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"Effect of Priming on Intubating Conditions Produced By Atracurium"

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Abstract: *Thisis a prospective randomised study where 120 patients of either sex are scheduled for elective surgery under general anaesthesia were randomly allocated into three groups. Group A consist of patients who received priming with 0.1mg/kg atracurium and intubating at 90 seconds after giving intubating dose of 0.6mg/kg atracurium . Group B patients received placebo with saline and intubation at 90 seconds after single dose of atracurium. Group C patients received priming with 0.1mg/kg atracurium and intubation at 120 seconds after second dose of 0.6 mg/kg.In this study we assess the effect of priming on intubating conditions produced by atracurium at 90 and 120 seconds.Intubating conditions were assessed with parameters like jaw relaxation, response to intubation [coughing, straining or muscular movement] hemodynamic responses to intubation-rise in blood pressure and pulse rate and number and strength of twitches to train of four stimulus just before intubation. With above parameters, scoring system was devised and intubating conditions were considered excellent, good, fair or poor depending upon the score.*
Statistical analysis were carried out using Chi-square test and Fisher's exact test. Demographic data like mean age, weight, sex were comparable in all the three groups. The total score were significantly less in Group B compared to Group A and Group C at the time of intubatiom. None of the patients had any serious complications after the priming dose of atracurium. Among Group A and Group C, Group C had highest mean jaw relaxation, best rima glottides opening, least coughing, straining and muscular movements and mean total score is also higher.

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I. Introduction

Speed of onset of neuromuscular block is one of the requirements to rapidly secure the airway and this is consistently provided by succinylcholine within 60 – 90 seconds, but its use has serious complications that occur occasionally, such as hyperkalemia, increased intra-ocular pressure, sudden cardiac arrest especially in infants and adolescents[1,2]. Atracurium is a benzyl-isoquinolinium diester, non-depolarizing neuromuscular blocking agent of intermediate duration of action. Its introduction in early 1980's has revolutionized anaesthetic practice by providing muscle relaxation withfaster onset and a more rapid measurablerecovery.[3,4] Priming principle refers to the administration of a small priming dose ofanon-depolarizing relaxant, which whenfollowed by the larger intubatingdose, after 2-4 minutes, produces a relativelyrapid and profound blockade to ensure a suitable condition for End otrachealintubation[5,6,7,8]. However, priming carries risk ofaspiration, difficulty inswallowing and the visual disturbances, which evenin subtledegree may beuncomfortable for the patient[9,10].

II. Material And Methods

This study was conducted in the Department of Anaesthesiology at Government Medical college Kota over a period of 24 months from July 2017 to July 2019. After institution's ethical committee approval, the study was conducted on 120 patients of ASA I and ASA II grade of either sex admitted to MBS Hospital, Kota who required surgery under general anaesthesia.

Study Design: Prospective open label observational study
Study Location: MBS Hospital , Kota (Rajasthan)
Study Duration: July 2017 to July 2019
Sample Size: 120 patients

Inclusion Criteria:

- ASA I and ASA II patients.

- Age >20 years <60 years.
- Patients admitted for elective surgeries under general anaesthesia.

Exclusion Criteria:
- Patients with anticipated airway difficulty.
- Patients with neuromuscular disease.

Procedure methodology:

After written informed consent,120 patients selected with the help of the inclusion/exclusion criteria were randomly allocated into 3 groupsin a double-blinded manner. Random numbers will be generated using computer programme.

Group A (n=40): Priming with 0.1 mg/kg Atracurium and intubating at 90 seconds after giving intubating dose of 0.6 mg/kg Atracurium.

Group B (n=40): Placebo with normal saline and intubation at 90 seconds after single dose of 0.7 mg/kg Atracurium.

Group C (n=40): Priming with 0.1 mg/kg Atracurium and intubation at 120 seconds after second dose of 0.6 mg/kg Atracurium.

The patients were premedicated with Tab Ranitidine 150mg the night before surgery and in the morning of surgery and Tab Diazepam 5mg the night before surgery. All operations were performed under general anaesthesia, induced withinj Fentanyl 1-2 µg/kg iv and injPropofol 2mg/kg iv 3minutes after administration of priming dose.The patients in group A and group C received 0.6mg/kg and those in group B received 0.7mg/kg of atracurium as intubating dose.Anaesthesia was maintained with N_2O:O_2(60:40), intermittent positive pressure ventilation, isoflurane and additional doses of atracurium were given as required.

