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Original Research Article.

A Double Blind, Randomized Comparison of Intubating Conditions between Rocuronium, Atracurium and Atracurium with Priming

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ABSTRACT

Background and Aims: The present study was undertaken to evaluate and compare rocuronium, with atracurium (with and without priming dose) for the purpose of intubation with emphasis on intubating conditions, haemodynamic changes and incidence of any adverse events.

Methods: This prospective, comparative randomized study was conducted at Rajindra Hospital, Patiala, Punjab. A total of 150 patients aged between 18-60 years of either sex and ASA physical status I and II scheduled for elective surgery under general anaesthesia were randomly divided into three groups as follows: Group A (n=61): Rocuronium (0.6mg/kg), Group B (n=47): Atracurium (0.7 mg/kg), Group C (n=42): priming with 0.1 mg/kg prior to second dose of Atracurium 0.6 mg/kg. Intubating conditions and hemodynamic parameters were analyzed with one way ANOVA or Chi-Square Test or Fisher's Exact Test as applicable.

Results: Rocuronium produced fastest onset of apnea (48.75 ± 8.91 seconds) and for the shortest period (29.82 ± 4.64 minutes). Atracurium without priming in comparison to Atracurium with priming had delayed onset of apnea (91.45 ± 28.89 seconds versus 73.31 ± 22.58 seconds) and longer duration of action (36.34 ± 12.77 minute versus 34.38 ± 10.34 minutes) respectively. (P value < 0.001) In group A, (Rocuronium), 100% patients had acceptable intubating condition at the end of 90 seconds. The hemodynamic parameters were comparable among three groups. Anaphylactic reactions were seen with atracurium usage both with and without priming.

Conclusion: Rocuronium produces the better intubating conditions compared to Atracurium with or without priming at 90 seconds and is associated with shorter duration of action.

Key words: Rocuronium, Atracurium, Endotracheal Intubation.

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INTRODUCTION

Muscle relaxants have become essential parts of the anaesthetist armamentarium. They help in endotracheal intubation, mechanical ventilation, reduce anaesthetic requirements, prevent patient movement, facilitate surgery, and decrease oxygen consumption. The ideal muscle relaxant for intubation should have a fast onset, brief duration of action, provide profound relaxation & be free from hemodynamic changes.[1] Rocuronium Bromide is a mono-quaternary amino steroidal neuromuscular blocking agent with a faster onset and a brief duration of neuromuscular blockade.[2,3] The duration of action of rocuronium is about 30 minutes with a 0.6mg/kg dose, full spontaneous recovery taking about an hour.[4]

Atracurium is a non-depolarizing neuromuscular blocking agent of intermediate duration of action.[5] Atracurium is more accessible and cheaper than other NDMRs. Onset time to maximum block at 0.6 mg/kg of Atracurium is 1.4 minutes. The hemodynamic changes resulting from release of histamine after administering atracurium can be a problem especially in cardiovascular patients. Clinical duration of response is 46 minutes. When Atracurium is used for endotracheal intubation, intubation cannot be accomplished satisfactorily in 90 seconds. In order to overcome this priming principle used.

Miguel et al concluded that Rocuronium at a dose of 0.45 mg/kg has faster onset and shorter duration than atracurium at 0.5 mg/kg when used with desflurane.

Priming principle refers to administration of small *(*subparalysing) dose of a nondepolarizing relaxant, which when followed by larger intubating dose, after 120 seconds produces relatively rapid and profound blockade to ensure a suitable condition for endotracheal intubation. Atracurium in a total dose 0.7 mg/kg utilizing priming principle provides excellent intubating conditions at 120 seconds after *intubating* dose. A priming dose of 0.1mg/kg appeared satisfactory and devoid of any side effects.[6]

We designed a randomized study to compare the intubating conditions, hemodynamic changes, time of onset of apnea and duration of action by rocuronium and atracurium (with and without priming) were compared. The haemodynamic parameters between rocuronium and atracurium during anaesthesia or any adverse reactions were also monitored.

