Indian Journal of Basic and Applied Medical Research;
December 2020: Vol.-10, Issue- 1, P.414 – 420
DOI: 10.36848/IJBAMR/2020/36215.55821

Original article:

Study of comparison of Cisatracurium besylate and Atracurium Besylate on the quality of tracheal intubating condition at onset of anaesthesia

Dr. Aman Barthwal* , Dr Niharika Aurora , Dr Subhro Mitra , Dr Gopal Krishnan , Dr Malti Agarwal

Rohilkhand Medical College, Bareilly
Corresponding author*

Abstract:

Introduction: Monitoring of neuromuscular function is a significant advancement in the world of muscle relaxants. It is recommended by authors due to varied response to the relaxants and narrow dose range

Material and methodology: In this randomized, prospective study, we evaluated and compared cisatracurium besylate and Atracurium Besylate on the basis of onset time to complete neuromuscular blockade, quality of tracheal intubating condition, duration of action of loading dose, vitals in first 10 minutes of administration and signs of histamine release in each group of 50 patients from Age 18-40 years. We excluded hepatic and renal insufficiency, neuromuscular disorders, pregnancy and anticipated difficult intubation. All our data was assessed by VIBY MOGENSEN SCORING SYSTEM and was graded as Excellent, Good or poor.

Results: The mean duration of action was shorter in patients of Atracurium group compared to Cisatracurium group which was statistically significant. We also found that that they were no signs of any histamine release, skin changes and bronchospasm in any of the patients. All patients remained hemodynamically stable till 10 minutes post intubation, and no statistically significant difference was found between the two groups.

Conclusion: None of the previous studies found signs of histamine release in patients receiving cisatracurium. In our study, signs of histamine release; skin changes (flush, erythema), hemodynamic changes (hypotension, tachycardia) and bronchospasm were not encountered in any of the patients receiving atracurium or cisatracurium.

Introduction:

Monitoring of neuromuscular function is a significant advancement in the world of muscle relaxants. It is recommended by authors due to varied response to the relaxants and narrow dose range. Studies shown that without the use of neuromuscular monitoring in up to 42% of patients have showed signs of inadequate reversal in the recovery room[1] (Padmaja D, Mantha, 2002). Atracurium has been in clinical use since 1980[2] (Stenlake et al, 1983). It is a bis benzyl tetrahydroisoquinoline which is eliminated by Hofmann degradation. The marketed product has 10 isomers which include cis-cis, cis-trans, trans-trans depending upon configuration. The spontaneous degradation by atracurium has advantage over other neuromuscular blocking drugs leading to its safety in geriatric and organ failure patients. However, histamine release and haemodynamic instability are its major limiting effects[3] (Elbradie, 2004; Grattan and Marsland, 2016).

It is unclear that if this effect is due to atracurium causing histamine release alone or a combination of the other agents used for induction of sedation. The hemodynamic effects of atracurium is to be associated with

the initial infusion, and these hemodynamic effects persist when atracurium is used as a continuous infusion. A histamine 1 (H1) receptor antagonist and a histamine 2 (H2) receptor antagonist are often used to attenuate histamine release and help prevent this cardiovascular side effect[4] (Fukushima et al, 1990; Doenicke et al, 1994).

The histamine release is not affected by cistarcurium which is an isomer of atracurium(R-cis-R-cis) and provides stable hemodynamics and equivalent neuromuscular blockade as compared to atracurium so it is considered as a potent neuromuscular blockade[5]. (Reisch et al, 1998).

Material and methodology:

In this randomized, prospective study, we evaluated and compared cisatracurium besylate and Atracurium Besylate on the basis of onset time to complete neuromuscular blockade, quality of tracheal intubating condition, duration of action of loading dose, vitals in first 10 minutes of administration and signs of histamine release in each group of 50 patients from Age 18-40 years. We excluded hepatic and renal insufficiency, neuromuscular disorders, pregnancy and anticipated difficult intubation. All our data was assessed by VIBY MOGENSEN SCORING SYSTEM and was graded as Excellent, Good or poor.

In our study, we included total 100 patients, 50 in each group. There was no significant difference in mean age and BMI of patients in between Atracurium and Cistracurium groups.

All patients were evaluated for onset time to neuromuscular blockade, heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, duration of action and, signs of histamine release clinically, intubating conditions, vocal cord position and movement, reaction to intubation and cuff inflation and movements of limbs or coughing.

Onset time

The mean onset time was higher in Cisatracurium group than Atracurium group and there was significant difference in mean onset time of patients between Cisatracurium and Atracurium groups. In our study of 100 patients 50 in each group, the mean time of onset to complete neuromuscular block of Atracurium was 3.22 minutes +/- 0.65 minutes and mean time of onset to complete neuromuscular block of cisatracurium was 2.24 +/- 0.42 minutes and the difference was statically significant.

