Original Research Article

Comparative evaluation of intubating dose of atracurium with Cisatracurium for abdominal surgeries

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Abstract

Background: Muscle relaxation is used to facilitate endotracheal intubation and surgical relaxation. For tracheal intubation main aim is to provide neuromuscular blocking agent with better intubating conditions, longer duration of action, better hemodynamic stability and good spontaneous reversal. Atracurium besylate is an intermediate-duration, nondepolarizing, skeletal muscle relaxant and Cisatracurium, an isomer of atracurium is devoid of histamine release when compared to atracurium. **Objectives:** To compare the efficacy of atracurium with that of cisatracurium, to look for adverse effects like hemodynamic instability and signs of histamine release. **Methods**: 60 patients of either sex, ranging in age from 18-55 years belonging to ASA grade 1 and 2 undergoing abdominal surgeries under general anaesthesia were taken up for study. Patients were randomly allocated to one of the two groups of 30 patients each. Group 1 received atracurium with loading dose of 0.5 mg/kg iv and Group 2 received cisatracurium with loading dose of 0.2mg/Kg iv. **Results:** There was no statistically significant difference in age distribution, gender distribution, ASA status , type of surgery, oxygen saturation, Etco2 and signs of histamine release between both groups (p value>0.05). There was statistically significant difference with respect to jaw relaxation, difference of vocal cords in all stages (closing, moving, open) and response to intubation in both groups (p value<0.05). Group 2 was found to be better than group 1.On intergroup comparison, there was statistically significant difference in Heart rate , Systolic blood pressure and Diastolic blood pressure at 1 minute and 3 minutes after intubation (p value<0.05) with less changes in group 2 as compared to group 1 and at all other intervals both groups were comparable. **Conclusion:** Cisatracurium(0.2mg/kg) provides better intubating conditions, stable hemodynamic status and no signs of histamine release as compared to atracurium(0.5mg/kg). Thus cisatracurium appears a better alternative for preventing undesirable effects of atracurium.

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INTRODUCTION

Evolution of muscles relaxants for the placement of endotracheal tube to secure the airway in early twentieth century has revolutionized the practice of anaesthesiology. The neuromuscular blocking drugs form an essential part of anaesthetists armamentarium.[1] Neuromuscular blocking agents are divided into depolarizing and non depolarizing. Depolarizing muscle relaxants act as acetylcholine receptor agonists. Non depolarising muscle relaxants competitively bind to the alpha subunit of acetylcholine receptors at the neuromuscular junction to produce muscle paralysis. They are reversed with anticholinesterases such as neostigmine. Atracurium and cisatracurium are non-depolarizing neuromuscular blockers, intermediate acting, benzylisoquinolone compounds.[2] Atracurium besylate was first made in 1974 by George H Dewar. Onset of atracurium is 2-3 min and intubating dose is 0.5mg/kg and maintenance dose is 0.1mg/kg. Allergic reactions like skin

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flushing, bronchospasm can be seen due to histamine release. Atracurium has a significant advantage over other neuromuscular blocking drugs due to its spontaneous degradation and non- organ dependent elimination leading to its safety in geriatric and organ failure patients. However histamine release and hemodynamic instability are its limiting factors.[3] Cisatracurium besylate formerly recognized as 51W89 is a Bisbenzyl tetrahydroisoquinolone. Onset of action is within 2-3 min and Duration of action is 55-65 minutes but they are dose dependent. It is metabolized by hofmann elimination. It has minimum propensity to release histamine and has a higher autonomic stability. Cisatracurium has potency of approximately 3 to 4 times greater than that of atracurium. Cisatracurium with higher dose (0.2mg/kg and 0.3mg/kg) has no effect on mean arterial pressure[4] and provide more effective, more rapid neuromuscular blocking with longer duration of action and stable hemodynamic status.[5]

AIMS AND OBJECTIVES: were to compare the efficacy of Atracurium with that of Cisatracurium, to look for adverse effects like hemodynamic instability and signs of histamine release.

MATERIAL AND METHODS

After obtaining informed written consent and approval from the hospital ethical committee, comparative controlled study was conducted in the Department of Anaesthesiology and Intensive care unit, Government Medical College and Associated Hospitals, Jammu. 60 patients of either sex, ranging in age from 18-55 years belonging to ASA grade 1 and 2 undergoing abdominal surgeries under general anaesthesia were taken up for study. Patients were randomly allocated to one of the two groups of 30 patients each.