METHODS

This prospective, comparative randomized study was conducted at Rajindra Hospital, Patiala. A total of 150 patients aged between 18-60 years of both sex and American Society of Anaesthesiologists physical status I and II were scheduled to undergo elective surgery under general anaesthesia were selected. Patients having cardiovascular diseases, renal, hepatic disorders, neuromuscular disorders or history of allergic reaction to rocuronium, atracurium or its constituents, those who had anticipatory difficult intubation or undergoing emergency surgeries were excluded from the study.

After institution ethical committee's approval and getting written informed consent patients were randomly divided into three groups by using random number table as follows: Group A (n=61): Rocuronium (0.6mg/kg body weight), Group B (n=47): Atracurium (0.7 mg/kg body weight), Group C (n=42): priming with 0.1 mg/kg body weight prior to second dose of Atracurium 0.6 mg/kg body weight.

All patients had preanaesthetic checkup which included detailed clinical history, general physical examination, systemic examination, airway assessment and baseline pulse rate, blood pressure, oxygen saturation and respiratory rate. Routine blood investigations were also obtained in all patients. All patients were premedicated with inj. midazolam (2mg) and inj. phenargan (25mg) 30 min before the elective surgery. All patients were kept fasting at least for six hours pre-operatively. Venous access was established with 18G cannula and connected to IV fluid. Inj. glycopyrrolate (0.04mg/kg), inj. fentanyl (2 µg/kg) were given prior to induction. Group A and Group B were administered placebo with isotonic saline whereas Group C was administered priming dose of 0.1 mg/kg atracurium. Following preoxygenation with 100% O_2 for three minutes, patients of all groups were received Inj. propofol (2-2.5mg/kg) and loss of eye lash reflex was noted and patients were controlled ventilated with O2 and N_2O with bag and mask. Group A received 0.6 mg/kg Rocuronium, group B received 0.7 mg/kg Atracurium and group C received 0.6 mg/kg of Atracurium as intubating dose respectively.

The time of onset of apnea was noted. Intubating conditions were assessed at 60 second after administration of muscle relaxant then every 30 seconds (upto 180 seconds) until clinically acceptable conditions were observed according to Cooper Scoring system.[7] Oral endotracheal intubation was done with proper size endotracheal tube. After inflating the cuff of endotracheal tube, it was connected to closed circuit and controlled ventilation was done with Bains circuit. $ETCO_2$ was kept in a range of 30-35. The excellent and good intubating conditions were taken as acceptable whereas the fair and poor intubating conditions were considered as unacceptable. Any adverse reactions associated with use of rocuronium and atracurium at the time of laryngoscopy were noted. Pulse rate, systolic and diastolic blood pressure, mean arterial pressure, SpO_2 and $EtCO_2$ were recorded at 1minute, 3minute, 5minute and every 5 minutes till 20 minutes and then at 30 minutes. At the end of surgery the neuro-muscular block were reversed by using inj. glycopyrrolate 10µg/kg and inj. neostigmine 40µg/kg. Oropharyngeal suction was done and patients were extubated when fully awake and fulfilled the criteria of extubation. Any post-operative hoarseness, sorethroat and myalgia were noticed post operatively.

Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Continuous variables were analysed with one way ANOVA among three groups. Categorical variables were analysed with the Chi-Square Test or Fisher's Exact Test. P value < 0.05 two sided was considered statistical significant. The data was analysed using SPSS version 22 .0 and Microsoft Excel 2007.