Evaluation and Observations:

Pulse rate, automated non-invasiveblood pressure, oxygen saturation and ECG were monitored. Neuromuscular blockade was assessed by train of four responses, using peripheral nerve stimulator by stimulating the ulnar nerve at wrist non-invasively and observing number of twitches and strength of contraction of adductor pollis muscle. For this study only those where train of four responses were seen just before intubation were taken into consideration. Strength of twitch was observed as normal (N), reduced (R),markedly reduced (RM),only flicker (F).

Intubating conditions were assessed with the followingparameters:
- Jaw relaxation
- Position of vocal cord
- Response to intubation (coughing, straining or muscular movements)
- Haemodynamic response to intubation
- Number and strength of twitches to train of four stimuli just before intubation.

With the above parameters, a scoring system was devised. The intubating conditions were considered as excellent,good, fair or poordepending upon the score tabulated as follows:

Table-1

Score	Jaw Relaxation	Position of vocal cord	Response to intubation		Rise in BP &Pulse	Number and strength of twitches on TOF
			Coughing /Straining	Muscular movements		
0	Poor	Closed	Severe	Severe	Increase in BP and Pulse > 20% of basal value	1,2,3twitch with reduced strength 75% block
1	Moderate	Semi-closed	Mild	Mild	Increase in BP and Pulse 10-20% of basal value	1-2 twitch with reduced/ marked reduced strength 80% block
2	Good	Open	Nil	Nil	Increase in BP and Pulse < 10% of basal value	1 twitch with just flicker or no twitch 90-100% block

Condition	Total Score
Excellent	10-12
Good	7-9
Fair	4-6
Poor	0-3

Also any side effects–diplopia, difficulty in swallowing, evidence of hypoventilation or fall in oxygen saturation after receiving a priming dose of 0.1mg/kg were noted.

Statistical Analysis: Descriptive statistical analysis has been carried out in the present study.Results on continuous measurements are presented on Mean ±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients. Post-hoc test namely Tukey test has been used to find the pair-wise significance 3x3 and 4x3 Fisher Exact test has been used to find the significance of study parameters oncategorical scale between groups. Analysis of variance has been used to test the homogeneity samples based on the age (or continuous parameters) and Chi-square test to test the homogeneity of samples based on parameters on categorical scale between the two groups.

III. Result

1. Demographic data

Table 1: Basic characteristics of patients studied between three groups

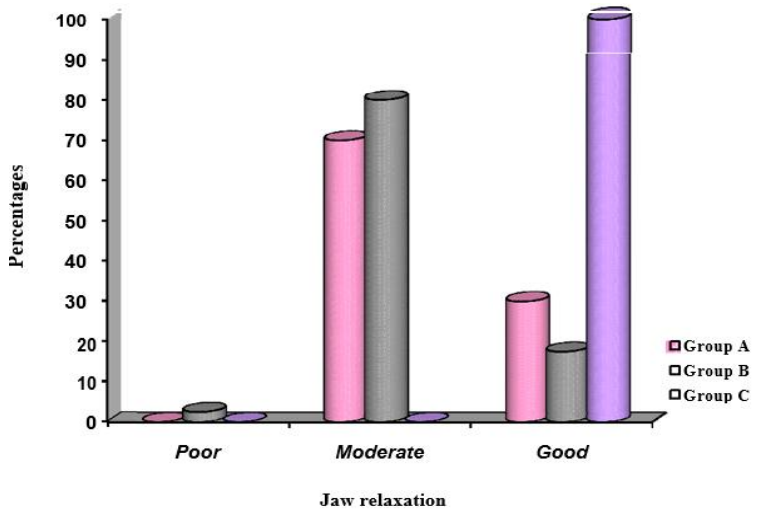
Basic characteristics	Group A	Group B	Group C	P value
Number of patients	40	40	40	-
Age in years; Mean±SD	39.40±11.44	40.42±12.36	40.20±11.49	0.920
Weight (kg); Mean±SD	62.63±9.23	61.45±9.53	61.30±8.48	0.776
Male; No (%)	19(47.5%)	21(52.5%)	20(50.0%)	0.905
Female; No (%)	21(52.5%)	19(47.5%)	20(50.0%)	0.905
ASA Grade I; No (%)	26(65.0%)	27(67.5%)	20(50.0%)	0.222
ASA Grade II; No (%)	14(35.0%)	13(32.5%)	20(50.0%)	0.222

The demographic parameters like age, sex and body weight were comparable in all the three groups.The distribution of patients with respect to ASA grade was also comparable.

