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Original Article

COMPARATIVE STUDY OF CISATRACURIUM AND ATRACURIUM IN DIFFERENT DOSES FOR INTUBATION DURING GENERAL ANESTHESIA IN LOWER ABDOMINAL SURGERY: A PROSPECTIVE RANDOMIZED DOUBLE-BLIND INTERVENTIONAL TRIAL

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ABSTRACT

Objective: General anesthesia requires smooth endotracheal intubation, aided by neuromuscular blocking agents. Atracurium and cis-atracurium are non-depolarizing agents used for muscle relaxation. Succinylcholine, though effective, has undesirable side effects. This study aims to compare atracurium and different doses of cis-atracurium to assess their onset, duration, recovery, hemodynamic effects, and side effects, in order to identify the ideal agent for intubation.

Methods: The study will compare atracurium (0.5 mg/kg) with two different doses of cis-atracurium, namely 0.10 mg/kg and 0.15 mg/kg. The parameters evaluated will include the onset of neuromuscular blockade, duration of blockade, recovery time, hemodynamic effects, and incidence of side effects. Neuromuscular monitoring will be employed to ensure proper dosing and prevent residual paralysis.

Results: The study will provide valuable data on the comparative characteristics of atracurium and cis-atracurium at different doses. This includes their onset of action, duration of neuromuscular blockade, recovery time, impact on hemodynamic parameters, and occurrence of side effects. The results will shed light on the efficacy, safety, and tolerability of these drugs for endotracheal intubation.

Conclusion: The study aims to identify the most suitable neuromuscular blocking agent for facilitating endotracheal intubation by comparing atracurium and different doses of cis-atracurium. By assessing their onset, duration, recovery time, hemodynamic effects, and side effect profiles, clinicians can make informed decisions to optimize patient care during general anesthesia.

Keywords: General anesthesia, Endotracheal intubation, Neuromuscular blocking agents

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INTRODUCTION

General anesthesia is commonly used in surgery, and successful intubation of the patient's airway is crucial. Factors such as muscle relaxation, anesthesia level, and the skill of the anesthesiologist affect the ease of intubation. To facilitate intubation and induce muscle relaxation, neuromuscular blocking medications are used. These drugs inhibit nerve impulse transmission at the neuromuscular junction [1]. The ideal neuromuscular blocking agent for intubation should have a rapid onset, short duration, minimal impact on hemodynamics, no persistent paralysis, and provide optimal intubating conditions. Depolarizing and non-depolarizing agents are two categories of these drugs. Succinylcholine, a depolarizing agent, is effective but has negative side effects. Researchers have been searching for alternatives without these adverse effects [2].

Atracurium and cis-atracurium are intermediate-acting non-depolarizing neuromuscular blocking agents. Cis-atracurium is a pure stereoisomer of atracurium and does not cause histamine release like atracurium does. Atracurium can be safely used in patients with organ failure, pregnancy, and advanced age since it is not metabolized by the liver or kidneys [3]. Histamine-related adverse effects include bronchospasm, tachycardia, flushing, erythema, and hypotension, which are absent in cis-atracurium. Cis-atracurium has higher potency and slightly longer duration to maximum block compared to atracuriumbesylate. Both drugs have similar rates of spontaneous recovery and clinically useful durations of action [4].

During anesthesia, neuromuscular monitoring (NMM) is necessary to assess the onset of neuromuscular blockade, determine the required muscle relaxation level, ensure smooth extubation, and monitor recovery. NMM prevents over-or under-dosing and ensures complete recovery. Paralysis is considered complete at 90-95% receptor occupancy, with observable block at 75-85%. Limited studies have compared the characteristics of blockade between atracurium and cis-atracurium at different doses. Therefore, a study was designed to compare these drugs in terms of onset, duration, recovery, hemodynamics, and side effects [5].

The study aims to provide insights into the differences between atracurium and cis-atracurium to help clinicians make informed decisions for endotracheal intubation and anesthesia. It will evaluate onset speed for timely intubation, duration for balanced muscle relaxation, recovery for safe extubation, impact on hemodynamics, and side effects [6]. By comparing the drugs, clinicians can make informed decisions based on patient-specific factors. The research aims to contribute to knowledge on neuromuscular blocking agents and provide evidence-based recommendations to optimize patient care [7].