Table 1: Baseline characteristics of patients in three groups

	Group A (n=61)	Group B (n=47)	Group C (n=42)	p-value
Age in years (Mean ± SD)	39.64 ± 12.30	42.26 ± 12.90	41.02 ± 11.35	0.543
Sex (male : female)	22 : 39	18 : 29	14 : 28	0.888
Weight in kgs (Mean ± SD)	62.2 ± 8.78	61.51 ± 8.91	61.64 ± 8.86	0.912
ASA physical status(I and II)	40 : 21	28 : 19	30 : 12	0.502
Malampatti grading (grade 1:grade 2)	34 : 27	19 : 28	24 : 18	0.194

Table 2: Onset and duration of action

	Group A	Group B	Group C	P-value	Significance	Group A Vs Group B	Group B Vs Group C	Group A Vs Group C
Onset of action (seconds) Mean ±SD	48.75 ± 8.91	91.45 ± 28.89	73.31 ± 22.58	< 0.001	HS	< 0.001 (HS)	< 0.001 (HS)	< 0.001 (HS)
Duration (minutes) Mean ±SD	29.82 ± 4.64	36.34 ± 12.77	34.38 ± 10.34	0.002	S	0.002 (S)	0.995 (NS)	0.053 (NS)

RESULTS

The age, gender distribution, weight, ASA class and Malampatti grading of the three groups were comparable. Rocuronium had fastest onset of apnea (48.75 ± 8.91 seconds) and shortest duration of action (29.82 ± 4.64 minutes). Atracurium took longest time for onset of apnea (91.45 ± 28.89 seconds) and its duration of action was also longest among three groups (36.34 ± 12.77 minute). Atracurium with priming the time of onset of apnea was

73.31 ± 22.58 seconds and duration was 34.38 ± 10.34 minutes and values are statistically significant. (P value < 0.001)

Rocuronium had higher Cooper scores compared to atracurium with or without priming at 60, 90, 120, 150 and 180 seconds. Atracurium with priming had higher Cooper score compared to atracurium without priming at 60, 90, 120, 150 and 180 seconds and it was statistically significant (p <0.001)

In group A (Rocuronium), excellent intubating conditions were obtained in 70.5%, 91.8% of the patients at 60 seconds and 90 seconds respectively. In group B (Atracurium) no patient had excellent intubating conditions at 60 seconds and 90 seconds. In group C (Atracurium with priming), at 60 seconds no patient had excellent intubating conditions where as 7.1%, patients achieved excellent intubating conditions at 90 seconds.

In group A (Rocuronium), 96.7% of patients had acceptable intubating conditions (excellent + good) compared to group B (Atracurium) with 2.1% patients and group C (atracurium with priming) with 4.8% patients at the end of 60 seconds.

The systolic blood pressure, diastolic blood pressure, mean blood pressure, heart rate, oxygen saturation, end tidal CO2 readings during preoxygenation, at 1min, 3min, 5min,10min,15min , 20min and 30min after intubation were comparable. No significant difference was found in the measurements between the three groups. (p>0.05) Anaphylactic reactions did not occur with Group A (Rocuronium) but seen with Group B and Group C. There were 4 cases (8.5%) of anaphylaxis in Group B (Atracurium) compared to 1 case (2.4%) in Group C (Atracurium with priming) and it was statistically significant. (P value < 0.05)

