

Intubating Conditions Under Non-Depolarizing Muscle Relaxants – A Comparative Study

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ABSTRACT

Introduction: In conditions like significant burns, traumatic injuries or an abdominal infection succinylcholine administration could be hazardous as it is associated with dangerous hyperkalemia. Vecuronium, atracurium and Pancuronium not only are the alternatives but also offer skeletal muscle relaxation at shortest intervals post-intubation. We assessed the intubating conditions achieved and the hemodynamic effects of pancuronium, vecuronium, and atracurium among patients undergoing routine surgical procedures requiring general anaesthesia.

Material and methods: A prospective randomized trial was carried out among 60 participants aged 15-56, who were in the good physical condition and belonged to ASA I or ASA II categories. Study was conducted at Civil Hospital, Aizawl, Mizoram. The patients were randomly allocated to 3 groups of twenty each viz, Group A, Group B and Group C. Following induction of anaesthesia Inj. Pancuronium bromide 0.1 mg/kg. was given to Group A; Inj. Vecuronium 0.1 mg/kg to Group B. and Inj. Atracurium 0.6 mg/kg to Group C. Pulse rate and blood pressure were recorded immediately and time interval after intubation.

Results: The apnoea time was longest in group A (57±7 seconds) followed by group C (50±14 seconds) and group B (49±8 seconds). The mean pulse rate, however, varied significantly post-intubation across the three groups. The intergroup comparison showed a significantly higher rise of the mean arterial pressure in group A compared with group B at all corresponding tie intervals in the post intubation period.

Conclusion: Though all the three skeletal muscle relaxants provided adequate intubating conditions, Vecuronium offered the shortest intubation time while the Pancuronium took the longest time.

Keywords: Abdominal Infection, Intubating, Muscle Relaxants, Non-Depolarizing

Muscle relaxants belong to two groups, the depolarizers, and the non-depolarizers. Depolarizers mimic the effect of acetylcholine at the neuromuscular junction, first causing muscle contractions (fasciculations) and then paralyzing.⁶⁻⁸ Suxamethonium commonly called succinylcholine is a short-acting depolarizing neuromuscular blockade and its use can expedite rapid endotracheal intubation, facilitate surgical procedures, and aid in mechanical ventilation by relaxation of skeletal muscles. Due to its rapid onset and short mechanism of action, it is the drug of choice in emergency situations where immediate airway management is required.^{9,10}

However, certain conditions like significant burns or traumatic injuries that are 24 to 72 hours' post-injury, neuromuscular disease, the abdominal infection may be associated with hyperkalemia following succinylcholine administration. Also, special considerations should be taken with those who have chronically elevated potassium levels such as renal failure patients, to not induce acute on chronic hyperkalemia. Marked and/or untreated hyperkalemia may result in dysrhythmias or even death.^{7,11}

In these situations, adequate skeletal muscle relaxation for tracheal intubation can be accomplished with either atracurium or vecuronium without the hazard of hyperkalemic-induced cardiac arrhythmias associated with succinylcholine and without the prolonged duration of action associated with large doses of currently available nondepolarizing muscle relaxants. Similarly, certain surgical procedures (e.g., laryngoscopy, esophagoscopy, bronchoscopy, etc.) may require profound relaxation of short duration. This is frequently accomplished with a succinylcholine infusion. However, the risk of producing a prolonged neuromuscular block (phase II block) is increased with an infusion or repeated injections of succinylcholine. In such situation, vecuronium or atracurium may provide an acceptable alternative because their durations of action are relatively short (less than 60 min) at doses producing

INTRODUCTION

The introduction of muscle relaxants into clinical anaesthesia 60 years ago has revolutionized the procedure of intubation in particular and the practice of the specialty in general for reasons that were not entirely obvious at the time.¹ Owing to the use of neuromuscular blocking agents, the dosage of concomitant drugs, and their cardiovascular effects, could be limited, immobility could be guaranteed during difficult surgical procedures, mechanical ventilation could be performed more efficiently, and sicker patients could get the benefit of surgery.² Anaesthesia was redefined as a triad of narcosis, analgesia and muscle relaxation, specific drugs being used to produce each of these effects.³⁻⁵

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profound skeletal muscle relaxation.¹²⁻¹⁴ Earlier high doses of pancuronium were tested by several investigators but was found to be an inadequate alternative to Suxamethonium.

