

Comparison of the hemodynamic and neuromuscular effects of atracurium and cisatracurium - A prospective, randomised, comparative study.

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Authors:

Sneha K (ORCID ID: 0009-0004-1989-1146), 1. Consultant , department of Critical care medicine, Nirmala Hospital, Calicut

Rajesh MC (ORCID ID: 0009-0002-8646-1256), 2. Senior Consultant, department of Anaesthesiology & Academic coordinator, BMH, Calicut

Nidhin Chandradas (ORCID ID: 0009-0009-3417-1434), Associate consultant, Department of Anaesthesiology, BM H, Calicut

Access This Article Online



Website:
theanaesthesiologist.com

Corresponding Author:

Nidhin Chandradas. Sreegovilakam, Ocheri house, Pantheerankave post, Calicut, Kerala - 673019.

Email : nidhin.chandradas@yahoo.co.in

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ABSTRACT

Introduction: Atracurium and cisatracurium are both intermediate-acting, non-depolarising neuromuscular blocking agents cleared largely through Hofmann elimination, making them relatively independent of hepatic or renal function. Atracurium causes dose-dependent histamine release, an effect absent in cisatracurium, its purified stereoisomer — though whether this translates into any real haemodynamic difference between the two remains worth examining directly.

Objectives: To compare the neuromuscular and haemodynamic effects of atracurium and cisatracurium in ASA I and ASA II patients undergoing elective surgery under general anaesthesia.

Methodology: Two hundred and fifty-six patients were randomly divided into two equal groups, receiving either atracurium 0.5 mg/kg or cisatracurium 0.2 mg/kg intravenously. Heart rate and blood pressure were recorded at baseline and at 1, 3, and 5 minutes after drug administration, and neuromuscular block was assessed via train-of-four count at 3 and 5 minutes. Results: Blood pressure did not differ significantly between groups at any point. Heart rate fell somewhat more with cisatracurium, reaching significance at one minute, though this did not persist. Train-of-four count was significantly lower with cisatracurium at both 3

minutes ($p = 0.0013$) and 5 minutes ($p < 0.001$), indicating a more complete block. Sex had no meaningful effect on outcomes with either drug.

Conclusion: Cisatracurium achieved a more complete neuromuscular block than atracurium, while blood pressure remained comparable throughout; cisatracurium was associated with only a modest, short-lived drop in heart rate at one minute. These findings favour cisatracurium where dependable neuromuscular blockade is the priority, with both drugs otherwise comparable in overall haemodynamic stability.

Keywords: Atracurium; Cisatracurium; Neuromuscular blockade; Train-of-four; Haemodynamic stability; Non-depolarising muscle relaxant

Introduction

In general anaesthesia practice, the neuromuscular blocking drugs (NMBDs) are given for skeletal muscle relaxation only in anaesthetised individuals, as analgesia and amnesia are not their properties. The pharmacological effect of these drugs is to interrupt the transmission of impulses at the neuromuscular junction. They act on the nicotinic acetylcholine receptor. There are two types of neuromuscular blocking drugs depending on their mechanism of action: depolarising NMBDs and non-depolarising NMBDs. The depolarising NMBDs act as acetylcholine receptor agonists, while non-depolarising NMBDs act as competitive antagonists.

The most widely used depolarising NMBD is succinylcholine. The non-depolarising muscle relaxants bind to the receptors but cannot produce any conformational change needed for ion channel opening. They are further classified according to their duration of action into long-, intermediate- and short-acting drugs. The intermediate-acting drugs last for 20 to 50 minutes. There are different intermediate-acting neuromuscular blocking agents like atracurium, cisatracurium, vecuronium and rocuronium. They differ from each other in their pharmacokinetic and pharmacodynamic properties.

Atracurium and cisatracurium both are benzylisoquinolinium compounds. Atracurium is metabolised by ester hydrolysis and Hofmann elimination. Cisatracurium is the 1R cis-1'R cis isomer of atracurium, which is metabolised by Hofmann elimination. Atracurium causes histamine release and its effects, which are absent in cisatracurium. As it causes histamine release, it can result in hypotension and tachycardia. This effect is related to the dose of the drug and is of short duration. It can also cause increased airway resistance and bronchospasm in patients with hyperactive airway disease. These changes will not be seen after cisatracurium administration, as per previous studies.

In this study, we intend to compare the neuromuscular and hemodynamic properties of cisatracurium and atracurium in ASA 1 and ASA 2 patients. The hemodynamic properties are assessed by heart rate and blood pressure measurements at regular intervals and the neuromuscular properties by train of four count. The better of these two can be then recommended for patients with hemodynamic instability.

