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ORIGINAL ARTICLE

Comparison of Mean Onset and mean duration of action between Atracurium and Cisatrcurium in patients undergoing Elective Surgery

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ABSTRACT

Background: Neuromuscular monitoring is required in an anesthetized patient to ensure complete recovery from a neuromuscular blockade. Cisatracurium and atracurium are used in adult patients undergoing diagnostic and surgical procedures with general anesthesia.

Objective: To compare the mean onset time and mean duration of action between atracurium and cisatracurium in patients undergoing elective surgery.

Methodology: This randomized control trial was conducted in the Department of Anesthesia/ICU at Jinnah Hospital Lahore from March 10, 2022, to September 10, 2022. A total of 68 patients were enrolled with 34 patients assigned to each of the two groups. Participants were randomly selected to receive either atracurium (Group A) or cisatracurium (Group B). On completion of the surgery, patients were reversed with injection neostigmine 0.05 mg/kg and 0.4 mg glycopyrrolate. Mean onset time and duration of action were noted.

Results: The mean onset time of the patients in Group A was 3.94±1.52 minutes and in Group B the mean onset time of the patients was 2.50±1.18 minutes (p=<0.001). In the atracurium group, the mean duration of action of the patients was 34.94±3.06 minutes, and in the cisatracurium group, the mean duration of action of the patients was 58.97±7,25 minutes (p-value=<0.001).

Conclusion: The cisatracurium group has significantly shorter mean onset time and longer mean duration of action as compared to the atracurium group in patients undergoing elective surgery

Keywords: Anesthesia, Atracurium, Cisatracurium, Duration of action, Onset time.

INTRODUCTION

Neuromuscular blocking is an essential element of anesthesia, utilized for endotracheal intubation, surgical procedures, and mechanical breathing. Neuromuscular blocking agents (NMBAs) are classified into depolarizing and non-depolarizing categories. The selection of neuromuscular blocking agents is contingent upon patient characteristics and the specific technique.[1] Succinylcholine is preferred for its quick onset and brief duration, inducing muscle paralysis by binding to cholinergic receptors, with effects lasting 7-12 minutes.[2] Nondepolarizing drugs, like rocuronium and atracurium, function as competitive antagonists of acetylcholine (ACh), inhibiting muscular contraction.[3] Neuromuscular blockade monitoring is commonly performed using train-of-four stimulation, which evaluates recovery from blockage by counting the detected twitches.[3] A train-of-four ratio under 0.9 signifies persistent blocking, necessitating reversal drugs such as neostigmine or sugammadex.3 Historically, the implementation of neuromuscular blocking agents has revolutionized anesthetic treatment by establishing a trinity of narcosis, analgesia, and muscle relaxation.[4] The mechanism of action entails the neuromuscular junction, where neuromuscular blocking agents impede acetylcholine transmission.[5] neuromuscular blocking agents (NMBAs) are supplied via intravenous or intramuscular routes, with dosages determined by optimal body weight to mitigate problems.[6]

Atracurium is a non-depolarizing neuromuscular blocking agent utilized as an adjuvant to general anesthesia to allow endotracheal intubation and ensure muscle relaxation during surgical interventions or mechanical ventilation. It is especially efficacious in facilitating the deployment of a laryngeal mask airway, as research indicates that its administration results in enhanced jaw relaxation and expedited insertion relative to propofolalone.[7] As a competitive antagonist of the nicotinic receptor at the neuromuscular junction, atracurium prevents acetylcholine from binding, thereby inhibiting muscle contraction without inducing receptor conformational changes. The primary contraindication for atracurium is hypersensitivity to its components, including benzyl alcohol, which is present in multi-dose vials. Caution is advised in patients with a history of anaphylactic reactions to neuromuscular blockers.[8] Atracurium is administered intravenously, either as a bolus or continuous infusion, with an effective dose (ED95) of 0.23 mg/kg for adults and 0.5 mg/kg for intubation.[9] Its onset of action is approximately 2 minutes, and it has an intermediate duration of action lasting about 40 to 45 minutes, with a half-life of around 20 minutes. Atracurium undergoes metabolism primarily through Hofmann elimination, accounting for 45% of its breakdown, and ester hydrolysis by non-specific esterases.[10] This metabolism is advantageous for critically ill patients, as it is not significantly affected by renal or hepatic dysfunction. However, a metabolite, laudanosine, can accumulate with prolonged use and may cross the blood-brain barrier, raising concerns about potential central nervous system effects, although no seizure activity has been documented in humans.[11] Adverse effects of atracurium are mainly related to histamine release, which can cause flushing, hypotension, and bronchospasm, among other symptoms.[12] Monitoring neuromuscular blockade can be achieved through clinical signs or nerve stimulation methods, with a train-of-four stimulation technique being the most common.[13]