Figure 1: Onset of action of the three agents

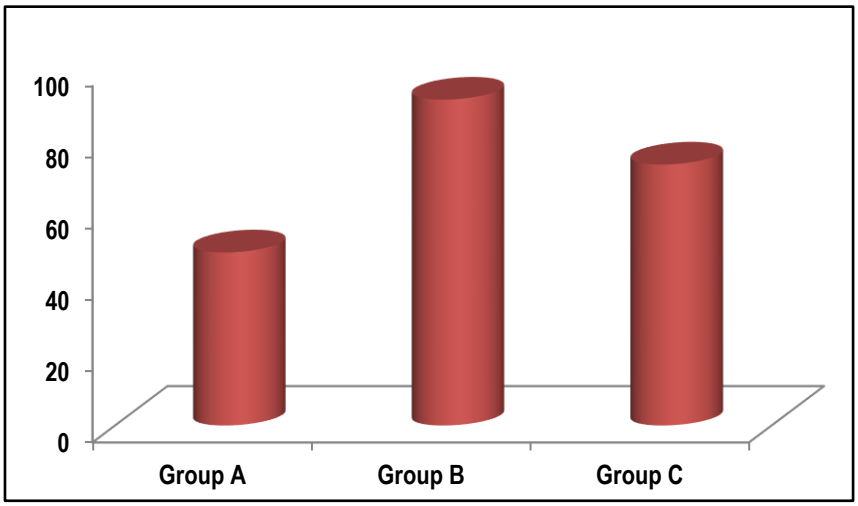


Figure 2: Duration of action of three agents

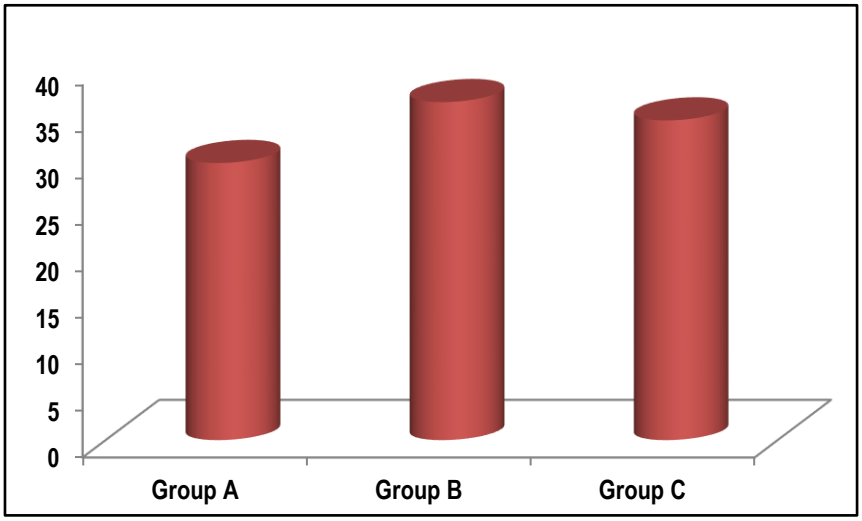


Table 3: Intubating score at 60 and 90 seconds:

At 60 seconds	Group A	Group B	Group C	P-value	At 90 seconds	Group A	Group B	Group C	P-value
Excellent	43(70.5%)	0	0	< 0.001	**Excellent**	56(91.8%)	0	3(7.1%)	
Good	16(26.2%)	1(2.1%)	2(4.8%)	(S)	**Good**	5(8.2%)	4(8.5%)	26(61.9%)	< 0.001
Fair	2(3.3%)	13(27.7%)	34(81%)		**Fair**	0	33(70.2%)	13(31%)	(S)
Poor	0	33(70.2%)	6(14.3%)		**Poor**	0	10(21.3%)	0	