Methods

This prospective, randomised, comparative study was carried out after obtaining clearance from the institutional scientific and ethical committee. Two hundred and sixty-eight adult patients, all of ASA physical status I or II and aged between 18 and 70 years, with body weight ranging from 40 to 90 kg, were enrolled after they gave informed consent and were found suitable for elective surgery under general anaesthesia. Using simple randomisation generated through WinPepi software (version 11.65), patients were divided into two equal groups of 134 each. Group A received cisatracurium at a dose of 0.2 mg/kg, while Group B received atracurium at 0.5 mg/kg, both administered intravenously. Patients presenting with an anticipated difficult airway, those who needed more than one attempt at intubation, pregnant women, and patients with a full stomach were not included in the study.

Before induction, nil-per-oral status and consent were verified once again for every patient, and premedication was administered in the form of injection midazolam 1 mg along with injection emeset 4 mg. Once shifted to the operating room, patients were connected to standard monitoring equipment — five-lead ECG, pulse oximetry, and non-invasive blood pressure. After three minutes of preoxygenation with 100% oxygen, anaesthesia was induced using injection fentanyl at 1.5 µg/kg and injection propofol at 2 mg/kg. Mask ventilation was confirmed to be adequate in each patient before the study drug was given. Heart rate and blood pressure readings were then taken at one, three, and five minutes following drug administration, with any deviation of more than 20% from baseline managed as clinically indicated. Neuromuscular block was evaluated using train-of-four stimulation via a peripheral nerve stimulator set at 40 mA, checked three minutes after the muscle relaxant was administered and again at five minutes if

intubating conditions were not yet adequate. Any patient who turned out to have an unanticipated difficult airway, or who needed multiple attempts at intubation, was excluded from the final analysis. Observation for each patient concluded five minutes after the muscle relaxant had been given.

All data were entered into an Excel spreadsheet and subsequently analysed with STATA (release 11). Comparisons of means between dichotomous variables, such as sex, were made using the two-sided independent-samples t-test, while one-way ANOVA was applied for variables spanning more than two categories. Percentages, proportions, and mean values were calculated as required, and a p-value below 0.05 was taken to indicate statistical significance throughout.

Results

256 patients completed the study, split evenly between the two groups — 128 on atracurium, 128 on cisatracurium. Overall, 127 (49.6%) were women and 129 (50.4%) were men, a near-even split. By ASA status, 78 patients (30.5%) were class I and 178 (69.5%) class II. Looking at the two drug groups separately, atracurium had 41 ASA I patients (32.0%) and 87 ASA II (68.0%), while cisatracurium had 37 ASA I (28.9%) and 91 ASA II (71.1%) — so the groups were well matched on ASA status.

Heart rate

Baseline heart rate was similar between groups (atracurium 78.72 ± 15.76 beats/min vs cisatracurium 79.35 ± 12.75 ; $p = 0.7242$). After the study drug, heart rate dropped in both groups, but more so with cisatracurium — a difference that reached

significance at one minute (78.09 ± 15.30 vs 72.98 ± 11.03 ; $p = 0.0025$), though not at three minutes

(73.04 ± 13.73 vs 70.02 ± 11.39 ; $p = 0.0563$) or five minutes (74.97 ± 14.55 vs 71.99 ± 11.74 ; $p = 0.0512$).

Time point	Atracurium (mean $\pm$ SD)	Cisatracurium (mean $\pm$ SD)	p value
Baseline	78.72 ± 15.76	79.35 ± 12.75	0.7242
1 minute	78.09 ± 15.30	72.98 ± 11.03	0.0025
3 minutes	73.04 ± 13.73	70.02 ± 11.39	0.0563
5 minutes	74.97 ± 14.55	71.99 ± 11.74	0.0512

Table: Heart rate (beats/min) at baseline and at 1, 3, and 5 minutes after study drug administration (N = 128 per group).

Blood Pressure

Systolic blood pressure fell in both groups after induction and the study drug — from a baseline of 123.19 ± 15.39 mmHg (atracurium) and 117.05 ± 11.19 mmHg (cisatracurium). At one, three, and five minutes the two groups tracked closely (93.27 ± 14.60 vs 93.56 ± 14.67 , $p = 0.8745$; 90.42 ± 14.50 vs 91.26 ± 15.08 , $p = 0.6516$; 99.10 ± 12.85 vs 96.51 ± 12.13 , $p = 0.0980$), with nothing clinically meaningful separating the two drugs at any of these points.

Diastolic pressure followed the same pattern — from a baseline of 72.34 ± 10.63 mmHg (atracurium) and 69.14 ± 8.94 mmHg (cisatracurium) down to comparable readings at one minute (56.07 ± 10.07 vs 53.88 ± 9.58 , $p = 0.0751$), three minutes (54.79 ± 9.60 vs 53.40 ± 11.58 , $p = 0.2966$), and five minutes (59.88 ± 10.52 vs 57.72 ± 10.35 , $p = 0.0982$). None of these post-drug differences reached significance.

