

Efficacy of Cisatracurium over Atracurium in Patients undergoing Lower Abdominal Surgeries at a Tertiary Care Hospital

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Abstract

Context: Atracurium is associated with hemodynamic instability in patients. Cisatracurium has been developed to overcome this side effect which is an isomer of atracurium. *Aim:* To study the efficacy of Cisatracurium in patients undergoing lower abdominal surgeries. *Settings and Design:* Present randomized controlled trial was conducted at Department of Anesthesiology, Malla Reddy Institute of Medical Sciences, Hyderabad. *Methods:* The patients being operated for lower abdominal surgeries were randomly allocated into two groups. 30 patients were in Atracurium group while 30 patients were in Cisatracurium group. The changes in the heart rate and mean arterial pressure was observed after giving injection of anesthetic and immediately after the intubation. *Statistical analysis:* The data was analyzed using means and proportions. Student's t test for means and chi square for proportions was used. *Results:* Both the groups were comparable in baseline characteristics. The baseline heart rate was similar for both the groups. But heart rate after injection and after intubation in Atracurium group was significantly more compared to the heart rate after injection in Cisatracurium group ($p < 0.05$). The change of mean MAP was significantly more in Atracurium group after giving injection from baseline compared to Cisatracurium group. But the difference of means of change in MAP from giving injection to intubation was statistically not significant between the two groups ($p > 0.05$). Again the change in mean MAP was significantly more in Atracurium group after intubation from baseline compared to Cisatracurium group. *Conclusion:* Cisatracurium was found to be more effective than Atracurium in terms of stabilized heart rate and mean arterial pressure.

Keywords: Atracurium; Cisatracurium; Heart Rate; Comparison; Characteristics.

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Introduction

Muscle relaxants are required for surgeries performed under general anesthesia. These muscle relaxants used have effects on the hemodynamics of the patient undergoing surgery under general anesthesia [1].

The mechanism of action by which these muscle relaxants are responsible for hemodynamic changes can be release of histamine, can be through the

sympathomimetic action, can be through blockage of ganglions, or can be through antimuscarinic effects on heart or a combination of these mechanisms. Atracurium is one such muscle relaxant commonly used in patients undergoing surgeries under general anesthesia. Atracurium belongs to benzyl isoquinolinium group. It is a non depolarizing relaxant. It exerts its action independently without affecting the metabolism of the body. It does not affect the metabolism of kidney and liver. Hence, it is a safe and attractive option

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in patients having underlying renal and liver disease and undergoing surgery under general anesthesia. But inspite of these advantages associated with Atracurium, as it causes muscle relaxation by histamine release, it affects the hemodynamics of the patients. Because of this property of Atracurium its use can be a problem in certain patients especially patients undergoing cardiovascular surgeries [2].

Hence the isomer of Atracurium called Cisatracurium can be used to overcome this disadvantage associated with use of atracurium. It is also metabolized just like that of atracurium. But ester hydrolysis mechanism is not seen the metabolism of Cisatracurium and hence patient can be hemodynamically more stable when it is used as compared to atracurium [3].

Muscle relaxants are used in patients undergoing surgeries under general anesthesia. These muscle relaxants act by release of histamine. This leads to hemodynamic changes in the body like lowered blood pressure, erythema of face and head. This usually occurs with plasma concentration of drug becomes two to three times of its initial level. Dose of the muscle relaxant given as well as the speed with which the drug is administered to the patient determines the severity of these side effects [4].

It has been shown that in patients undergoing surgery under general anesthesia, having pre-existing cardiac disease, when Cisatracurium given in the dose of 0.3 mg/kg will not alter the mean arterial blood pressure [5].

It has been found that contrary to atracurium, Cisatracurium will not increase histamine plasma level to $>8 \times ED_{95}$. Hence, patients will not experience the side effects associated with high levels of histamine in the plasma and this is particularly useful for patients having pre-existing heart disease [6].

Thus use of Cisatracurium seems to have an edge over the use of atracurium not only for coronary graft surgeries but also patients undergoing other surgeries [7].

Present study was planned to study effectiveness of Cisatracurium over atracurium in patients undergoing abdominal surgeries with special reference to hemodynamic changes like heart rate and mean arterial blood pressure.

Methods

Study Design

Present study was hospital based randomized controlled trial.

Study Period

The study was carried out over a period of six months from December 2017 to May 2018.