Figure 3: Cooper score comparison between three groups

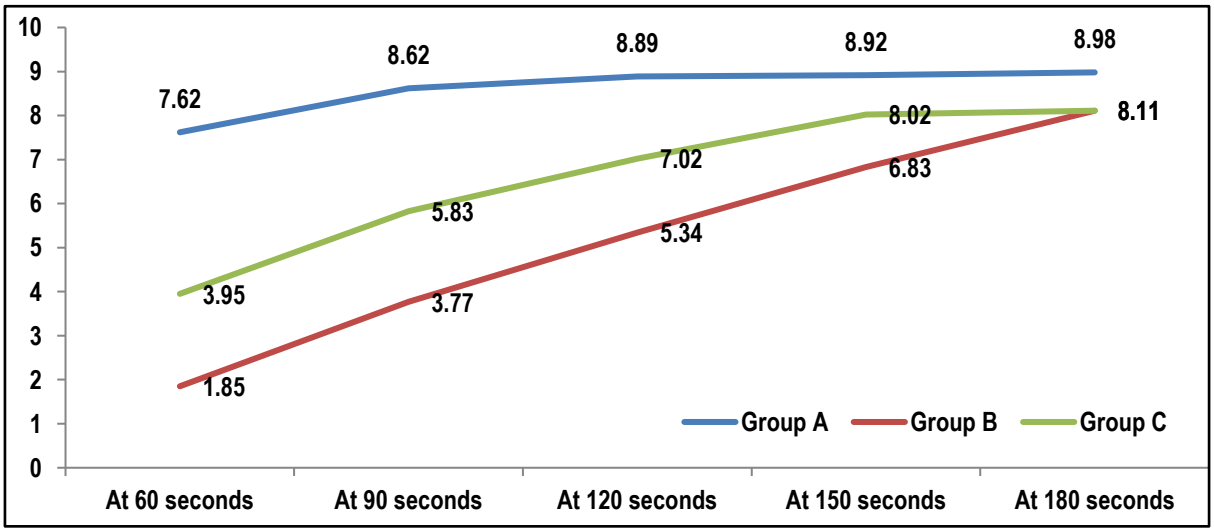
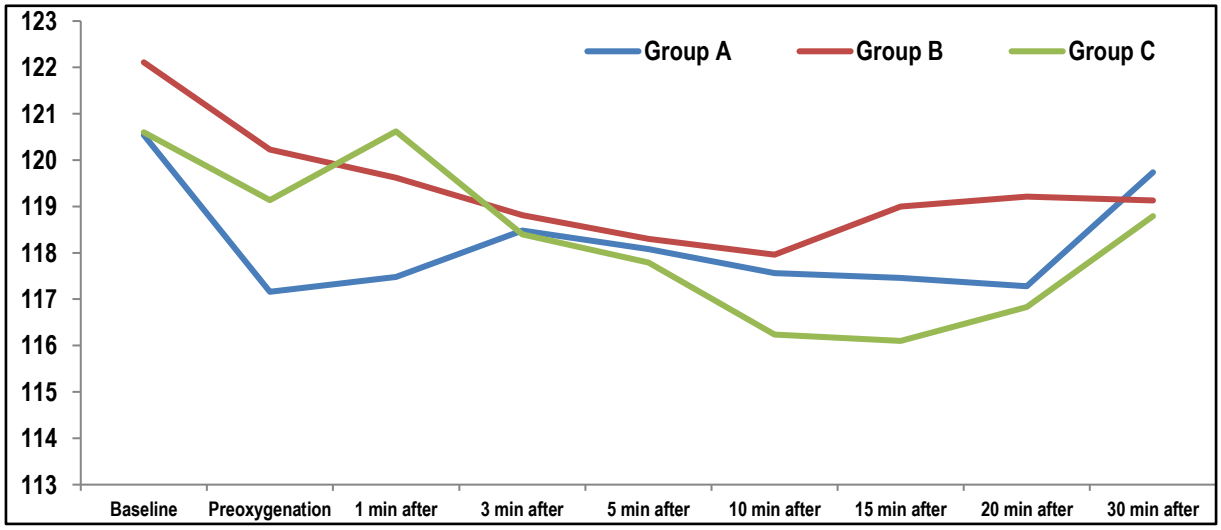


Figure 4: SBP in mm of Hg among three groups



DISCUSSION

The onset of action of Rocuronium at a dose of 0.6mg/kg varied from 41 to 60 seconds as per various studies.[8-10] The onset of action of atracurium without priming and the reported onset of action below 2 minutes (Range = 69 seconds to 100 seconds).[5,7,11] With priming dose of atracurium the onset of action improved as compared to atracurium without priming.[6,7,11]

In our study, the time of onset of apnea was 48.75 ± 8.91 seconds in patients receiving rocuronium and the mean onset of apnea was 91.45 ± 28.89 seconds in patients who received atracurium whereas who received atracurium with priming, the time of onset of apnea was 73.31 ± 22.58 seconds. (p- Value <0.001) This is in agreement with the hypothesis that onset time is proportional to potency. The lowest potency drug, Rocuronium, was found to have the shortest onset time.[12,13]