Cisatracurium, a more potent isomer of atracurium, is also a non-depolarizing neuromuscular blocker indicated for similar uses. It is contraindicated in patients with known hypersensitivity and should be used cautiously in those with myasthenia gravis due to the risk of profound effects.[14] Cisatracurium is stored under refrigeration and has a potency of approximately 3 times that of atracurium, with similar recovery profiles.[15] Its metabolism also relies on Hofmann elimination, making it suitable for patients with renal or liver dysfunction.[16] The typical dose for cisatracurium is 0.15 to 0.2 mg/kg for intubation, achieving optimal conditions within 1.5 to 2 minutes.[17] Adverse effects are rare, occurring in less than 1% of cases, and include bradycardia and prolonged neuromuscular blockade.[14,17] Monitoring for cisatracurium follows similar protocols as atracurium, utilizing peripheral nerve stimulation to assess neuromuscular function.[18] In emergency settings, rapid sequence induction (RSI) often employs succinylcholine or high-dose rocuronium; however, atracurium is a safe alternative for patients with contraindications to these agents.[19] Its renal-independent elimination and lack of cumulative effects make it advantageous for rapid intubation.[20] Comparatively,

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while cisatracurium is more potent, atracurium may facilitate quicker intubation under certain conditions.[21] In the ICU, the use of neuromuscular blockers remains debated, but cisatracurium is frequently employed due to its favorable pharmacokinetics, including rapid degradation and minimal impact from organ dysfunction.[22] The recommended dosing for cisatracurium in the ICU may differ from elective surgery patients, necessitating adjustments based on individual patient factors.[23] Cisatracurium and atracurium are both non-depolarizing neuromuscular blocking agents (NMBAs) that play a crucial role in facilitating endotracheal intubation during general anesthesia. The ideal NMBA should provide rapid onset, optimal intubation, and a short duration of muscle paralysis, especially in emergencies where rapid sequence induction is necessary due to the risk of aspiration.[24] Among the available NMBAs, rocuronium is noted for its rapid onset, making it a popular choice in clinical anesthesia. Notably, cisatracurium does not induce histamine release at clinical doses, which is advantageous for cardiovascular stability.[22] However, its slower onset and less favorable intubating conditions compared to other NMBAs limit its use.

Atracurium revolutionized anesthetic practice by providing muscle relaxation with a faster onset and measurable recovery. The potency of cisatracurium is approximately 3-4 times greater than that of atracurium, with a 95% effective dose of 50 µg/kg for cisatracurium compared to 0.2 mg/kg for atracurium.[24] The pharmacodynamics of cisatracurium highlight its organ-independent metabolism, making it preferable for patients with compromised liver function. The degradation of cisatracurium is primarily through Hoffmann elimination, similar to atracurium, and its lower dosage requirement results in reduced histamine release.[25] Inhalational anesthetics can potentiate the effects of NMBAs, with desflurane being the most potent, followed by sevoflurane, isoflurane, halothane, and nitrous oxide. Local anesthetics can also enhance the effects of both depolarizing and non-depolarizing NMBAs, although they do not significantly shorten onset times. Patients with neuromuscular transmission disorders or central nervous system conditions may exhibit increased sensitivity to NMBAs.[26] Monitoring neuromuscular function post-administration is critical for ensuring appropriate dosing and patient safety. This involves stimulating a peripheral nerve and assessing the muscle response.[27]

