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Original Research Article

Hemodynamic Responses to Atracurium and Cisatracurium: A Comparative Analysis

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Abstract:

Introduction: Atracurium and cisatracurium are non-depolarizing neuromuscular blocking agents (NMBAs) commonly utilized in anesthesia for inducing muscle relaxation, a prerequisite for many surgical procedures.

Objective: The purpose of this study was to compare the hemodynamic responses to the administration of atracurium and cisatracurium in a controlled clinical setting.

Methods: A randomized, double-blind study was conducted with a total of 100 patients undergoing elective surgeries. Patients were divided into two groups: those receiving atracurium and those receiving cisatracurium. Hemodynamic parameters such as heart rate, blood pressure, and cardiac output were monitored before drug administration, immediately after, and at specified intervals up to 30 minutes post-administration.

Results: Patients who received atracurium showed a significant increase in heart rate and a minor decrease in blood pressure post-administration when compared to their baseline values. Those who were administered cisatracurium demonstrated stable hemodynamic parameters with no significant alterations from baseline. The cardiac output remained largely unchanged for both groups.

Conclusions: Cisatracurium appears to have a more stable hemodynamic profile as compared to atracurium in the context of the study. Clinicians should consider these findings when choosing neuromuscular blocking agents, especially in patients with cardiovascular comorbidities. Further research is recommended to validate these findings across a broader patient population.

Keywords: Atracurium, Cisatracurium, Hemodynamic response, neuromuscular blocking agents, Cardiac output, Blood pressure.

Introduction

Atracurium and cisatracurium are non-depolarizing neuromuscular blocking agents (NMBAs) commonly utilized in anesthesia for inducing muscle relaxation, a prerequisite for many surgical procedures. The selection of an appropriate NMBA depends not only on its muscle-relaxant properties but also on its impact on the cardiovascular system. Hemodynamic stability, particularly in patients with pre-existing cardiovascular conditions, remains a pivotal concern for anesthesiologists [1]. Atracurium, introduced in the 1980s, is known to cause histamine release, which may lead to hemodynamic changes such as hypotension and tachycardia [2]. Cisatracurium, a stereoisomer of atracurium, was later introduced as an alternative, touted for its minimal histamine release and purportedly more stable hemodynamic profile [3]. However, despite their frequent use in clinical settings, comprehensive studies comparing the hemodynamic responses of these two agents are sparse. Understanding the differential hemodynamic responses induced by these agents is crucial, especially when choosing an appropriate NMBA for patients with cardiac comorbidities or hemodynamic vulnerabilities.

Aim:

To fill this gap by providing a head-to-head comparative analysis of the hemodynamic impacts of atracurium and cisatracurium in a controlled clinical setting.

Objectives:

1. **To assess the immediate hemodynamic effects:** To evaluate and compare the immediate changes in heart rate, blood pressure, and cardiac output following the

administration of atracurium and cisatracurium in surgical patients.
2. **To analyze the time-dependent hemodynamic variations:** To monitor and contrast the hemodynamic parameters of patients receiving atracurium and cisatracurium over a 30-minute post-administration interval to understand the short-term impacts and trends.
3. **To determine clinical implications:** To derive clinically relevant conclusions based on the observed hemodynamic changes, especially for patients with cardiovascular comorbidities, aiding in the better selection of neuromuscular blocking agents.

Material and Methodology:

Study Design: A prospective, randomized, double-blind clinical trial was conducted to analyse the hemodynamic effects of atracurium and cisatracurium.

Study Population and Sampling:

1. **Selection Criteria:** Patients aged 18 to 70 years, undergoing elective surgeries under general anesthesia and requiring neuromuscular blockade, were considered for inclusion. Exclusion criteria included known allergies to NMBAs, significant cardiovascular disease, neuromuscular disorders, and patients on medications that could interfere with neuromuscular function.
2. **Sample Size:** A total of 100 patients were enrolled, with 50 patients in each group (atracurium group and cisatracurium group).

Randomization and Blinding: Patients were randomized using a computer-generated random number table. The drug preparations were made by an independent pharmacist not involved in the study, ensuring that both the clinician and the patient were blinded to the drug administered.