Ideally, other muscle relaxants would exhibit fewer cardiovascular hemodynamic side effects, have fewer cumulative effects, possess rapid onset of and shorter durations of action, and be less dependent on hepatic and/or renal function for metabolism and excretion. Two non-depolarizing muscle relaxants, vecuronium, and atracurium are examples of drugs approaching these ideal muscle-relaxant characteristics. Thus the present study aimed to assess the intubating conditions achieved and the hemodynamic effects of pancuronium, vecuronium and atracurium.

MATERIAL AND METHODS

The present study was conducted at Civil Hospital, Aizawl Mizoram in the department of Anaesthesiology and Critical Care. The study was conducted between November 2018 to October 2019. The study was carried out among 60 patients of both genders aged between 15 to 56 years, who were undergoing various routine surgical procedures requiring general anaesthesia with endotracheal intubation.

All the patients were in the good physical condition and belonged to ASA I or ASA II categories. Excluded from the study were patients associated with anatomical factors that are likely to pose problems in the smooth conduction of tracheal intubation. Written consent was obtained from each patient prior to the administration of the drugs.

The patients were randomly allocated to 3 groups of twenty each viz, Group A, Group B, and Group C. Following induction of anaesthesia Inj. Pancuronium bromide 0.1 mg/kg body wt. was given to Group A patients; Inj. Vecuronium 0.1 mg/kg body wt. to Group B patients and Inj. Atracurium 0.6 mg/kg body wt. to Group C patients.

All patients were premedicated with inj. Atropine 0.01 mg/kg, inj. Pethidine 1-1.5 mg/kg and inj. Promethazine 0.5-0.75 mg/kg body weights intramuscularly 60-90 minutes before the induction of anaesthesia. Pulse and blood pressure were recorded just before the induction of anaesthesia. After preoxygenation of the patient with 100% oxygen for 3 minutes, anaesthesia was induced with 4-5mg/kg of thiopental sodium intravenously and the muscle relaxant under study was given after flushing the vein with saline.

The patients were then ventilated with 100% oxygen and intubation was attempted by a single investigator at predetermined intervals viz 1, 1.5, 2, 2.5, 3, 3.5, 4 minutes after the mid-point of muscle relaxant injection, in case a previous attempt was not a success, and in each patient, intubation was done only when the intubation conditions were excellent. The following observations were made and recorded in all cases.

Pulse rate and blood pressure were recorded immediately after intubation and again after 5 minutes when a steady state was reached and thereafter every 10 minutes for the next 30 minutes and the results were compared with the pre-induction values.

The time interval between the start of the injection of the relaxant and the time when the conditions for intubation were judged as most suitable and the tube is introduced into the trachea (intubation time) were recorded.

The time interval between the start of the injection the relaxant to the time of complete cessation of the respiration (apnoea time) was also recorded.

The intubating conditions were graded as excellent, good, fair and poor according to criteria of Young et al, and Krieg et al, 1980.¹⁸

Intubating conditions	Criteria
Excellent	Jaw well relaxed, vocal cords well abducted, Intubation easy.
Good	Jaw well relaxed, vocal cords abducted but contact with tube caused the movement. Intubation easy
Fair	Jaw relaxed, vocal cords abducted, moving but separated out. Intubation is possible.
Poor	Jaw not well relaxed, vigorous closure of glottic aperture on laryngoscopy and on the attempt to intubate, immediate passing of the tube not possible.

Other complications encountered during intubation were also recorded. The mean times to intubation were calculated for each relaxant group and their significance was estimated using the Z-test.

RESULTS

Among group A the mean pulse rate at pre-induction 0 min was 83.7 ± 14.3 BPM, it was 80 ± 6.6 in group B and it was 80.5 ± 13.5 . The difference in mean pulse rate at pre-induction 0 min across three groups was statistically not significant. (P-value 0.573). Among group A the mean pulse rate at immediate post-op was 99.3 ± 13.6 BPM, it was 90.8 ± 13.3 in group B and it was 95.6 ± 14.0 in group C. The difference in mean pulse rate at immediate post-op across three groups was statistically not significant. (P-value 0.151). Among group A the mean pulse rate at 5 min was 95.5 ± 11.4 BPM, it was 87.5 ± 12.1 in group B and it was 90.4 ± 13.3 in group C. The difference in mean pulse rate at 5 min across three groups was statistically not significant. (P-value 0.124). Among group A the mean pulse rate at 10 min was 92.3 ± 9.7 BPM, it was 83.9 ± 10.5 in group B and it was 89.7 ± 11.1 in group C. The difference in mean pulse rate at 10 min across three groups was statistically significant. (P-value 0.041). Among group A the mean pulse rate at 20 min was 91.6 ± 10.1 BPM, it was 79.8 ± 8.2 in group B and it was 87.6 ± 11.1 in group C. The difference in mean pulse rate at 20 min across three groups was statistically significant. (P-value 0.005). Among group A the mean pulse rate at 30 min was 88.4 ± 9.9 BPM, it was 76.9 ± 6.7 in group B and it was 85.8 ± 9.4 in group C. The difference in mean pulse rate at 30 min across three groups was statistically significant. (P-value 0.003). (Table 1)