2. Jaw Relaxation:

Table 2:Jaw Relaxation

Jaw relaxation	Group A (n=40)	Group B (n=40)	Group C (n=40)
Poor	0	1(2.5%)	0
Moderate	28(70.0%)	32(80.0%)	0
Good	12(30.0%)	7(17.5%)	40(100.0%)

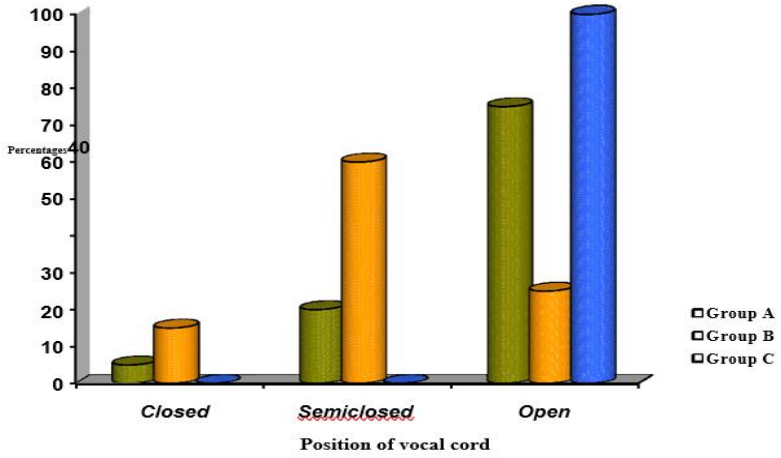


Jaw relaxation: In group C 100% (40) patients had good relaxation, whereas only30.0% (12) had good and 70% (28) had moderate jaw relaxation among group A patients. Group B showed only 17.5% (7) had good and 8% (32) had moderate jaw relaxation. There was statistically significant difference between the groups**.**

3. Position of Vocal Cords:

Table 3:Position of vocal cord

Position of vocal cord	Group A (n=40)	Group B (n=40)	Group C (n=40)
Closed	2(5.0%)	6(15.0%)	0
Semi-closed	8(20.0%)	24(60.0%)	0
Open	30(75.0%)	10(25.0%)	40(100.0%)

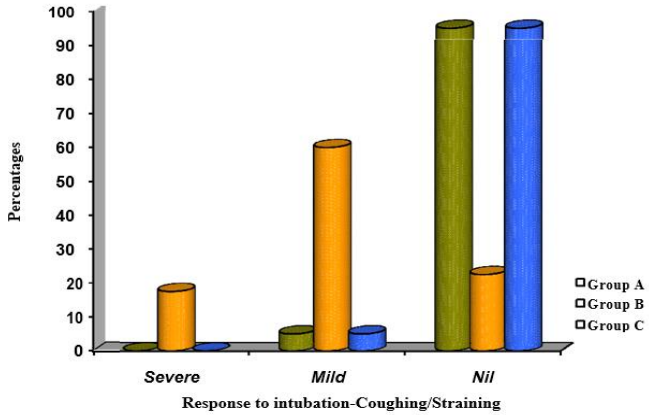


Position of vocal cords: This was assessed in 3 grades closed, semi-closed and openi.e. unacceptable, partial and full relaxation of the cords. In groups C 100% (40) patients had open vocal cords, whereas group A had 75.0% (30) open, 20% (8) semi closed and 5.0 % (2) closed vocal cords. In group B 25.0% (10) had open, 60.0 %(24) semi closedand remaining 10% (4) had closed vocal cords. There was a statistically significantdifference between the groups.

4. Response to intubation:

Table 4: Response to intubation- Coughing/Straining

Response to intubation-Coughing/Straining	Group A (n=40)	Group B (n=40)	Group C (n=40)
Severe	0	7(17.5%)	0
Mild	2(5.0%)	24(60.0%)	2(5.0%)
Nil	38(95.0%)	9(22.5%)	38(95.0%)