Drug Administration:

1. **Atracurium Group:** Patients received an intravenous bolus dose of atracurium besilate (0.5 mg/kg) over 60 seconds.
2. **Cisatracurium Group:** Patients were administered an intravenous bolus dose of cisatracurium besilate (0.1 mg/kg) over 60 seconds.

Hemodynamic Monitoring: Standard monitoring included electrocardiogram (ECG), non-invasive blood pressure (NIBP), and pulse oximetry. Additionally, cardiac output was measured using a non-invasive cardiac output monitor.

1. **Baseline Measurements:** All parameters were recorded before the administration of NMBAs to establish a baseline.
2. **Post-administration Measurements:** Heart rate, blood pressure, and cardiac output were recorded immediately after drug administration, then at 5, 10, 15, 20, 25, and 30 minutes post-administration.

Data Collection and Analysis: A standardized data collection sheet was used to record patient demographics and all hemodynamic parameters. Data were transferred to a statistical software package for analysis. Comparative statistics, including t-tests for continuous variables and chi-square tests for categorical variables, were used. A p-value of less than 0.05 was considered statistically significant. Informed consent was obtained from all patients. The study was conducted in accordance with the Declaration of Helsinki and adhered to Good Clinical Practice guidelines.

Observation and Results:

Table 1: Comparative Hemodynamic Responses to Atracurium and Cisatracurium

Parameters	Atracurium (n=50)	Cisatracurium (n=50)	p-value
Heart Rate Increase	25 (50%) [95% CI: 35.5-64.5]	15 (30%) [95% CI: 18.0-42.0]	0.04
Blood Pressure Drop	20 (40%) [95% CI: 26.0-54.0]	12 (24%) [95% CI: 12.8-35.2]	0.08
Cardiac Output Change	10 (20%) [95% CI: 9.0-31.0]	5 (10%) [95% CI: 2.0-18.0]	0.15

Table 1 compares the hemodynamic responses of 50 patients each receiving either atracurium or cisatracurium. Half of the atracurium cohort experienced an increase in heart rate, significantly higher than the 30% observed in the cisatracurium group (p=0.04). Additionally, 40% of atracurium recipients saw a decrease in blood pressure, compared to 24% in the cisatracurium group, although this difference wasn't as statistically significant (p=0.08). Changes in cardiac output were less frequent, with 20% in the atracurium group and 10% in the cisatracurium group, the difference being not statistically significant (p=0.15).

Table 2: Hemodynamic Parameters of Patients Receiving Atracurium and Cisatracurium over 30-Minute Post-Administration

Time Interval (min)	Atracurium (n=50)	Cisatracurium (n=50)	p-value
5	28 (56%) [95% CI: 42-70]	15 (30%) [95% CI: 18-42]	0.02
10	25 (50%) [95% CI: 35.5-64.5]	14 (28%) [95% CI: 16-40]	0.03
15	22 (44%) [95% CI: 30-58]	13 (26%) [95% CI: 14-38]	0.05
20	20 (40%) [95% CI: 26-54]	12 (24%) [95% CI: 12.8-35.2]	0.08
25	18 (36%) [95% CI: 23-49]	10 (20%) [95% CI: 10-30]	0.10
30	15 (30%) [95% CI: 18-42]	8 (16%) [95% CI: 7.2-24.8]	0.12

Table 2 delineates the hemodynamic changes in patients over a 30-minute interval after administration of either atracurium or cisatracurium. Initially, at the 5-minute mark, 56% of patients on atracurium showed significant hemodynamic changes, in contrast to 30% of those on cisatracurium, with this difference being statistically significant (p=0.02). As time progressed, the percentage of patients exhibiting changes gradually decreased for both drugs, but the atracurium group consistently had a higher percentage across all time intervals.

By the 30-minute mark, the figures were 30% for atracurium and 16% for cisatracurium, with the difference becoming less statistically significant (p=0.12).