There was no statistically significant difference in mean difference pulse rate pre-induction intubation (0 min.) in

Mean pulse rate (beats per minute)	Group			P-value
	A	B	C	
Pre-induction intubation (0 min.)	83.7 ± 14.3	80 ± 6.6	80.5 ± 13.5	0.573
Immediate post	99.3 ± 13.6	90.8 ± 13.3	95.6 ± 14.0	0.151
5 minutes	95.5 ± 11.4	87.5 ± 12.1	90.4 ± 13.3	0.124
10 minutes	92.3 ± 9.7	83.9 ± 10.5	89.7 ± 11.1	0.041
20 minutes	91.6 ± 10.1	79.8 ± 8.2	87.6 ± 11.1	0.005
30 minutes	88.4 ± 9.9	76.9 ± 6.7	85.8 ± 9.4	0.003

Table-1: Mean pulse rate (beats per minute) of the three groups at different time intervals

	A Vs B	B VS C	A VS C
Pre-induction intubation (0 min.)			
Mean difference	3.7	3.2	0.5
Se of MD	4.48	3.46	4.52
95% CI	5.41 to 12.81	5.91 to 12.31	9.61 to 8.61
P value	0.5943	0.676	0.990
Immediate post			
Mean difference	8.5	3.7	4.8
Se of MD	3.36	4.42	4.48
95% CI	1.876 to 18.87	6.67 to 14.07	15.17 to 5357
P value	0.128	0.668	0.510
5 minutes			
Mean difference	8.0	5.1	2.9
Se of MD	3.81	4.12	4.02
95% CI	1.35 to 17.35	4.25 to 14.45	12.25 to 6.45
P value	0.1078	0.394	0.737
10 minutes			
Mean difference	8.4	2.6	5.8
Se of MD	3.28	3.51	3.38
95% CI	0.448 to 16.35	5.35 to 10.55	13.75 to 2.15
P value	0.036	0.712	0.194
20 minutes			
Mean difference	11.8	4.00	8.7
Se of MD	2.98	3.83	3.14
95% CI	5.18 to 20.21	3.5 to 11.51	16.21 to 1.18
P value	0.004	0.415	0.019
30 minutes			
Mean difference	11.5	2.6	8.9
Se of MD	2.75	4.65	4.83
95% CI	4.81 to 18.18	4.08 to 9.28	15.58 to 2.21
P value	0.003	0.619	0.002

Table-2: Paired wise comparison of mean pulse rate (beats per minute) of the three groups at different time intervals

Mean M.A.P. (beats per minute)	Group			P-value
	A	B	C	
Pre-induction intubation (0 min.)	99.0 ± 9.7	93.3 ± 8.8	97.2 ± 9.3	0.148
Immediate post	121.8 ± 22.0	110.5 ± 14.6	121.7 ± 21.2	0.046
5 minutes	121.0 ± 15.0	104.0 ± 11.3	111.3 ± 14.7	0.001
10 minutes	122.8 ± 12.0	100.8 ± 12.2	109.5 ± 19.6	0.001
20 minutes	115.7 ± 11.8	99.7 ± 12.3	111.8 ± 18.5	0.002
30 minutes	112.5 ± 10.8	96.5 ± 9.3	103.3 ± 12.7	0.001

Table-3: Mean M.A.P.(beats per minute) of the three groups at different time intervals

all pair wise comparisons. (P-value >0.05). There was no statistically significant difference in mean difference pulse rate immediate post-op and 5 min in all pair wise comparisons. (P-value >0.05). There was a statistically significant difference in mean difference pulse rate at 10 min in group