Group 1: received atracurium with loading dose of 0.5 mg/kg iv.

Group 2: received cisatracurium with loading dose of 0.2mg/Kg iv.

Exclusion criteria were patients refusal, hypersensitivity to drugs, history of progressive cardiac, renal, hepatic and central nervous system disease or psychiatric illness, anticipated difficult intubation (MPG grade 3 or 4 and thyromental distance < 6cm)

PRE ANAESTHETIC CHECK UP

A detailed pre- anaesthetic check up was done one day prior to surgery which include detailed history, thorough clinical examination and relevant investigations. An informed written consent was taken. All patients were prepared by overnight fasting. Tab Alprazolam 0.5 mg was given at bed time the night before surgery and Tab Pantoprazole 40mg was given with a sip of water in the morning of surgery.

PROCEDURE

All patients were premedicated with injection Diclofenac sodium 75mg im 15 minutes before surgery. After arrival in operative room, monitors attached and baseline readings like heart rate, non invasive arterial blood pressure (systolic blood pressure, diastolic blood pressure and mean arterial pressure) and oxygen saturation were recorded and patients were infused with 4-6 ml/kg/min of RL. Patients were given inj. Ondansetron 0.1 mg/kg iv and inj. Tramadol 1 mg/ kg iv. After preoxygenation for 3 minutes the patient was induced with inj. Propofol 2-2.5mg/kg iv given slowly till loss of verbal contact with the patient. Gas mixture of 50%oxygen, 50% nitrous oxide and isoflurane was started and ventilation was assisted. Thereafter the muscle relaxant was given to the patients.

Group 1: patients received 0.5 mg/kg iv of atracurium over 5-10 seconds. **Group 2:** patients received 0.2mg/kg iv of cisatracurium over 5-10 seconds.

After administration of specific muscle relaxant according to groups, the time was recorded from giving of muscle relaxant to relaxation of jaw. The tracheal intubation was performed with appropriate size cuffed endotracheal tube and intubating conditions were assessed as per Cooper's criteria (jaw relaxation, Status of vocal cords and response to intubation). Systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, heart rate, SPO2 and ETCO2 were recorded after 1 minute, 3 minutes, 5 minutes and every 10 minutes of intubation till end of surgery.

Table: Cooper's criteria – Cooper *et al*. in 1992

Score	0	1	2	3
Jaw relaxation (ease of laryngoscopy)	Poor (impossible)	Minimal (difficult)	Moderate (fair)	Good (easy)
Vocal cords	Closed	closing	Moving	Open
Response to intubation	Severe coughing or bucking	Mild coughing	Slight diaphragmatic movement	None

SCORING: EXCELLENT 8-9, GOOD 6-7, FAIR 3-5, POOR 0-2

Maintenance of anaesthesia was provided by isoflurane with 60% nitrous oxide and 40% oxygen and top up of muscle relaxant (0.02 mg/kg of cisatracurium and 0.1 mg/kg of atracurium). Patients were mechanically ventilated to maintain end expiratory carbon dioxide concentration of 35-45 mmHg.

At the end of surgery, patients were reversed with inj Neostigmine [50ug/kg iv] and inj Glycopyrrolate [10ug/kg iv] and extubated.The data tabulations were done by done using MS excel 2010 and statistical analysis was done using the SPSS

software 20.0 version (SPSS Inc., Chicago, Illinois, USA) Student's independent t-test was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. A P-value of less than 0.05 was considered statistically significant. All P-values were two tailed.

RESULTS

There was no statistically significant difference in age distribution, gender distribution, ASA status and type of surgery. In group 1 good, moderate and minimum jaw relaxation were found in 53.3%, 33.3% and 13.3% patients respectively. In group 2 good and moderate jaw relaxation was found in 83.3% and 16.7% patients and minimal jaw relaxation was not found in any patient. Jaw relaxation in group 2 was found to be better with statistically significant difference (p value <0.05). In group 1 open, moving and closing vocal cords were found in 46.7% ,43.3% and 10% patients respectively where as in group 2 open and moving vocal cords were found in 76.7% and 23.3% patients and closing vocal cords were not found in any patient. Difference of vocal cords in all stages (closing, moving, open) was found to be better in group 2 with statistically significant difference(p value < 0.05) . In group 1 no response, slight diaphragmatic movement and mild coughing were found in 50%, 36.7 % and 13.3% patients respectively. In group 2 no response, slight diaphragmatic movement were found in 80% and 20 % patients respectively where as mild coughing was not found in any patient. Response to intubation was also found to be better in group 2 with statistically significant difference (p<0.05). In group 1 excellent intubating conditions, good intubating conditions and fair intubating conditions were found in 53.3%, 30% and 16.7% patients whereas in group 2 excellent intubating conditions and good intubating conditions were found in 76.7% and 23.3% patients and no patient had fair intubating conditions. Intubating conditions in group 2 were better with statistically significant difference between group 2 and group 1 (p<0.05).