In terms of safety, both cisatracurium and atracurium have similar characteristics, but cisatracurium is associated with a lower incidence of histamine release, which is particularly beneficial for patients with cardiovascular issues or those undergoing neurosurgery.[28] The primary disadvantage of atracurium is its potential for hemodynamic instability, making cisatracurium a more favorable option in certain clinical scenarios.[29] The choice between agents like atracurium and cisatracurium depends on individual patient factors, clinical indications, and potential contraindications, highlighting the importance of personalized anesthesia care. This purpose was to compare the mean onset time and mean duration of action between atracurium and cisatracurium in patients undergoing elective surgery.

MATERIALS AND METHODS

The study was designed as a randomized control trial conducted in the Department of Anesthesia/ICU at Jinnah Hospital Lahore over six months, from March 10, 2022, to September 10, 2022. A total of 68 patients were enrolled, with 34 patients in each group, based on a calculated sample size that considered the mean onset times for Atracurium (3.28±0.64 minutes) and Cisatracurium (2.7±0.12 minutes), achieving a power of 80% and a confidence level of 95% using an online calculator (www.openepi.com). Non-probability consecutive sampling was employed, with inclusion criteria specifying ASA grade I & II patients aged 20 to 60 years undergoing elective surgery, while exclusion criteria eliminated those under 18 or over 65 years, pregnant women, ASA grade III or higher patients, individuals with a BMI over 30 kg/m², those with anticipated difficult airways, patients with neuromuscular diseases, and those undergoing emergency surgeries. To mitigate confounding variables, strict adherence to the exclusion criteria was maintained. Data collection involved obtaining written informed consent from all participants, who were then randomly assigned to either Group A or Group B by selecting a slip from a mixed pool of labeled slips. Group was included those patients who managed with atracurium and Group B included those patients who managed with cisatracurium. In addition, all the biodata age, gender, weight, and height were noted. In the operation room, full multiparameter monitoring, including Heart Rate (HR), Non-Invasive Blood Pressure (NIBP), Oxygen Saturation (SpO2), Capnography (EtCO2), and Temperature (T) probe, was connected to the patient. A neuromuscular monitoring device was affixed to the ulnar nerve using two electrodes, and an acceleromyogram was connected to the thumb. Intravenous access was established, and fluids were initiated. All patients received premedication with 1 mg of butorphanol administered intravenously and 0.03 mg/kg of midazolam administered intravenously. Following preoxygenation with 100% oxygen, general anesthesia was initiated with 2 mg/kg of propofol. Group A was administered a loading dosage of 0.5 mg/kg atracurium, whereas Group B got 0.1 mg/kg cisatracurium for neuromuscular blockade. A neuromuscular blocker was administered intravenously, diluted in isotonic normal saline over a duration of 10 seconds, followed by a fluid bolus administered by a blinded individual. The location of the ETT was verified by capnography. Anesthesia was sustained with 50% N2O in O2 and isoflurane at 0.6-1% concentration. Upon completion of the procedure, the patients were administered neostigmine at a dosage of 0.05 mg/kg and 0.4 mg of glycopyrrolate for reversal. Mean onset time and duration of action were noted by a blind person. The data was entered and analyzed through SPSS-16. The t-test was utilized to compare the mean start time and mean duration of activity between the two groups. P-values ≤0.05 were deemed statistically significant.

RESULTS

There were 16 (47.1%) males and 18 (52.9%) females in group A whereas in group B, 17 (50%) males and 17 (50%) females respectively. Seventeen (50%) patients have ASA 1 and 17 (50%) patients have ASA II while in group B, 16 (47.1%) patients have ASA I and 18 (52.9%) patients have ASA II (Table 1). The mean age of the patients were 38.91±10.93 years of group A and 41.17±12.31 years of group B. The mean BMI of the patients were 21.83±1.99 kg/m^2 of group A and 25.22±3.98 kg/m^2 of group B (Table 2).