Mean arterial pressure told the same story — no significant between-group difference, falling from

91.69 ± 12.25 mmHg (atracurium) and 86.80 ± 8.41 mmHg (cisatracurium) at baseline to closely matched values at one minute (70.77 ± 10.46 vs 69.59 ± 11.01 , $p = 0.3801$), three minutes (69.77 ± 12.88 vs 69.27 ± 12.57 , $p = 0.7536$), and five minutes (76.75 ± 13.82 vs 74.69 ± 10.11 , $p = 0.0541$).

Neuromuscular blockade

TOF count, checked at three and five minutes, was consistently lower with cisatracurium than atracurium at both points — meaning a more complete block. At three minutes, mean TOF count was 3.46 ± 1.07 (atracurium) vs 2.93 ± 1.51 (cisatracurium); at five minutes the gap widened, to 1.62 ± 1.75 vs 0.82 ± 1.21 ($p = 0.0013$ at three minutes; $p < 0.001$ at five minutes). In short, cisatracurium produced a faster, more complete onset of block than atracurium at the doses used here.

Breaking TOF count down by sex within each drug group turned up no significant differences. In the atracurium group, mean TOF at three minutes was 3.48 ± 1.11 (women) vs 3.44 ± 1.04 (men), $p = 0.8647$

at five minutes, 1.66 ± 1.73 vs 1.57 ± 1.78 , $p = 0.7725$. In the cisatracurium group, three-minute TOF was 3.19 ± 1.27 (women) vs 2.68 ± 1.67 (men), $p = 0.0545$; at five minutes, 0.85 ± 1.23 vs 0.79 ± 1.21 , $p = 0.7563$. So the neuromuscular effects of both drugs held up regardless of sex.

Discussion

Atracurium and cisatracurium are both intermediate-acting, non-depolarising relaxants whose clearance barely depends on liver or kidney function — which is exactly why they've become popular in patients with multiple comorbidities. We compared the two agents, at their usual clinical doses of 0.5 mg/kg and 0.2 mg/kg, for their haemodynamic and neuromuscular effects in ASA I and ASA II patients.

On the haemodynamic side, both drugs saw heart rate and blood pressure drop relative to baseline after induction and drug administration — which looks more like an effect of the induction agents than of either muscle relaxant specifically. Heart rate dropped somewhat more with cisatracurium, significantly so at one minute, though that difference didn't hold at three or five minutes. Blood pressure changes tracked closely between groups throughout, with nothing clinically meaningful separating them at any point.

For neuromuscular blockade, TOF count at three and five minutes was consistently — and significantly — lower with cisatracurium, pointing to a more complete block at the doses used. That doesn't line up neatly with the rest of the literature, though. Rochana et al. found a faster onset with cisatracurium 0.2 mg/kg versus atracurium 0.5 mg/kg, but without statistical significance, which broadly agrees with what we found here.

Mellingoff et al. went the other way, finding atracurium 0.5 mg/kg reached maximal twitch suppression faster than cisatracurium 0.1 mg/kg. El Kasaby et al. also found atracurium had the better onset at twice its ED95, though cisatracurium pulled ahead — with fewer side effects — at higher ED95 multiples. Sparr et al. reported a similar edge for atracurium at twice ED95. These seemingly contradictory results probably come down to the specific doses and ED95 multiples each study used, rather than any clear-cut superiority of one drug over the other.

We found no significant sex difference in TOF count within either drug group, suggesting the neuromuscular response to both agents held steady regardless of sex at the doses used. That sits alongside Shi HJ et al., who reported a notably higher cisatracurium ED95 in men (67.4 ± 4.4 mcg/kg) than women (48.7 ± 1.0 mcg/kg), though without a matching difference in onset time. One likely reason we didn't see a sex effect here is that we used a single fixed dose per kilogram for everyone, rather than individualising doses around each sex's ED95.

Limitation

Our findings diverge from earlier reports that described a more favourable haemodynamic profile with cisatracurium, particularly regarding blood pressure stability, but we found no such difference: blood pressure tracked closely between groups throughout, and heart rate fell slightly more with cisatracurium if anything.

This discrepancy may reflect our study population, which was predominantly ASA I–II and therefore less likely to reveal haemodynamic differences that might emerge in higher-risk patients — for example,

those with compromised left ventricular function or significant cardiovascular disease. A larger or more targeted sample may also have been needed to detect the hemodynamic effects reported previously. Future studies in larger, more heterogeneous, higher-risk populations would help clarify whether this reflects a true absence of difference or simply limited power in our study.

Conclusion

Overall, atracurium and cisatracurium gave comparable haemodynamic stability, with no significant blood pressure difference between groups at any point studied. Cisatracurium did produce a modest but significant fall in heart rate at one minute — an effect atracurium didn't show — though it faded at later time points. On neuromuscular blockade, cisatracurium clearly outperformed atracurium, with a consistently lower TOF count at both three and five minutes. Sex made no difference to either drug's effects. Altogether, this points to cisatracurium as the preferable choice when a more reliable, complete block matters most, while both drugs remain reasonable options haemodynamically — including for patients with limited cardiovascular reserve.

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