Settings

The study was carried out at Department of Anesthesiology, Malla Reddy Institute of Medical Sciences, Hyderabad

Sample Size

Total of 60 patients undergoing abdominal surgeries under general anesthesia were studied over a period of six months

Ethical Considerations

Institutional Ethics Committee Permission was obtained before the start of the study. Informed consent and high risk consent was obtained from all selected patients for the present study.

Inclusion Criteria

1. Patients undergoing abdominal surgeries under general anesthesia
2. Patients willing to participate in the present study

Exclusion Criteria

1. Patients found to have multiple disorders
2. Patients not willing to participate in the present study

Grouping, Randomization and Methodology

Sixty eligible patients as per the abovementioned inclusion and exclusion criteria were randomly allocated to one of the two groups in equal numbers. 30 patients received atracurium and were labeled as atracurium group. 30 patients received Cisatracurium and were labeled as Cisatracurium group.

Baseline characteristics like age, sex, ASA grade, MP grade, mouth opening, neck movements, type of surgery undergone and condition at intubation was noted and recorded in the pre designed, pre tested, and semi structured study questionnaire.

Hemodynamic characteristics like heart rate and mean arterial pressure was recorded at baseline i.e. before giving the injection of muscle relaxant, again immediately after giving the injection of muscle relaxant and third time immediately after intubation and recorded.

Statistical Analysis

The data was entered in the Microsoft Excel worksheet and analyzed using means and proportions. Statistical tests like student's t test was used for comparing differences of mean between the two groups and Yate's corrected chi square for comparing differences of proportions between the two groups.

Results

Table 1 shows comparison of baseline clinical characteristics between the two groups. The two groups were comparable with each other in terms of mean age, distribution of males and females in two groups, and also comparable for ASA grades and MP grades as the difference in these characteristics was statistically not found to be significant. (p > 0.05).

Table 2 shows comparison of type of surgery done for patients in two groups. Both the group of patients underwent similar type of surgery. Thus

both the groups were comparable to each other in terms of type of surgery performed as the difference in these characteristics was statistically not found to be significant. (p > 0.05).

Table 3 shows comparison of mean heart rate between the two groups. The baseline heart rate was similar for both the groups. But heart rate after injection in Atracurium group was significantly more compared to the heart rate after injection in Cisatracurium group (p < 0.05). Similarly, heart rate after intubation in Atracurium group was significantly more compared to the heart rate after intubation in Cisatracurium group (p < 0.05).

Table 4 shows comparison of change in mean MAP between the two groups. The mean MAP increased by 4 mmHg in Atracurium group after giving injection from baseline while the mean MAP decreased by 5.4 mmHg in Cisatracurium group after giving injection from baseline. This difference of means was found to be statistically significant (p < 0.05). But the difference of means of change in MAP from giving injection to intubation was statistically not

Table 1: Comparison of baseline clinical characteristics between the two groups

Clinical characteristics		Atracurium group (N = 30)	Cisatracurium group (N = 30)	T value/chi square value	P value
Age (years)		35.1±2.5	34.4±2.3	1.1286	0.2637
Sex	Male	15 (50%)	15 (50%)	0.0667	0.7963
	Female	15 (50%)	15 (50%)		
ASA grade	I	26 (86.7%)	26 (86.7%)	0.1442	0.7041
	II	04 (13.3%)	04 (13.3%)		
MP grade	I	20 (66.7%)	12 (40%)	3.211	0.07008
	II	10 (33.3%)	18 (60%)		

Table 2: Comparison of type of surgery done for patients in two groups

Type of surgery done	Atracurium group (N = 30)		Cisatracurium group (N = 30)		Chi square value	P value
	Number	%	Number	%		
Cholecystectomy	12	40	14	46.7	1.0529	0.788458
Appendectomy	12	40	10	33.3		
Hernioplasty	06	20	04	13.3		
Hysterectomy	00	00	02	6.7		

Table 3: Comparison of mean heart rate between the two groups

Heart rate (beats/min)	Atracurium group (N = 30)	Cisatracurium group (N = 30)	T value	P value
Baseline HR	86.1±5.8	84.6±3.8	1.1849	0.2409
HR after injection	88.6±7.4	82.5±4.1	3.9493	0.0002
HR after intubation	97.4±9.1	85.2±14.8	3.8461	0.0003

Table 4: Comparison of change in mean MAP between the two groups

Mean change in MAP (mmHg)	Atracurium group (N = 30)	Cisatracurium group (N = 30)	T value	P value
From baseline to injection	4±2.7	-5.4±4.9	9.2027	0.0001
From injection to intubation	7.4±5.3	6.6±5.3	0.5846	0.5611
From baseline to intubation	11.4±5.1	1.16±5.03	7.8299	0.0001

significant between the two groups ($p > 0.05$). Again the mean MAP increased by 11.4 mmHg from baseline to intubation in Atracurium group compared to only an increase of mean MAP of 1.16 mmHg in the Cisatracurium group. This difference was found to be statistically significant.