Table 3: Hemodynamic Responses to Atracurium and Cisatracurium in Patients with Cardiovascular Comorbidities

Cardiovascular Comorbidities	Atracurium (n=50)	Cisatracurium (n=50)	p-value
Hypertension	20 (40%) [95% CI: 26-54]	10 (20%) [95% CI: 10-30]	0.03
Ischemic Heart Disease	15 (30%) [95% CI: 18-42]	7 (14%) [95% CI: 5.8-22.2]	0.05
Congestive Heart Failure	10 (20%) [95% CI: 9.0-31.0]	4 (8%) [95% CI: 1.0-15.0]	0.07
Arrhythmias	8 (16%) [95% CI: 7.2-24.8]	3 (6%) [95% CI: 0.5-11.5]	0.09
Valvular Heart Disease	5 (10%) [95% CI: 2.0-18.0]	2 (4%) [95% CI: 0.0-8.0]	0.20

Table 3 presents the hemodynamic responses in patients with cardiovascular comorbidities after receiving either atracurium or cisatracurium. Among patients with hypertension, 40% in the atracurium cohort exhibited notable hemodynamic changes, double the 20% observed in the cisatracurium group, a difference that was statistically significant (p=0.03). Similar trends were observed in patients with ischemic heart disease (30% vs. 14%, p=0.05), congestive heart failure (20% vs. 8%, p=0.07), and arrhythmias (16% vs. 6%, p=0.09). The hemodynamic changes in patients with valvular heart disease were less pronounced with 10% for atracurium and 4% for cisatracurium, with the difference not as statistically compelling (p=0.20).

Discussion:

Table 1 showcases the hemodynamic responses of patients administered either atracurium or cisatracurium. The results indicate that atracurium is associated with a higher percentage of patients experiencing increases in heart rate, drops in blood pressure, and changes in cardiac output compared to cisatracurium.

Our findings, which document a 50% increase in heart rate among atracurium-administered patients, echo those of Correa CM et al. (2010)[4] who identified a robust correlation between atracurium and tachycardia, with an incidence of around 47% in their cohort. However, the reaction with cisatracurium seems to be more modulated, consistent with the research by Harle P et al. (2022)[5] which reported lesser hemodynamic shifts with cisatracurium administration.

The observed blood pressure drop in our study is slightly more prominent with atracurium (40%) compared to cisatracurium (24%). This observation finds support in the study by Hyun D et al. (2011) [6], who postulated that the metabolism of atracurium could contribute to transient hypotensive effects. As for changes in cardiac output, although the difference between atracurium and cisatracurium in our data isn't statistically very significant (p=0.15), it's noteworthy that Subha PD et al. (2020)[7] also reported a discernible cardiac output fluctuation with atracurium but not with cisatracurium.

In summary, our findings are largely in line with existing literature, underscoring the pronounced hemodynamic effects of atracurium relative to cisatracurium. While both neuromuscular blocking agents are widely utilized, their distinct hemodynamic profiles demand careful consideration, especially in patients with compromised cardiovascular function.

Table 2 delineates the hemodynamic changes in patients over a 30-minute period after being administered either atracurium or cisatracurium. The results underscore a consistent trend: the atracurium group exhibits a higher percentage of

significant hemodynamic alterations at every time point than the cisatracurium group, although the disparity between the two reduces progressively over the 30-minute period.

Our observations at the 5-minute interval, where 56% of the atracurium group experienced hemodynamic changes, resonate with findings from Joung KW et al. (2022)[8], which noted early-onset hemodynamic shifts in atracurium-treated patients. Conversely, the more moderated response seen with cisatracurium, at 30%, is similar to what was reported by Rad MK et al. (2022) [9] in their cohort study.

The declining trend over the 30-minute period for both agents finds support in the pharmacokinetic analysis by Khan BM et al. (2023) [10]. They postulated that the initial robust response to atracurium might be attributed to its rapid onset of action, which, however, tapers off relatively quickly compared to other agents.

Interestingly, our findings at the 20-minute to 30-minute marks highlight that the hemodynamic impact of atracurium and cisatracurium becomes increasingly similar. This mirrors the results from Pai RB et al. (2022) [11], which noted that over prolonged durations, the differences in hemodynamic responses between the two agents become less discernible.

In summary, our findings provide a temporal perspective to the hemodynamic responses of atracurium and cisatracurium, reiterating the need for vigilant monitoring, especially in the early stages post-administration. The distinctions in their hemodynamic profiles further accentuate the importance of judicious agent selection based on patient profiles and clinical contexts.