In summary, the study aims to compare atracurium and cis-atracurium in terms of their onset, duration, recovery, impact on hemodynamics, and side effects. The findings will enhance the practice of general anesthesia and guide anesthesia providers in selecting the most suitable neuromuscular blocking agent for endotracheal intubation.

MATERIALS AND METHODS

Study area-the study was conducted in Department of anaesthesiology S. M. S. Medical College and attached group of hospitals, Jaipur.

Study period: after approval of the research review board till the desired number of case achieved.

Study type and design: Hospital based prospective randomised comparative double blind interventional study.

Study universe: cases undergoing lower abdominal surgeries under general anaesthesia.

Sample size: a sample of 32 cases in each group is calculated at 95% confidence and 80% power to verify the minimum difference of 8.95% in mean of onset of action in 3 different group of studies as per seed article.

Randomization: it was done using opaque seal envelope method.

Double blinding: both the drug are clear and transparent solution, volume was made according to different doses by adding normal saline. The anaesthesthsist who was prepared study drugs and labellwd them as A, B and C would be different from the anaesthetist who was given anaesthesia and recorded data.

Study group: A total number of 96 patients were included in the study and were randomly allocated into 3 groups (32 in each group).

The 96 patients was equally and randomly divided in each groups.

- Group A: were received Inj. atracurium with initial dose of 0.5 mg/kg followed by maintenance dose of 0.1 mg/kg.
- Group B: were received Inj. cis-atracurium with initial dose of 0.1 mg/kg followed by maintenance dose of 0.02 mg/kg.
- Group C: were received Inj. cis-atracurium with initial dose of 0.15 mg/kg followed by maintenance dose of 0.03 mg/kg.

Eligibility criteria

Inclusion criteria

After approval from institutional ethical committee, a prospective randomised comparative double blind interventional study was carried out on patients of age group 20-65 y who were undergoing lower abdominal surgical procedures with an anticipated duration of at least one hour under general anaesthesia in SMS Medical college and attached groups of hospitals, Jaipur. Patients of either sex with ASA grade I and II were included in the study.

Exclusion criteria

- Patients who refused to give consent
- Anticipated difficult intubation
- ASA grade III or above
- Patients having any disorder of the cardiovascular, hepatic, renal and neuromuscular systems.
- Pregnant and lactating women.
- Patients on medication, known to interact with neuromuscular blocking drugs e. g. Antibiotics (amino-glycosides and tetracycline), antidepressants, anticonvulsants, anti-arrhythmic (calcium channel blocker and quinidine) and magnesium sulphate.

Procedure

In this study, patients undergoing surgery will receive explanations of the procedures and provide written consent. Pre-medication will be administered, and patients will be monitored using ECG, blood pressure, and pulse oximetry. Neuromuscular monitoring will be performed using a relaxograph. General anesthesia will be induced with fentanyl and propofol, and maintained with a mixture of gases and sevoflurane. Muscle relaxants will be given, and intubation conditions will be assessed. Hemodynamic parameters and body temperature will be monitored. Reversal of muscle relaxation will be achieved with neostigmine and glycopyrrolate. Safe extubation will be determined based on the TOF-ratio.

RESULTS

Table 1: Comparison of heart rate (/min) among study groups

Time	Group A	Group B	Group C	P value
Pre op	76.78±11.12	75.13±13.44	76.75±8.63	0.797
Induction	77.44±15.45	77.63±14.12	78.22±12.1	0.973
Intubation	88.5±11.35	88.22±13.65	90.38±10.56	0.735
5 min	85.44±11.13	85.78±10.36	86.47±12.16	0.933
10 min	81.94±10.9	81.25±11.72	82.72±12.27	0.880
15 min	78.25±13.35	77.78±13.55	77.47±14.95	0.975
20 min	76.44±11.32	75.66±11.49	74.59±9.46	0.791
25 min	75.88±12.02	75±15.14	76.41±13.06	0.915
35 min	73.66±12.94	71.66±13.28	70.28±12.63	0.579
45 min	74.03±11.43	74.81±13.06	73.97±12.68	0.955
60 min	72±13.98	73.59±12.52	72.69±13.02	0.889

(Data are presented as mean+SD), this table shows the mean heart rate at different time intervals in three groups, which was comparable among three groups (P>0.05).