On intergroup comparison, there was statistically significant difference in heart rate, SBP, DBP, MAP at 1 minute and 3 minutes after intubation (p value<0.05) whereas at all other intervals both groups were comparable.

Table 1: Demographic profile of both groups

	Group 1	Group 2
Age (years)	32.5	31.4
Male	26.7	40
Female	73.3	60
ASA 1	76.7	86.7
ASA 2	23.3	13.3

Table 2: Comparison based on interoperative HR (beats/min) between two groups

Time Interval	Group 1	Group 2	P-value
Baseline	76.27	79.77	0.084
Before Induction	76.73	78.37	0.396
1 Min after Intubation	100.23	90.70	<0.001*
3 Min	81.53	85.27	0.048*
5 Min	77.10	79.10	0.301
10 Min	76.37	79.13	0.157
20 Min	75.47	78.60	0.098
30 Min	75.17	78.10	0.123
40 Min	76.27	79.77	0.084
50 Min	75.17	78.10	0.123
60 Min	75.37	78.03	0.177

Table 3: Comparison based on interoperative SBP (mmHg) between two groups

Time Interval	Group 1	Group 2	P-value
Baseline	121.13	122.73	0.378
Before Induction	120.50	121.80	0.465
1 Min after Intubation	141.07	135.63	0.001*
3 Min	137.23	132.50	0.003*
5 Min	122.03	123.53	0.406
10 Min	120.13	122.20	0.235
20 Min	120.50	120.77	0.878
30 Min	121.60	120.57	0.543
40 Min	121.10	120.00	0.501
50 Min	120.50	120.77	0.878
60 Min	121.60	120.57	0.543

Table 4: Comparison based on interoperative DBP (mmHg) between two groups

Time Interval	Group 1	Group 2	P-value
Baseline	77.20	76.73	0.735
Before Induction	76.17	76.47	0.824
1 Min after Intubation	91.10	85.67	<0.001*
3 Min	87.27	82.43	<0.001*
5 Min	78.87	76.37	0.053
10 Min	75.93	75.33	0.631
20 Min	76.77	75.17	0.224
30 Min	76.17	75.10	0.358
40 Min	77.20	75.10	0.087
50 Min	76.17	75.10	0.358
60 Min	77.20	75.10	0.087

Table 5: Comparison based on interoperative MAP (mmHg) between two groups

Time Interval	Group 1	Group 2	P-value
Baseline	91.84	92.07	0.847
Before Induction	90.94	91.58	0.569
1 Min after Intubation	107.76	102.32	<0.001*
3 Min	103.92	99.12	<0.001*
5 Min	93.26	92.09	0.274
10 Min	90.67	90.96	0.779
20 Min	91.34	90.37	0.346
30 Min	91.31	90.26	0.281
40 Min	91.83	90.07	0.076
50 Min	90.94	90.32	0.518
60 Min	92.00	90.26	0.086

Table 6: Comparison based on jaw relaxation in two groups

Jaw Relaxation	Group 1	Group 2	P-value
Minimal	13.3	0.0	<0.001*
Moderate	33.3	16.7	
Good	53.3	83.3	
Total	**100**	**100**	

Table 7: Comparison based on vocal cord in two groups

Vocal Cord	Group 1	Group 2	P-value
Closing	10.0	0.0	<0.001*
Moving	43.3	23.3	
Open	46.7	76.7	

Table 8: Comparison based on response to intubation in two groups

Response to intubation	Group 1	Group 2	P-value
Mild coughing	13.3	0.0	<0.001*
Slight diaphragmatic movement	36.7	20.0	
None	50.0	80.0	

Table 9: Comparison based on intubating conditions in two groups

Intubating Conditions	Group 1	Group 2	P-value
Excellent	53.3	76.7	<0.001*
Good	30.0	23.3	
Fair	16.7	0.0	