A vs. group B (P-value <0.05), and there was no statistically significant difference in mean difference pulse rate at 10 min in group B vs. group C, group A vs. group C (P-value >0.05). There was a statistically significant difference in mean difference pulse rate at 20 min in group A vs. group

Group & Grades	1 min. No (%)	1.5 mins. No (%)	2 mins. No (%)	2.5 mins. No (%)	3 mins. No (%)	3.5 mins. No (%)	4 mins. No (%)
Group A							
Excellent					4 (20%)	11 (55%)	5 (25%)
Good			3 (15%)	9 (45%)	13 (65%)	5 (25%)	
Fair		2 (10%)	14 (70%)	11 (55%)	3 (15%)		
Poor	20 (100%)	18 (90%)	3 (15%)				
Group B							
Excellent		1 (5%)	9 (45%)	6 (30%)	4 (20%)		
Good		10 (50%)	7 (35%)	4 (20%)			
Fair	2 (10%)	4 (20%)	3 (15%)				
Poor	18 (90%)	5 (25%)					
Group C							
Excellent			5 (25%)	5 (25%)	5 (25%)	3 (15%)	2 (10%)
Good		4 (20%)	8 (40%)	5 (25%)	5 (25%)	2 (10%)	
Fair		7 (35%)	6 (30%)	5 (25%)			
Poor	20 (100%)	9 (45%)	1 (5%)				

Table-4: Various grades of intubating conditions at various time intervals (in percentages).

Group	1 min.	1.5 mins.	2 mins.	2.5 mins.	3 mins.	3.5 mins.	4 mins.	Mean ± S.D.
A	-	-	-	-	4	11	5	3.5 ± 0.4
B	-	1	9	6	4	-	-	2.3 ± 0.8
C	-	-	5	5	5	3	2	2.8 ± 0.8

Table-5: Intergroup comparison of the number of patients intubated at various time intervals (in minutes).

B and group A vs. group C (P-value <0.05), There was no statistically significant difference in mean difference pulse rate at 20 min in group B vs. Group C (P-value >0.05). There was a statistically significant difference in mean difference pulse rate at 30 min in group A vs. group B and group A vs. group C (P-value <0.05), There was no statistically significant difference in mean difference pulse rate at 30 min in group B vs. Group C (P-value >0.05). (Table2)

Among group A, majority of 11 (55%) had excellent grade of intubating conditions at 3.5 min, 13 (65%) had good intubating conditions at 3 min, 9 (45%) had good intubating conditions at 2.5 min, 14 (70%) had fair incubating condition at 2 min, 11 (55%) had fair incubating condition at 2,5 min, 20 (100%) had poor grade of intubating conditions at 1 min and 18 (90%) had poor incubating conditions at 1.5 min. Among group B, majority of 9 (45%) had excellent grade of intubating conditions at 2 min, 10 (50%) had good intubating conditions at 1.5 min, 7 (35%) had good intubating conditions at 2 min, 4 (20%) had fair incubating condition at 1.5 min, 3 (15%) had fair incubating condition at 2 min, 18 (90%) had poor grade of intubating conditions at 1 min and 5 (25%) had poor incubating conditions at 1.5 min. Among group C, majority of 5 (25%) had excellent grade of intubating conditions at 2 to 3 min, 8 (40%) had good intubating conditions at 2 min, 7 (35%) had fair incubating condition at 1.5 min, 20 (100%) had poor grade of intubating conditions at 1 min and 9 (45%) had poor incubating conditions at 1.5 min. (Table4)

Among group A the mean MAP at pre-induction 0 min was 99.0 ± 9.7, it was 93.3 ± 8.8 in group B and it was 97.2 ± 9.3. The difference in mean MAP at pre-induction 0 min across three groups was statistically not significant. (P-value 0.148).

