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Original Research Article

Efficacy of Cisatracurium and Atracurium during Burn Surgeries under General Anaesthesia: A Comparative Study

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Conflict of interest: Nil

Abstract

Aim: The aim of our study was to compare onset of action, hemodynamic effects, intubating conditions and any adverse effects of cisatracurium and atracurium in patients posted for burn surgeries under general anaesthesia.

Method: Sixty patients were randomly assigned to one of two groups, group A received 0.5mg/kg of atracurium, and group C received 0.2mg/kg of cisatracurium for intubation. Onset time, duration of action, condition of intubation, hemodynamic effects, and clinical signs of histamine release were monitored.

Results: Onset time was found to be significantly less with cisatracurium compared to atracurium. At the same time, cisatracurium provided longer duration of action and better intubating condition compared to atracurium in burn surgeries.

Conclusion: Cisatracurium has a quicker onset time and provides better conditions for tracheal intubation, compared to atracurium. Cisatracurium have a better safety profile than atracurium in burn surgeries.

Keywords: Cisatracurium, Hemodynamic, Histamine, Atracurium, Burn.

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Introduction

Though many non-depolarizing neuromuscular blocking drugs have been used during general anaesthesia, each has its own side effects like cardiovascular instability, occurrence of recurarization and residual paralysis which were not suitable for use in certain clinical situations like burn.[1]Rapid and safe endotracheal intubation is an integral part of administration of general anaesthesia which depends upon degree of muscle relaxation and depth of anaesthesia in burn surgeries. [2]

Muscle relaxant is used to facilitate endotracheal intubation and provide surgical relaxation. The ideal neuromuscular blocking agent for intubation should have a rapid onset, brief duration of action, free from hemodynamic changes, devoid of residual paralysis and provide excellent intubating conditions like fully relaxed jaw, widely open vocal cord and absence of stress response. Among all muscle relaxants, atracurium and cisatracurium are widely used benzylisoquinolinium compounds that have distinct pharmacodynamic and pharmacokinetic profiles, influencing their clinical applications in burn surgeries. [3]Atracurium is having benzyl isoquinolinium structure and is an intermediate acting NDMR, a mixture of 10 optical isomers. It is metabolized by Hoffmann elimination and nonspecific ester hydrolysis. It is associated with histamine release leading to hypotension and anaphylaxis. [4] Cisatracurium besylate is an intermediate-acting, non-depolarizing neuromas cular blocking drug. Cisatracurium has a benzylisoquinolinium structure and is the 1R cis-1-prime R cis isomer of atracurium.[5]

Cisatracurium is a purified form of one of the 10 stereoisomers of atracurium with a potency of approximately 3 to 4 times greater than that of atracurium which, unlike the parent compound is not associated with dose dependent histamine release.[6]On metabolism cisatracurium produce 5 times less laudanosine compared to atracurium.[7]Few studies in literature have shown that cisatracurium may be preferred over atracurium

in burn surgeries due to its higher potency, greater hemodynamic stability, and lack of histamine release at clinically effective doses. Hence keeping in view of the above facts we have compared cisatracurium and atracurium during general anaesthesia in patients posted for burn surgery.