The difference has been quoted to be due to the higher potency of cisatracurium as compared to atracurium which produces slower onset at the laryngeal muscles[29] (Kirov et al, 2004).

Results:

Mean age of patients in group 1 was 34.86±10.79 yrs. and in group 2 was 35.02±11.72 yrs., Mean BMI of patients in group 1 was 21.34±1.49 (kg/m²) and in group 2 was 21.40±2.35 (kg/m²). There was no significant difference in mean age and BMI of patients in between group 1 and group 2.

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TABLE-1 COMPARISON OF MEAN HEART RATE AT DIFFERENT TIME INTERVAL IN BETWEN GROUP A AND GROUP B.

Heart Rate (beat/min)	GROUP 1	GROUP 2	P-Value
Baseline	87.22±8.05	88.32±5.83	0.346#
At pre-medication	94.70±5.54	95.26±5.47	0.529#
Induction	94.32±4.24	95.48±4.38	0.472#
Intubation	94.72±3.96	95.12±4.44	0.461#
5 min	94.76±3.71	94.94±4.61	0.498#
10 min	95.28±3.87	94.96±4.51	0.378#

#statistically not significant.

Mean heart rate(beat/min) at baseline in group 1 was 87.22±8.05, at pre medication was 94.70±5.54, at Induction was 94.32±4.24, at Intubation was 94.72±3.96, at 5 min after intubation was 94.76±3.71 and at 10 minutes after intubation was 95.28±3.87. In Group 2 mean heart rate at baseline in group 1was 88.32±5.83, at pre medication was 95.26±5.47, at Induction 95.48±4.38, at Intubation was 95.12±4.44, at 5 min after intubation was 94.94±4.61 and at 10 minutes after intubation was 94.96±4.51. There was no significant in mean Heart rate at different time interval in between Group 1 and Group 2.

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TABLE- 2 COMPARISON OF MEAN SBP AT DIFFERENT TIME INTERVAL IN BETWEN GROUP A AND GROUP B.

SBP (mmHg)	GROUP 1	GROUP 2	P-Value
Baseline	119.96±6.30	120.48±5.90	0.367#
At pre-medication	118.32±5.18	119.28±5.31	0.265#
Induction	114.52±3.56	115.20±3.98	0.370#
Intubation	115.98±3.41	115.36±3.53	0.374#
5 min	115.64±3.34	114.82±3.34	0.223#
10 min	114.32±2.80	113.82±3.44	0.427#

#statistically not significant.

Mean SBP (mmHg) at baseline in group 1 was 119.96±6.30, at pre medication was 118.32±5.18, at Induction was 114.52±3.56, at Intubation was 115.98±3.41, at 5 min after intubation was 115.64±3.34 and at 10 minutes after intubation was 114.32±2.80 and in Group 2 mean heart rate at baseline in group 1was 120.48±5.90, at pre medication was 119.28±5.31, at Induction was 115.20±3.98, at Intubation was 115.36±3.53, at 5 min after intubation was 114.82±3.34 and at 10 minutes after intubation was 113.82±3.44. There was no significant in mean SBP (mmHg) at different time interval in between Group 1 and Group 2.

Mean DBP(mmHg) at baseline in group 1 was 80.68±6.85, at pre medication was 79.25±6.80, at Induction was 79.02±7.91, at Intubation was 78.84±7.25, at 5 min after intubation was 78.20±7.99 and at 10 minutes after intubation was 80.16±8.06 and .in Group 2 mean heart rate at baseline in group 1was 80.02±8.00, at pre medication was 79.44±7.82, at Induction was 79.38±8.26, at Intubation was 79.27±7.61, at 5 min after intubation was 78.10±8.92 and at 10 minutes after intubation was 79.94±8.40. There was no significant in mean DBP (mmHg) at different time interval in between Group 1 and Group 2.

We found that 28 patients in atracurium group had excellent results compared to 22 patients in cisatracurium group whereas 26 patients had good results in atracurium group in comparison to 24 patients in cisatracurium group. None of our patients fell in poor score category. The mean onset time of patients was shorter in Cisatracurium group than Atracurium group and the difference was statistically significant. The mean duration of action was shorter in patients of Atracurium group compared to Cisatracurium group which was statistically

significant. We also found that that they were no signs of any histamine release, skin changes and bronchospasm in any of the patients. All patients remained hemodynamically stable till 10 minutes post intubation, and no statistically significant difference was found between the two groups.