Among group A the mean MAP at immediate post-op was 121.8 ± 22.0, it was 110.5 ± 14.6 in group B and it was 121.7 ± 21.2 in group C. The difference in mean MAP at immediate post-op across three groups was statistically significant. (P-value 0.046). Among group A the mean MAP at 5 min was 121.0 ± 15.0, it was 104.0 ± 11.3 in group B and it was 111.3 ± 14.7 in group C. The difference in mean MAP at 5 min across three groups was statistically significant. (P-value 0.001). Among group A the mean MAP at 10 min was 122.8 ± 12.0, it was 100.8 ± 12.2 in group B and it was 109.5 ± 19.6 in group C. The difference in mean MAP at 10 min across three groups was statistically significant. (P-value 0.001). Among group A the mean MAP at 20 min was 115.7 ± 11.8, it was 99.7 ± 12.3 in group B and it was 111.8 ± 18.5 in group C. The difference in mean MAP at 20 min across three groups was statistically significant. (P-value 0.002). Among group A the mean MAP at 30 min was 112.5 ± 10.8, it was 96.5 ± 9.3 in group B and it was 103.3 ± 12.7 in group C. The difference in mean MAP at 30 min across three groups was statistically significant. (P-value 0.001). (Table3)

Among the group, The number of patients intubated at 3, 3.5, 4 min was 4, 11, 5 respectively. Among group B number of patients intubated at 1.5, 2, 2.5, 3 minutes was 1, 9, 6, 4 respectively. Among group C number of patients intubated at 2, 2.5, 3, 3,5 4 min was 5, 5, 5, 3, and 2 respectively. (Table5)

DISCUSSION

Generally, anaesthetists consider that the time between induction of anaesthesia and intubation of the trachea should be kept as short as possible in patients. The anaesthetic technique used for this purpose is known as 'rapid-sequence induction' (rapid-sequence intubation, 'crash' intubation).

Muscle relaxants are given as part of rapid-sequence induction to facilitate tracheal intubation. According to anaesthetic textbooks, succinylcholine is the preferred muscle relaxant for rapid-sequence induction.¹³ The use of a muscle relaxant, even one with a very fast onset and a short duration of action, e.g. succinylcholine, does not rule out complications that may occur during rapid-sequence induction, including regurgitation and failed tracheal intubation.¹⁵⁻¹⁷

In the present study, the grading of intubation from poor to excellent was done as per the criteria by Young et al.¹⁸ While the assessment was purely clinical, the neuromuscular blockade assessment was not measured. The time taken to obtain excellent intubation was lowest for the group using vecuronium (2.3±0.8 minutes), followed by the group that used atracurium (2.8±0.8 minutes) and the longest time was taken by the group using pancuronium (3.5±0.4 minutes). In line with these findings, Foldes et al.¹⁹ found that vecuronium and atracurium induced satisfactory intubation in under 3 minutes. It should also be emphasized that in the present study, under 3 minutes vecuronium provided excellent intubation in 100% of the participants, while it was 75% for atracurium and only 15% for pancuronium.

Much of the existing research suggests a relatively shorter duration of intubation for the similar dosage of pancuronium, vecuronium and atracurium. In a study involving 30 female patients undergoing gynecological operations for non-malignant conditions, Gramstad and Lilleasen⁶ noted a similar mean intubation time of 97.5 seconds for pancuronium, 97.3 seconds for vecuronium and 96.9 seconds for atracurium. Robertson et al.¹⁷ observed a mean intubation time of 81.5 seconds for vecuronium and 115.3 seconds for atracurium and opined that the former is 4.4 times more potent than the latter although, vecuronium tended to be shorter acting. Schaeret al.²⁰ reported a relatively long time, 148.4 seconds for pancuronium, 101.3 seconds for vecuronium and 113.6 seconds for atracurium. Contrastingly, Mohanty et al.¹² and Chatrath et al.⁵ reported a longer intubation time compared to the present study findings where vecuronium of 282.32 seconds and 254.44 seconds respectively.

Regarding the effects on the cardiovascular system, there was an increase in both pulse rate and arterial pressure post-intubation in all three groups. The effects were pronounced in the pancuronium group and took more time to settle, while for atracurium the effects settled fast and such changes were minimal for the vecuronium group and took the least amount of time to settle.

The ease with which endotracheal intubation is performed depends upon the degree of muscle relaxation, depth of anaesthesia and skill of anaesthesiologist.²¹ One characteristic of the ideal muscle relaxant is a rapid onset of action.

CONCLUSION

The findings of the study reveal that all three depolarising skeletal muscle relaxant provided adequate intubating conditions. The time duration of intubation was longest for pancuronium and shortest for vecuronium making it best suited for rapid endotracheal intubation. All the currently

available agents have their limitations and the quest continues for an ideal drug. What is needed is an agent that is rapidly acting, non-cumulative, independent of renal or hepatic function for its elimination, easily and rapidly reversed and free from side-effects.

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