Duration of action is considered as time to first diaphragmatic contraction i.e. time to resumption of spontaneous breathing. The various authors who have studied the duration of action of rocuronium and the reported duration of action varied from 27 minutes to 38 minutes.[14-16] Duration of action of Atracurium without priming as reported in different studies from 33 minutes to 44 minutes.[5,17]

In our study in those who received rocuronium, the mean duration time was 29.82 ± 4.64 minutes while those receiving atracurium, the mean duration time was 36.34 ± 12.77 minute and patients who received atracurium with priming dose the duration of action was 34.38 ± 10.34 minutes.

Rocuronium group had significantly higher Cooper score at 60 seconds (7.62 ± 0.93) as compared to atracurium (1.85 ± 1.35) and atracurium with priming (3.95 ± 1.22) which was statistically significant as p value is < 0.001.

Rocuronium at a dose of 0.6 mg/kg provides an acceptable intubating condition in most of the patients within 1 minute.[10]

In our study, group A showed the overall best results. This group had highest mean jaw relaxation, best rima glottids opening and least coughing-straining and irregular muscular movements in response to intubation.

L D Mishra et al in their study observed that intubating conditions with atracurium without using the priming principle were not satisfactory after 90 seconds. Though the conditions improved on increasing the time interval to 120 seconds; it still remained less than satisfactory. But on utilizing priming principle, Atracurium provided excellent intubating conditions at 120 seconds.[6]

Mehta et al[18] observed that when nondepolarizing relaxants were administrated in divided doses, neuromuscular blockade adequate for tracheal intubation was achieved in less than 90 seconds. The same findings were also observed by Naguib et al[19] reported the same findings with Atracurium. Rocuronium had excellent

intubating conditions were obtained within 90 seconds (91.8%) compared to Atracurium without priming (0%) and with priming (7.1%) respectively. The patients who received Rocuronium, 96.7% had acceptable intubating conditions (excellent + good) at 60 seconds compared to 2.1% patients who received atracurium and 4.8% patients who received Atracurium with priming. This is found to be highly statistically significant ($p < 0.001$).

In the present study, the haemodynamic parameters during conduct of anaesthesia with rocuronium in the dose of 0.6 mg/kg are comparable with atracurium with or with priming. The difference in mean HR, SBP, DBP and MAP between the three groups were not statistically significant at any time interval ($p>0.05$). This finding is in correlation with the studies of Whalley et al,[20] Vinik et al[17] and Miguel RV et al[21] who have all found no difference in any of the haemodynamic variables between the groups during comparison. Maddineni VR et al[16] who studied the haemodynamic effects of Rocuronium in the doses of 0.6mg/kg and 0.9 mg/kg under balanced and volatile anaesthesia concluded that no significant change in heart rate occurred with both doses and both techniques. Levy JH et al[22] studied the cardiovascular profile of Rocuronium in three intubating doses (0.6, 0.9, 1.2 mg/kg) and did not observe any significant differences in heart rate or mean arterial pressure or any adverse effects.

Anaphylactic reactions did not occur with rocuronium but seen with atracurium with or without priming.

CONCLUSION

The results of our study showed that rocuronium (0.6mg/kg) after 60seconds produces the best intubating condition. It is recommended to wait for 90seconds with rocuronium to achieve excellent intubation conditions. Atracurium in a total dose of 0.7 mg/kg utilizing priming principle provided excellent intubating conditions at 120 seconds after the intubating dose. The intubating conditions without using the priming principle were not satisfactory after 90 seconds. Though the conditions improved on increasing the time interval to 120 seconds; it still remained less than satisfactory. A priming dose of 0.1 mg/kg appeared satisfactory and devoid of any untoward effects. Risk of anaphylaxis is present with atracurium in both bolus dose regimen and priming dose regimen but rocuronium was devoid of any such adverse effects. No significant hemodynamic parameter alterations observed in of the groups.

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