw relaxed, vocal cords moving bucking and coughing), or inadequate (jaw relaxed, vocal cords closed).

The neuromuscular blockade monitoring was started 2 minutes before the administration of study drug on the contralateral arm to the intravenous line by using nerve stimulator of the adductor pollicis to a train-of-four at 10 seconds interval with submaximal current. The resulting conditions were recorded. The onset time was depending as the time from the end of injection of vecuronium to maximal depression of the first twitch of train-of-four stimulation. The presence of arrhythmias on the ECG was noted. Since the number of patients was randomized by using random numbers table, the effects of the confounding variables got eliminated. All that information was recorded on a predesigned performa.

Data analysis: Data was entered and analyzed by SPSS version 11.0. Descriptive statistics was calculated. Mean$\pm$SD was calculated for age, weight, pulse, blood pressure, temperature, height and onset time. Percentages were calculated for sex, ASA classification and diagnosis. The difference between the mean onset time of each group was compared by using independent student “t” test. P value $\leq$0.05 was taken as significant.

RESULTS

During the study period of 6 months, total 60 patients were included in the study. They were allocated in two groups of the 30 patients in each group. Group-A received ephedrine + vecuronium and Group-B received saline and vecuronium. The patients included in this study were 18 to 45 years of age. In group-A, the highest number of patients were between 20-40 years of age contributing 20 patients (66.6%) while in group-B, there were also 20 patients (66.6%) between 20-40. Mean age was observed 35.5+4.3 and 35.9+5.2, in group A and B, respectively (Table 1).

ASA classification showed 20 patients (66.7%) in group A and 18 patients (60%) in group B belong to ASA-I, while 10 patients (33.33%) in group A and 12 patients (40%) in group B were ASA-II (Table 2).

Excellent intubating conditions were in 15 patients (50.0%) in group-A, and 10 patients (33.33%) in group B while good intubating conditions found in 15 patients (50%) in group A and 17 patients (56.7%) in group B. Poor conditions were found in 3 patients (10%) in group B. (Table 3).

Table 4 depicts mean values of onset time 120.0+9.6 and 170.0+27.1 in group-A and B, respectively. The difference between two groups was statistically significant (P< 0.001).

Table 1: Distribution of cases by age (n=60)

Age (yrs)	Group-A(n=30) (ephedrine+Vecuronium)	Group-B (n=30) (Saline+ Vecuronium)
<20	05(16.7%)	05(16.7%)
20-30	10(33.3%)	08(26.6%)
31-40	10(33.3%)	12(40%)
≥41	05(16.7%)	05(16.7%)
Total	30(100%)	30(100%)
Mean±SD	35.5±4.3	35.9±5.2

Table 2: Distribution of cases by ASA classification (n=30)

ASA Classification	Group-A (n=30) (ephedrine+Vecuronium)	Group-B (n=30) (Saline+ Vecuronium)
I	20(66.7%)	18(60%)
II	10(33.3%)	12(40%)
Total	30(100%)	30(100%)

Chi Square=0.29, df=1, P value=0.592

Table 3: Distribution of cases by Intubating conditions

Intubating conditions	Group-A (n=30) (ephedrine+Vecuronium)	Group-B(n=30) (Saline+ Vecuronium)
Excellent	15(50%)	10(33.3%)
Good	15(50%)	17(56.7%)
Poor	-	03(10%)
Total	30(100%)	30(100%)

Chi Square=4.13, df=2, P value=0.127

Table 4: Distribution of cases by onset time (minutes)

Onset time	mean	Standard deviation
Group-A (n=30) (ephedrine+Vecuronium)	120.0	9.6
Group-B (n=30) (Saline+Vecuronium)	170.0	27.1

T value= -9.480, Df=58, P value=<0.001

DISCUSSION

The circulating time to the target organ and its blood flow partly determines the onset time of the neuromuscular block for example, onset time is faster when a neuromuscular blocking drug is injected directly into the pulmonary artery rather than into a peripheral vein[10].

Similarly, neuromuscular block is especially rapid in highly perfused muscles.[11] both circulation time and blood flow depend on cardiac output, a variable confirmed to be a primary determinant of the onset time of the neuromuscular blocker succinylcholine[12]. Ephedrine increase leg blood flow and leg muscle oxygen consumption[13].