The mean onset time of the patients were 3.94±1.52 minutes of group A and 250±1.18 minutes of group B. The mean duration of action of the patients were 34.94±3.06 minutes of group A and 58.97±7,25 minutes of group B. The significant (p<0.001) difference was found both groups in mean onset of time and mean duration of action (Table 3).

Table 1: Demographic information of the patients (n=68)

Variable	Group A	Group B
Gender		
Male	16 (47.1%)	17 (50%)
Female	18 (52.9%)	17 (50%)
ASA		
I	17 (50%)	16 (47.1%)
II	17 (50%)	18 (52.9%)

Table 2: Descriptive statistics of the patients (n=68)

Variable	Group A	Group B
Age (years)	38.91±10.93	41.17±12.31
BMI (kg/m^2)	21.83±1.99	25.22±3.98

Table 3: Comparison of onset time (minutes) and duration of action (minutes) between study groups

Variable	Group A	Group B	P value
Onset time (minutes)	3.94±1.52	2.50±1.18	<0.001
Duration of action (time)	34.94±3.06	58.97±7.25	<0.001

DISCUSSION

When choosing a neuromuscular agent for tracheal intubation or skeletal muscle relaxation, the primary objective of an anesthesiologist is to select an agent that offers quick onset, prolonged clinical duration, enhanced hemodynamic stability, and effective spontaneous reversal. Numerous studies have already examined cisatracurium to assess its pharmacokinetics, pharmacodynamics, safety, and efficacy. In the present study, the atracurium group exhibited a mean onset time of 3.94±1.52 minutes, while the cisatracurium group demonstrated a mean onset time of 250±1.18 minutes (p=<0.001). The atracurium group exhibited a mean length of action of 34.94±3.06 minutes, while the cisatracurium group had a mean duration of action of 58.97±7.25 minutes (p-value=<0.001).

Athaluri et al[30] demonstrated this in their research. Cisatracurium yields superior intubating conditions characterized by a rapid onset, extended duration of action, and negligible hemodynamic alterations compared to cisatracuriumand atracurium, thus establishing cisatracurium as an optimal non-depolarizing muscle relaxant for intubation. Pooja and Rahul[31] discovered in their research that the mean onset length of atracurium was 3.28±0.64 minutes, whereas the mean onset for cisatracurium was 2.7±0.12 minutes, which is statistically significant (p=0.05). The mean duration was 36 minutes for atracurium and 64 minutes for cisatracurium, respectively (p=0.01).

The mean onset of action, or the time to maximum blockade, was significantly more rapid in Group C compared to Groups B and A. The onset of action was 97 seconds for Group C, 128 seconds for Group B, and 142 seconds for Group A, as demonstrated by Duggappa et al[32] and Deepika et al.[33] The mean duration of action was markedly prolonged in Group C compared to Group B and Group A, with durations of 52 minutes in Group C, 43 minutes in Groups B and A, consistent with the findings of El-Kasaby et al.[21]

Khobragade et al[34] demonstrated that atracurium and cisatracurium have equivalent intubating circumstances and hemodynamic stability, with no adverse consequences related to histamine release. Hemodynamic parameters were analogous in both groups. El-Kasaby et al[35] reported that a dose of 2×95% effective dose of atracurium serves as a more potent neuromuscular blocking agent compared to cisatracurium. Conversely, higher doses of cisatracurium, specifically 4×95% effective dose, and 6×95% effective dose, yield enhanced and expedited neuromuscular blockade with prolonged duration, stable hemodynamic parameters, and no clinically observable signs of histamine release.

CONCLUSION

The study concluded that the cisatracurium group has a significantly shorter mean onset time and longer mean duration of action as compared to the atracurium group in patients undergoing elective surgery.

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