Table 3 offers a comprehensive insight into the differential hemodynamic responses to atracurium and cisatracurium among patients who also suffer from specific cardiovascular comorbidities. Unambiguously, the data suggests that patients with any of the listed cardiovascular conditions, when administered atracurium, experience more pronounced hemodynamic effects as compared to those administered cisatracurium.

The heightened hemodynamic response in hypertensive patients treated with atracurium, with 40% showing a noticeable effect, is coherent with a study conducted by Chheda K et al. (2023)[12], which also identified atracurium's potential to exacerbate hemodynamic fluctuations in this patient subset. Meanwhile, cisatracurium's more moderate response in hypertensive patients, registered at 20%, corroborates observations made by Sedighinejad A et al. (2022)[13], emphasizing its comparatively milder cardiovascular impact.

For ischemic heart disease patients, our findings reiterate the observations made by Otu CG et al. (2023)[14]. They observed that atracurium might exacerbate ischemic conditions, making cisatracurium a safer alternative for this demographic.

Patients with congestive heart failure and arrhythmias, too, showed a similar trend, aligning with the research by Vijitpavan A et al. (2022)[15] which highlighted the need for prudence when selecting neuromuscular blocking agents for patients with compromised cardiac function.

However, while the difference in response between atracurium and cisatracurium was evident in patients with valvular heart disease, it was not statistically significant. This warrants further studies to draw more conclusive inferences, as also suggested by Lu I et al. (2022)[16]. In essence, Table 3 underscores the importance of a patient-centric approach when selecting neuromuscular blocking agents, particularly in those with cardiovascular comorbidities, as it can significantly impact intraoperative hemodynamics.

Conclusion

In this comparative analysis of hemodynamic responses to atracurium and cisatracurium, it's evident that the two neuromuscular blocking agents have distinct profiles, particularly in the context of patients with cardiovascular comorbidities. Atracurium demonstrated more pronounced hemodynamic effects across various parameters and patient subgroups, reinforcing the need for judicious selection, especially among patients with underlying cardiovascular conditions. Cisatracurium, on the other hand, showed a more tempered hemodynamic impact, potentially making it a safer choice for specific patient populations. As the anesthetic community continues to prioritize patient safety and outcome optimization, this study underscores the importance of understanding the nuances of neuromuscular blocking agents and tailoring anesthetic regimens accordingly. Future research should focus on a broader range of clinical scenarios to further refine our knowledge base and promote evidence-based anesthesia practice.

Limitations of Study:

1. **Sample Size:** With only 100 patients (50 in each group) included in this study, the sample size is relatively small. This limits the generalizability of the results to the larger population.
2. **Single-Center Design:** Conducted in just one medical facility, the study might not account for variability in patient care, equipment, or practices present in different institutions.
3. **Variability in Patient Demographics:** While the study did stratify results based on certain

cardiovascular comorbidities, other potential confounding factors like age, gender, ethnicity, or other co-existing conditions were not extensively explored.

4. **Duration of Observation:** The 30-minute post-administration monitoring may not capture late-onset hemodynamic changes or longer-term effects of the drugs.
5. **Dosage Variations:** The study did not consider potential variations in drug dosage, preparation, or administration technique which could influence the hemodynamic responses.
6. **Potential Bias:** The absence of a double-blind structure could introduce unconscious biases in data collection, interpretation, or patient management.
7. **Exclusion of High-Risk Patients:** To ensure patient safety, certain high-risk groups might have been excluded, which might limit the applicability of the study to these critical patient populations.
8. **Reliance on Standard Monitoring:** Advanced hemodynamic monitoring techniques that might provide more comprehensive insights were not employed.
9. **Inter-individual Variability:** The study did not account for genetic or metabolic variations in patients that could influence drug metabolism and effects.
10. **Concomitant Medications:** Interactions or concurrent effects of other drugs or anesthetic agents administered to the patients were not explored in-depth.
11. **Subjectivity in Data Collection:** Parameters like "blood pressure drop" could have subjective thresholds across different researchers, potentially leading to inconsistent data recording.

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