Similarly i/v ephedrine increases cardiac output with a decrease in total peripheral and forearm's vascular persistence[14]. There findings thus indicate that the increased cardiac output caused by ephedrine is accompanied by increase in the muscle blood flow of the extremities.

In this study it is observed that ephedrine 70ug/kg could improve intubating conditions two minutes after vecuronium. The rapid onset of vecuronium was attributed to an increased cardiac output. Previous studies with vecuronium have demonstrated a significant reduction in onset time with the use of priming dose before the administration of the intubating dose and increased dose[15,16].

Although there alternatives could reduce the onset time vecuronium some could lead to adverse effects such as development of muscle weakness, loss of airway control[17] or increased duration of neuromuscular blockade[18].

In present study, it is suspected that pretreatment with ephedrine 70ug/kg reduces the onset time of vecuronium by almost 30%. The mean onset time of group A (ephedrine and vecuronium) in 30 patients was 120.0 + 9.6 seconds, while the mean onset time of group B (saline and vecuronium) 170.0 + 27.1. The difference between two groups was statistically significant (P< 0.001).

When I compared the results of current study with the study carried out by Munoz et al in which it was observed that ephedrine 70ug/kg reduces the onset time of rocuronium from 98 to 72 seconds[19] and reduced the onset time of cisatracurium from 234.9 to 167 seconds[20].

In this study it was observed that pretreatment with ephedrine 70ug/kg reduced the onset time of vecuronium by 23% was equally as effective as priming with vecuronium 0.01mg/kg and was certainly safer. It is also suspected that pretreatment with ephedrine is applicable to other competitive antagonists to reduce the onset time.

Ephedrine in doses of 70,120, 210 and 280ug/kg is very effective at obtunding the hypotensive response to propofol[21,22]. Marked tachycardia and hypertension associated with the use of ephedrine in combination with propofol after tracheal intubation occurred in most patients. Because of the risk of this tachycardia-induced myocardial ischemia, the use of any of the ephedrine/propofol mixture is not recommended for elderly patients[23]. It is also found

that ephedrine 110ug/kg was associated with marked hypertension and tachycardia (30% and 32% more than control, respectively) at one minute after intubation. An appropriate dose of ephedrine (70ug/kg) should be used to minimize the adverse effects and reduce the onset time of vecuronium.

Another study was done in the department of Anesthesiology, Tokyo Women's Medical University Tokyo, Japan[5], in which it was observed that ephedrine increased cardiac index and caused a considerable increase in blood pressure. However, ephedrine failed to accelerate the onset time of vecuronium neuromuscular blockade. The combination of ephedrine and vecuronium thus cannot be substituted for rapid acting non-depolarizing muscle relaxants. Results of current study not agree with this. The limitations of this study were that vecuronium was administrated after 11 minutes of stable propofol anesthesia to standardize the duration of control ulnar nerve stimulation.

Hemodynamic conditions at the administration of vecuronium in this study were depressed. Therefore, these results might not be applicable in the typical clinical situation in which vecuronium is given just after propofol administration at induction, when blood pressure at cardiac index are substantially higher than during our study condition. In addition, the effect of ephedrine could be different if it was given at induction with propofol.

Another study which was done in Italy by Leykin et al[2] in which it was observed that combination of ephedrine and propofol significantly improved clinical intubating conditions 30sec after priming with ,rocuronium compared to without priming and propofol alone.

Neuromuscular testing in awake patients is further limited by patient discomfort. The use of less painful submaximal stimulating currents may facilitate neuromuscular monitoring[24].

TOF ratios obtained at submaximal current correlate highly with those at supramaximal current[25]. The reliability of submaximal current at 20mA suggests that could deliberately use a low amperage, for evaluating the degree of neuromuscular block in awake patients[26]. Therefore, generally use submaximal current (20mA).

In present study, although, severe adverse effects were not found after the administration of ephedrine in healthy patients, incidence of adverse effects might be more frequent in patients with cardiovascular disease or with use of a different induction technique.

CONCLUSION

In conclusion, ephedrine 70ug/kg given before the induction of anesthesia improved intubating conditions at 2 min after vecuronium by increased cardiac output without significant adverse haemodynamic effects.

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