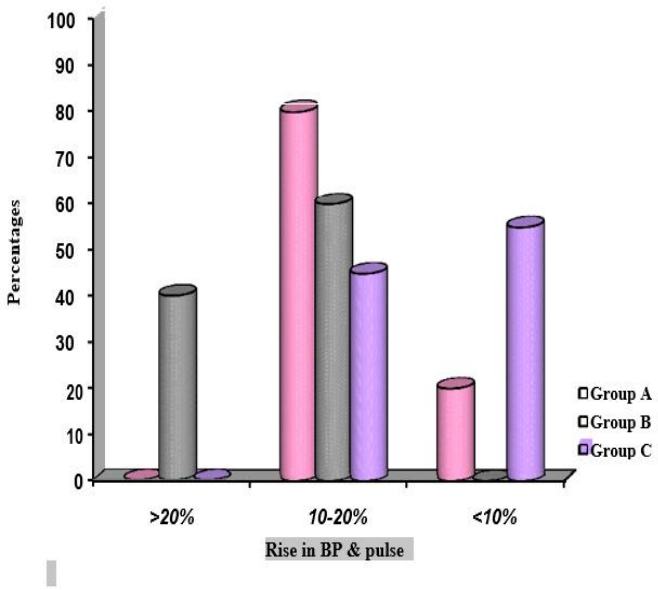


Coughing/straining in response to intubation: These were also assessed by 3 grades viz. severe, mild and nil. In both groups A and C, 95% (38) had nilincidence of coughing/straining, whereas in group B only 32.5% (13) had nil and 45% (18) had moderate incidence.

5. Rise in BP and Pulse:

Table 5: Rise in BP & Pulse

Rise in BP & pulse	Group A (n=40)	Group B (n=40)	Group C (n=40)
Increase in BP & PULSE > 20% of basal value	0	16(40.0%)	0
Increase in BP & PULSE 10-20% of basal value	32(80.0%)	24(60.0%)	18(45.0%)
Increase in BP & PULSE <10% of basal value	8(20.0%)	0	22(55.0%)



Rise in BP and Pulse: Assessed in 3 grades more than 20% increase,10-20% increase and less than 10% increase. In group C 55.0%(22) had less than 10% increase, 45% (18) had 10-20% increase in BP &Pulse. There was a statistically significant difference between the groups as shown.

6. Extent of Neuromuscular blockade:

Table 6: Number & strength of twitches on TOF

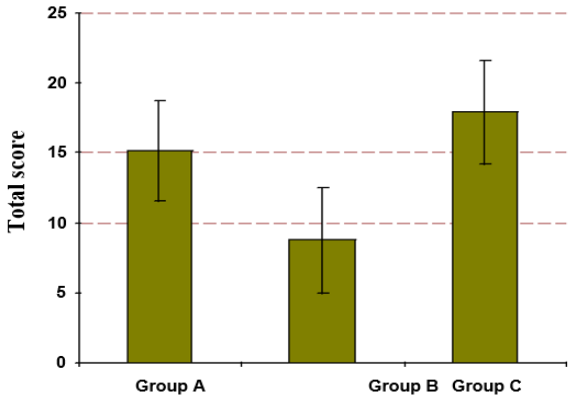
Number & strength of twitches on TOF	Group A (n=40)	Group B (n=40)	Group C (n=40)
1,2,3 Twitch with reduced strength 75% block	31(77.5%)	40(100.0%)	22(55.0%)
1,2, Twitch with reduced strength 80% block	9(22.5%)	0	18(45.0%)
1 twich with just flicker or no twitch 90-100% block	0	0	0

Extent of Neuromuscular blockade: This was assessed in 3 grades – 75% or less block, 80% block and 90-100%block. In group A 77.5% (31) showed 75% of less block, 22.5%(9) showed 80% block. In group B100.0% (40) had 75% or less block and in Group C55.5% (22) showed 75% or less blockand45.5%(18) showed 80% block. Thus, there was a statistically significant difference between the groups.

7. Total score:

Table 7: Comparison of total score between three groups

Total score	Group A (n=40)	Group B (n=40)	Group C (n=40)
Min-Max	6-20	2-18	8-21
Mean □ SD	15.15□3.63	8.75□3.75	17.90□3.71
95%CI	13.99-16.31	7.55-9.95	16.71-19.09

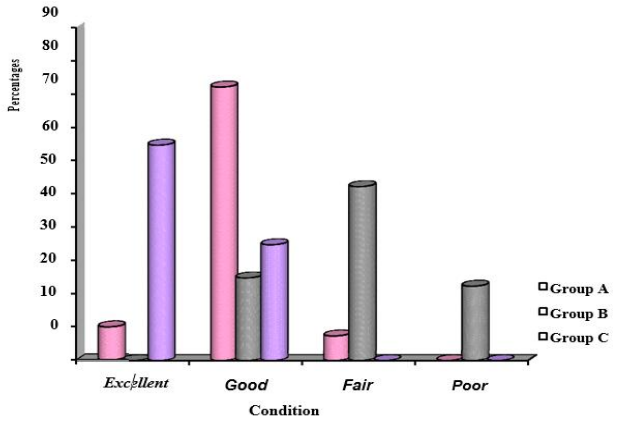


Statistically there is a significant difference among the groups**.**

8. Condition based on total score:

Table 8: Comparison of condition based on Total score

Condition	Group A (n=40)	Group B (n=40)	G roup C (n=40)
Excellent	4(10.0%)	0	26(65.0%)
Good	33(82.5%)	10(25.0%)	14(35.0%)
Fair	3(7.5%)	21(52.5%)	0
Poor	0	9(22.5%)	0