Table 10: Signs of histamine release in two groups

Signs of Histamine release	Yes	No	P-value
Group 1	6.7	93.3	0.492
Group 2	0	100	

DISCUSSION

The demographic parameters of the patients including age, weight, sex and ASA status were comparable in both groups (p value > 0.05). There was statistically no significant difference between group 1 and group 2 as far as type of surgeries was concerned. In our study intubating conditions were assessed using jaw relaxation, vocal cord position and intubating response as per the Cooper's Criteria. It was found that intubating conditions were most favourable in group 2 followed by group 1. Our results were in accordance to Athaluri VV *et al.,* 2019[6] who found excellent intubating conditions with rapid onset of action with cisatracurium(0.15mg/kg) as compared to cisatracurium(0.1mg/kg) and atracurium(0.5mg/kg) and El kasaby AM *et al.*, 2010[5] who found excellent intubating conditions of cisatracurium in higher doses (0.2mg/kg, 0.3mg/kg) versus 2ED95 dose of cisatracurium(0.1mg/kg) and atracurium(0.5mg/kg). On intergroup comparison it was found that difference in Heart rate was statistically significant at 1 and 3 minutes after intubation. Group 1 produced a more significant increase in heart rate as compared to group 2 where as on intragroup comparison, the difference in heart rate from the baseline was greatest in group 1 than group 2 at 1 minute and 3 minutes after intubation which was statistically significant.

Our results were in accordance with Thukral S *et al.*, (2018)[7] who compared cisatracurium (0.2mg/kg) with atracurium (0.5mg/kg) and concluded that cisatracurium has a faster onset, good intraoperative hemodynamic parameters and better recovery profile. Kaur H *et al.*, 2018[8] studied recovery profile and haemodynamic profile of atracurium (0.5mg/kg) versus cisatracurium (0.1mg/kg) and reported that there was no statistically significant difference in heart rate. Our results are in contrary to this study as the dose of cisatracurium taken in this study was 0.1 mg/kg which was less than that taken in our study. On intergroup comparison we found that group 1 produced a more significant increase in systolic blood pressure, diastolic blood pressure and mean arterial pressure as compared to group 2 after 1 minute and 3 minutes after intubation where as on intragroup comparison, statistically significant difference in systolic blood pressure, diastolic blood pressure and mean arterial pressure from baseline was seen at 1 minute and 3 minutes after intubation in both groups which were greatest in group 1 than group 2. However the HR, systolic blood pressure, diastolic blood pressure and mean arterial pressure returned to baseline at 5 minutes after intubation and thereafter till 60 minutes. Change in HR, SBP, DBP, MAP was considered significant only when there is >20% deviation from baseline values.The more significant increase in HR, SBP, DBP, MAP in group 1 than group 2 might be because we had not taken equipotent doses i.e. 2ED95 of atracurium (0.5mg/kg) and cisatracurium (0.1mg/kg) in which the results are insignificant. The dose we had taken in our study was 2ED95 (0.5mg/kg) of atracurium and 4ED95 (0.2mg/kg) of cisatracurium. As we increase the dose of drug the cardiovascular stability also increases. Our results were also in accordance with that of Teymourian H *et al.*, 2014[9] who found that the same dose (2ED95) atracurium is more effective neuromuscular blocking agent than cisatracurium, but higher doses of cisatracurium 4ED95 and 6ED95 provide more effective, more rapid neuromuscular blocking with longer duration of action and stable hemodynamic status. Bhagat M *et al.*, 2018[10] concluded that atracurium and cisatracurium had similar safety profile. Oxygen saturation, ETCO2, signs of histamine release like erythema, wheal and flush were comparable in both groups which was statistically insignificant. The syndrome becomes clinically evident when doses of 0.5 mg/kg (two times ED95) or more are injected rapidly Basta SJ *et al.,*1992[11] Our study was in accordance with Mohanty AK *et al.*, 2018[12] who compared cisatracurium and atracurium and found that cisatracurium had no signs of histamine release. Similarly Kopman AF *et al.*, 2000[13] reported that cisatracurium is 3-4 times more potent than atracurium and it did not release histamine. Jammar P *et al.*, 2017[14] evaluated two intubating doses of

cisatracurium during general anaesthesia and stated that 0.2mg/kg of cisatracurium provides longer duration of action and more stable hemodynamic status than 0.15mg/kg. No associated signs of histamine release were detected clinically.

CONCLUSION

We concluded that cisatracurium(0.2mg/kg) provided better intubating conditions, stable hemodynamic status and no signs of histamine release as compared to atracurium(0.5mg/kg). Thus cisatracurium appears a better alternative for preventing undesirable effects of atracurium.

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