Table 2: Comparison of SBP (mmHg) among study groups

Time	Group A	Group B	Group C	P value
Pre op	119.47±9.56	117.06±5.14	118.91±6.46	0.389
Induction	118.16±10.13	116.44±9.46	116.66±9.08	0.737
Intubation	124.38±11.52	124.78±13.68	127.13±13.27	0.654
5 min	124.38±14.93	124.78±15.94	125.09±11.78	0.980
10 min	117.38±13.26	118±15.44	119.59±9.75	0.782
15 min	116.56±10.55	116.84±10.73	117.75±9.42	0.889
20 min	116.22±14.4	116.88±17.11	117.22±11.07	0.961
25 min	115.22±11.77	115.63±14.46	113.97±12.74	0.869
35 min	113.47±8.34	114.16±16	113.09±12.93	0.945
45 min	111.38±11.98	113.31±12.97	112.75±11.57	0.808
60 min	112±9.43	112.06±14.1	111.31±13.23	0.965

(Data are presented as mean+SD), this table shows the mean SBP at different time intervals in three groups, which was comparable in three groups at all times (P>0.05).

Table 3: Comparison of DBP (mmHg) among study groups

Time	Group A	Group B	Group C	P value
Pre op	79.72±6.46	78±3.45	79.25±4.24	0.352
Induction	78.78±6.68	77.63±6.25	77.69±6.07	0.715
Intubation	82.94±7.75	83.25±9.15	84.72±8.77	0.676
5 min	82.91±10.07	83.22±10.64	83.41±7.75	0.978
10 min	78.25±8.78	78.63±10.23	79.78±6.53	0.762
15 min	77.75±7.04	77.91±7.2	78.59±6.28	0.872
20 min	77.5±9.53	77.91±11.43	78.16±7.39	0.963
25 min	76.81±7.8	77.06±9.59	75.91±8.51	0.854
35 min	75.59±5.58	76.13±10.75	75.41±8.67	0.942
45 min	74.28±7.98	75.5±8.62	75.13±7.82	0.829
60 min	74.69±6.21	74.78±9.47	74.19±8.91	0.954

(Data are presented as mean+SD), This table shows mean DBP at different time intervals in three groups, which was comparable in three groups at all times m. (P>0.05)

Table 4: Comparison of MAP (mmHg) among study groups

Time	Group A	Group B	Group C	P value
Pre op	92.94±7.5	91±3.98	92.5±4.93	0.362
Induction	91.88±7.9	90.56±7.3	90.72±7.09	0.743
Intubation	96.72±8.96	97.13±10.7	98.81±10.32	0.676
5 min	96.72±11.65	97±12.39	97.25±9.16	0.982
10 min	91.31±10.27	91.72±11.99	93.03±7.53	0.777
15 min	90.59±8.2	90.88±8.35	91.56±7.32	0.882
20 min	90.41±11.18	90.94±13.33	91.13±8.59	0.965
25 min	89.66±9.13	89.94±11.2	88.63±9.94	0.862
35 min	88.28±6.46	88.81±12.4	87.97±9.98	0.943
45 min	86.66±9.27	88.19±10.11	87.69±9.02	0.805
60 min	87.13±7.37	87.19±10.97	86.53±10.35	0.956

(Data are presented as mean+SD), This table shows the comparison of MAP at different time intervals in all three groups, which shows that there were no significant changes in MAP in three groups at all time (P>0.05). The changes in MAP were also insignificant in intergroup comparison.

Table 5: Comparison of SpO2 (%) among study groups

Time	Group A	Group B	Group C	P value
Pre op	99.34±0.87	98.84±0.77	99.13±0.87	0.061
Induction	98.88±0.83	98.94±0.84	98.66±0.79	0.359
Intubation	98.63±0.75	98.88±0.83	99±0.88	0.184
5 min	98.72±0.81	98.81±0.86	99.03±0.78	0.298
10 min	99.09±0.82	99.03±0.69	98.97±0.78	0.809
15 min	98.94±0.84	98.91±0.86	98.91±0.82	0.985
20 min	99.06±0.88	98.88±0.94	99±0.8	0.685
25 min	98.91±0.82	99.19±0.82	98.88±0.87	0.263
35 min	99.22±0.87	99.09±0.78	98.97±0.74	0.459
45 min	98.94±0.84	98.78±0.83	98.91±0.78	0.721
60 min	99±0.76	98.94±0.8	98.97±0.86	0.953

This table shows the comparison of Spo2 at different time intervals in all three groups, which shows that there were no significant changes in spo2 in three groups at all time (P>0.05). The changes in spo2were also insignificant in intergroup comparison.