Comparison of condition based on Total score: The total scores in graded form as excellent, good, fair and poor and their statistical comparison showed a statistically significant difference among the groups ($p<0.01$).

IV. Discussion

The onset of action of a non-depolarising drug can be accelerated by preceding the intubating dose with a priming dose of neuromuscular blocker which provides rapid and good intubating conditions without undue prolongation of actionorundesirable side effects.[5,6,7,8] Patron and Ward conducted a study using priming dose of 20% of ED_{95} of non-depolarising agent. They recorded that greater than 75%of endplate receptors wereoccupied by that dose and this does not causeanyunpleasant symptoms.[11]In our study, priming dose of atracurium was taken as 0.1 mg/kg which was only 14.30% of the total dose. Han CG et al[12] in their study showed that optimal priming dose of atracurium was 0.09 mg/kg. The patients were instructed prior to receiving the priming dose to report development of diplopia, swallowing difficulty. Also we looked for evidence of hypoventilation and fall in oxygen saturation. Oxygen administration was given prior to administration of priming dose in every case. In our study none of the patients complained of diplopia or difficulty in swallowing or occurrence of hypoventilation after receiving priming dose of 0.1 mg/kg body weight. It has been advised that a total 2-3 times the ED_{95} of a non-depolarising agent may be used for intubation when priming principle is utilised.[13]This for atracurium comes to 0.46-0.69mg/kg. Here we used 0.7mg/kg.

In the study of Nageeb et al, priming interval were kept at 2min, 3min & 5min and comparison was done. They observed that priming interval of 3min gave optimal facilitation of intubating conditions and waiting upto 5min gave no significantadvantage over 3min and avoided unnecessary delay.[14] Mainly based on such study we kept an interval of 3 min in our study.

Analysis of variance has been used to find the homogeneity of demographic parameters. The Turkey Post-hoc test has been used to find the pair-wise significance between the three groups. Chi-square test was used to test the homogeneity of samples based on parameters as categorical scale between two groups.The demographic parameters like age, sex, bodyweight and ASA grading of all the 3 groups were comparable (table 1).

Assessment of Intubatinng Conditions:

Jaw relaxation, position of vocal cords, response to intubating coughing, straining or muscular movements, hemodynamic response to intubation and number and strength of twitches to train of four stimuli just before intubation were assessed and intubating conditions were considered excellent, good, fair or poor depending upon the score. Jaw relaxation in study Group C, 100% patients had good jaw relaxation where as 30% patients in Group A and 17.5% in Group B had good jaw relaxation and there was statistically significant difference between the two groups (table2) .Vocal cords fully open in all patients of Group C, while open vocal cords were 75% in Group A and 25% in Group B (table 3).

L D Mishraet al studied the intubating conditions of priming dose of Atracurium and concluded that Atracurium in a total dose of 0.7mg/kg utilisingpriming principle provided excellent intubating conditions at 120 sec.[15]None of the patients in Group A and Group C showed any adverse response to intubation like coughing, straining or muscular movements, which is around 95% patients in both Group A and Group C and it is significant.

These results were consistent with studies of Birsinger et al which showed that neuromuscular blockers in divided doses, significantly improved intubating conditions.[16] 45% patients in group C and 22.5% patients in group A showed 1-2 twitches with reduced strength, 80% block. By using scoring system mentioned in the text, the total score were calculated and compared between the three groups. The score were low in group B, which

denotes that intubating conditions were not satisfactory. Excellent and good conditions were significantly more in group A and group C when compared to group B. Statistically there is a significant difference among the groups.

V. Conclusion

The intubating conditions were not satisfactory even after 90 seconds when atracurium was used without priming. But when atracurium was used in a total dose of 0.7 mg/kg utilising priming principle, good intubating conditions were reached at 90 seconds and ideal conditions were reached at 120 second interval. Succinylcholine still remains the ideal drug for rapid sequence intubation. But in situations where succinylcholine is contraindicated atracurium may be used for securing airway rapidly**.**

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