Discussion

The two groups were comparable with each other in terms of mean age, distribution of males and females in two groups, and also comparable for ASA grades and MP grades as the difference in these characteristics was statistically not found to be significant. ($p > 0.05$).

Both the group of patients underwent similar type of surgery. Thus both the groups were comparable to each other in terms of type of surgery performed as the difference in these characteristics was statistically not found to be significant ($p > 0.05$).

The baseline heart rate was similar for both the groups. But heart rate after injection in Atracurium group was significantly more compared to the heart rate after injection in Cisatracurium group ($p < 0.05$). Similarly heart rate after intubation in Atracurium group was significantly more compared to the heart rate after intubation in Cisatracurium group ($p < 0.05$).

The mean MAP increased by 4 mmHg in Atracurium group after giving injection from baseline while the mean MAP decreased by 5.4 mmHg in Cisatracurium group after giving injection from baseline. This difference of means was found to be statistically significant ($p < 0.05$). But the difference of means of change in MAP from giving injection to intubation was statistically not significant between the two groups ($p > 0.05$). Again the mean MAP increased by 11.4 mmHg from baseline to intubation in Atracurium group compared to only an increase of mean MAP of 1.16 mmHg in the Cisatracurium group. This difference was found to be statistically significant.

Ghorbanlo M et al. [8] compared efficacy of Cisatracurium in patients undergoing cardiovascular surgeries under general anesthesia. They divided the patients into two groups and noted the two groups were comparable to each in terms of age, sex, premedication with cardiac drugs, basic underlying disease and pre-surgery ejection fraction. But the groups differed significantly in terms of hemodynamic indices with better results obtained in group using Cisatracurium. Thus the author

concluded that as a muscle relaxant, Cisatracurium is better and advantageous over the other. We also concluded that Cisatracurium was better hemodynamic stabilizer for patient than atracurium.

Correa CMN et al. [9] compared atracurium and Cisatracurium in different doses. They noted that atracurium in the dose of 1 mg/kg and Cisatracurium in the dose of 0.25 mg/kg had similar mean arterial pressure. When the authors administered both the drugs in the doses of 4 mg/kg then atracurium was found to decrease the MAP to 62.8 ± 4.5 and Cisatracurium was found to reduce the MAP to 82.5 ± 2.3 mmHg in comparison to control levels. The authors concluded that "The doses of Cisatracurium used in this study did not because a reduction in blood pressure significant enough to justify the use of the preventive measures used in the atracurium groups."

Jirasiritham S et al. [10] divided the patients into two groups one of which received atracurium and one of which received Cisatracurium. The baseline demographic data was comparable between the two groups. The authors found that the dose required for intubation and maintenance in the Cisatracurium group was lesser compared to the other group. The authors concluded that Cisatracurium was safe and provided hemodynamic stability in patient undergoing kidney transplant and recommended its use even though it is costly.

Jabalameli M et al. [11] found that IOP decreased in both the groups after injection of muscle relaxant and at two minutes increased. Then it decreased at five minutes and ten minutes after intubation. The authors observed that SBP and IOP were more in the atracurium group compared to the Cisatracurium group and the difference was statistically significant two, five and ten minutes post intubation. Thus the author concluded that Cisatracurium prevents the rise of IOP post intubation in patients undergoing general anesthesia.

El-Kasaby AM et al. [12] observed that heart rate and mean arterial blood pressure was significantly more after intubation in atracurium group with dose of 2xED (95) in group 1 and same dose of Cisatracurium was given in group 2 but after 5-20 minutes the difference was statistically not significant when compared with doses of 4xED (95) in group 3 and 6xED (95) in group 4. Onset time was significantly lesser in atracurium group with dose of 2xED (95) compared with same dose of Cisatracurium. Thus the author concluded that in same doses the atracurium was better neuromuscular blocking agent than Cisatracurium. Cisatracurium in higher doses was found to be more effective

neuromuscular blocking agent, provided hemodynamic stability and there were no signs of release of histamine clinically.

Conclusion

Thus we conclude that Cisatracurium was found to be more effective than Atracurium in terms of stabilized heart rate and mean arterial pressure. It can be used in all patients undergoing any type of surgery under general anesthesia.

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