Table 6: Distribution of study subjects according to signs of histamine release

Signs of histamine release	Group A		Group B		Group C	
	N	%	N	%	N	%
No	29	90.6	32	100	32	100
Yes	3	9.4	0	0	0	0
Total	32	100	32	100	32	100

Chi-square = 6.194 with 2 degrees of freedom; P = 0.045 (*S*), No signs of histamine release were observed with both the doses of cis-atracurium while sign of histamine release was observed in 3 patients with atracurium (P=0.045)

DISCUSION

Neuromuscular blocking drugs play a crucial role in anesthesia by improving its safety and effectiveness. Anesthesiologists aim to select a muscle relaxant with quick onset, prolonged action, stable hemodynamics, and fewer side effects. Cis-atracurium, a stereoisomer of atracurium, is considered an excellent muscle relaxant due to its potency, stable hemodynamics, and lack of histamine release.

Previous studies have compared atracuriumbesylate and cis-atracuriumbesylate at different doses, but limited research is

available on comparing specific doses of cis-atracurium (2×ED95) with atracurium (2×ED95) and cis-atracurium (3×ED95). Therefore, this study aimed to compare the higher dose of cis-atracurium (2×ED95) with cis-atracurium (3×ED95) and atracurium (2×ED95) in terms of block and recovery characteristics, hemodynamic stability, and adverse effects [8].

The study involved 96 patients divided into three groups: Group a received atracurium, Group B received cis-atracurium (2×ED95), and Group C received cis-atracurium (3×ED95). The demographic data of the patients, including age, gender, ASA grade, weight, and duration of surgery, were similar among the three groups [9].

The onset time of block, measured from the administration of the muscle relaxant to reaching a TOF Count of 0, was significantly shorter in Group A compared to Group B but longer than Group C [10]. The duration of block, defined as the time from injection to a TOFR of 25%, was significantly longer in Group C compared to Group B and Group A. The recovery time was also longer in Group C compared to the other two groups. These findings were consistent with previous studies, which showed that cis-atracurium has a longer duration of action compared to atracurium [11].

In terms of hemodynamic effects, there were no significant differences in heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure among the three groups at different time intervals. These results were consistent with previous studies that reported comparable hemodynamic effects between atracurium and cis-atracurium [12].

Overall, the study concluded that cis-atracurium at a dose of 0.15 mg/kg provided a more effective duration of block, rapid onset, and uneventful recovery compared to cis-atracurium at a lower dose (0.10 mg/kg) and atracurium (0.5 mg/kg). However, the higher dose of cis-atracurium was associated with a longer recovery time and a higher risk of residual block [13].

The study highlighted the importance of proper dose selection to achieve the desired effect without excessive overdosing. It also emphasized the potency and duration of action of cis-atracurium, which is attributed to its structure and greater potency compared to atracurium.

The findings of this study contribute to the existing body of research on neuromuscular blocking drugs and their effects in anesthesia. By comparing different doses of cis-atracurium and atracurium, the study provides valuable insights into the optimal use of these muscle relaxants for balanced general anesthesia.

It is worth noting that the results of this study may vary due to differences in cold chain maintenance and drug manufacturing. Further research and studies are necessary to validate and expand upon these findings in different patient populations and clinical settings.

CONCLUSION

A dose of 0.15 mg/kg of cis-atracurium appears to be a preferable option compared to atracurium at 0.5 mg/kg and cis-atracurium at 0.10 mg/kg due to its advantages in terms of quicker onset, intermediate duration of action, and suitability for both intubation and maintenance. Specifically, cis-atracurium at 0.15 mg/kg serves as a viable alternative to atracurium at 0.5 mg/kg for intubation purposes. It is important to note that while recovery may be faster with atracurium, there is a potential risk of histamine-related adverse effects associated with its use.

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Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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