Mean Onset time and mean duration was significantly lower among patients of Group 1(Atracurium) than Group 2(Cisatracurium). There were no signs of histamine release like skin change, hemodynamic change and Bronchospasm in Group 1 (Atracurium) and Group 2 (Cisatracurium). There was no significant difference in laryngoscope outcome, VC position, VC movement, RICI, MOV.L/C, hemodynamic parameters and mean score between the groups.

Discussion:

In our study , mean duration of action was shorter in patients who received Atracurium compared to Cisatracurium group and there was significant difference in mean duration between Cisatracurium and Atracurium groups. Bluestein et al[7] have studied that the duration of action of 0.1 mg/kg, 0.2 mg/kg of cisatracurium, and 0.5 mg/kg of atracurium was found to be 44 min, 55 min, and 43 min respectively. They stated that higher dose of cisatracurium hastened onset at the expense of prolonged duration of action. Similar results were reflected in our study.

El-kasaby AM et al[8] concluded that cisatracurium and atracurium have comparable duration of action at equipotent doses (2xED95 i.e., 0.5 mg/kg atracurium and 0.1 mg/kg cisatracurium).

In another study conducted by Bluestein LS et al[7], the duration of action of atracurium and cisatracurium in 2xED 95 doses was found to be statistically non-significant (Bluestein et al,1996).

Neuromuscular blocking drugs are extensively used by anaesthesiologists in the operating room and in the intensive care units. Among the array of muscle relaxants available, the most important concern for an anaesthesiologist after their administration, is the complete recovery of the muscle function post-surgery. Atracurium and cisatracurium have a significant advantage over other non depolarising muscle relaxants due to their non-organ dependent metabolism. This implies that postoperative recovery of muscle power is more predictable and ensures patient safety especially in the elderly as well as in patients with compromised organ functions. However, the major undesirable effect of this group of drugs is histamine release leading to anaphylactic or anaphylactoid reactions[9] (Mertes et al,). In addition, postoperative residual curarisation is also a possibility with all muscle relaxants in cases of excessive dosage or incorrect timing of the repeat dose. It has been seen that there is variable response to neuromuscular blockers in different patients that might lead to a varying degree of residual block present at the end of anaesthesia[10.11](Cammu et al, 2002; Beaussier and Boughaba, 2005).

In laryngoscopy outcome out of 50 patients, there was no significant difference in laryngoscopy outcome between Atracurium and Cisatracurium group.

Teymourian et al have compared modified dose and high dose of cisatracurium for rapid sequence induction (RSI) and found that 0.2 versus 0.4 mg/kg of cisatracurium had the same effect in providing appropriate laryngoscopy condition for RSI after 90 s. It is safer to use 0.2 mg/kg instead of 0.4 mg/kg cisatracurium to achieve acceptable conditions for RSI.

Mean heart rate (beat/min) was decreased from baseline to subsequent time periods in both the groups. There was no significant difference in mean heart rate at different time interval between Atracurium and

Cisatracurium group. In contrast to this study, Ranjan and Makker[42] showed that there was a statistically significant increase in heart rate post intubation when compared to baseline reading, in both atracurium and cis-atracurium group.

Mean SBP (mmHg) was decreased from baseline to subsequent time periods in both the groups. There was no significant difference in mean SBP (mmHg) at different time intervals between Atracurium and Cisatracurium group.

There were no significant changes in the hemodynamic variables during pre-operative, at the time of injecting the drug, during laryngoscopy and 1, 2, 3, 5, 10, and 15 min after laryngoscopy in all the groups. Niranjana et al[12](2020) found that heart rate changes were statistically insignificant between two groups. MAP was gradually decreased from preoperative values after 5 min of giving Atracurium. But this change was not observed with Cisatracurium. El –kasaby et al[8] in his study reported that hemodynamic stability for both heart rate and mean arterial blood pressure were more evident even with higher doses of cisatracurium. In their study they found that there was a statistically significant increase in HR and MABP post-intubation 120s post-injection of the muscle relaxant when compared to baseline and post-injection of 2×ED95 dose of atracurium in and the same dose of cis-atracurium due to stress of intubation.

Hosking MP et al[13], have stated that by using H1 and H2 receptor blockers before administering large dose atracurium (six times ED95), the haemodynamic manifestations of histamine release can be effectively prevented. They used diphenhydramine 1 mg/kg and cimetidine 4 mg/kg 30minutes before giving 1.5 mg/kg atracurium intravenously and found that atracurium induced reduction in MAP was decreased by 30 mmHg.

Conclusion:

None of the previous studies found signs of histamine release in patients receiving cisatracurium. In our study, signs of histamine release; skin changes (flush, erythema), hemodynamic changes (hypotension, tachycardia) and bronchospasm were not encountered in any of the patients receiving atracurium or cisatracurium.

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