Method

This trial was conducted at a tertiary care hospital after taking approval of Institutional Ethical Committee. Written informed consent was obtained from all patients.60 patients of ASA I/II and aged 18-70 years, posted for burn surgeries were enrolled in this study. Patients having hepatic, renal, cardiovascular and pulmonary diseases were excluded from the study. Using computer-generated random numbers, 60 patients were allocated to one of two groups of 30 each. Group A received atracurium with an initial dose of 0.5 mg/kg and maintenance dose of 0.1 mg/kg, whereas Group C received cisatracurium with an initial dose of 0.2 mg/kg and maintenance dose of 0.04 mg/kg. Pre anaesthetic check-up was done and any abnormality detected preoperatively was optimized before surgery. On arrival into the operating room non-invasive monitors like Electrocardiogram (ECG), Non-invasive BP, and pulse oximetry were connected to the patient. Intravenous access was done with an 18G cannula and infusion of crystalloid solution was started. All the patients were premedicated with injection butorphanol 1 mg and 0.03 mg/kg midazolam. After preoxygenation with 100% oxygen, general anesthesia was induced with 2 mg/kg propofol and study drug was administered according to group. Neuromuscular monitoring was carried out after obtaining the control values by supramaximal stimulus (50 mA, 2 Hz) at every 15s to stimulate the ulnar nerve through surface electrodes. From the injection of neuromuscular blocking agent (NMBA), the patient's blood pressure and pulse rate were monitored. The onset time was determined as the interval from the end of muscle relaxant injection until "Train of Four (TOF) score 0." [8] Endotracheal intubation was done using the proper size tube. Anesthesia was maintained with a mixture of 50% N_2O in O_2, isoflurane (0.8%–1%), with the maintenance dose of either atracurium 0.1 mg/kg or cisatracurium 0.04 mg/kg) was given at TOF score 2. Patients were monitored for any signs of histamine release clinically by observing skin changes graded as flush (if redness lasted >120 s), erythema, or wheals, and presence of any hemodynamic changes or bronchospasm. Intraoperatively, the patient was on volume-controlled ventilation and maintained normocapnia. Duration from the last dose of NMBA to 25% recovery of TOF was recorded. When TOF recovery was 25% from the last dose at the end of the surgery, the reversal was achieved by administering 0.05 mg/kg neostigmine and 8 µg/kg glycopyrrolate mixture. The patient was then shifted to the recovery room for postoperative monitoring. Data were recorded in Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS Inc.; Version 22.0, Chicago, IL, USA). Quantitative data were expressed as mean ± SD, whereas qualitative data were expressed as numbers and percentages (%). Student's t-test was used to test the significance of difference for the quantitative variables (HR, MAP) that follow a normal distribution, and Chi-square was used to test the significance of difference for qualitative variables. $P < 0.05$ was considered statistically significant

Results

60 patients were enrolled in this study. The demographic characteristics were comparable for age, weight, sex, and ASA status.

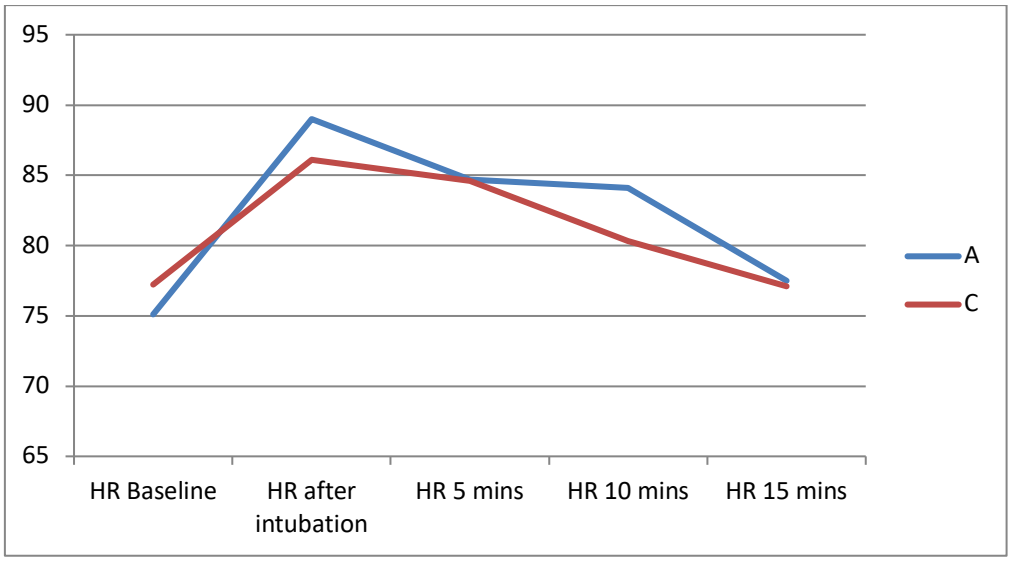

Figure 1: Heart rate changes before and after administration of atracurium and cisatracurium

The mean and standard deviation of baseline heart rate, heart rate after intubation and at different time intervals at 5,10,15 mins among two groups were compared. The results obtained from the analysis shows that there was an increase in heart rate compared to baseline in both groups after intubation and at 5 mins but gradually returns to baseline at 15mins but this may be due to stress response and there was no statistically significant difference. (Fig 1)

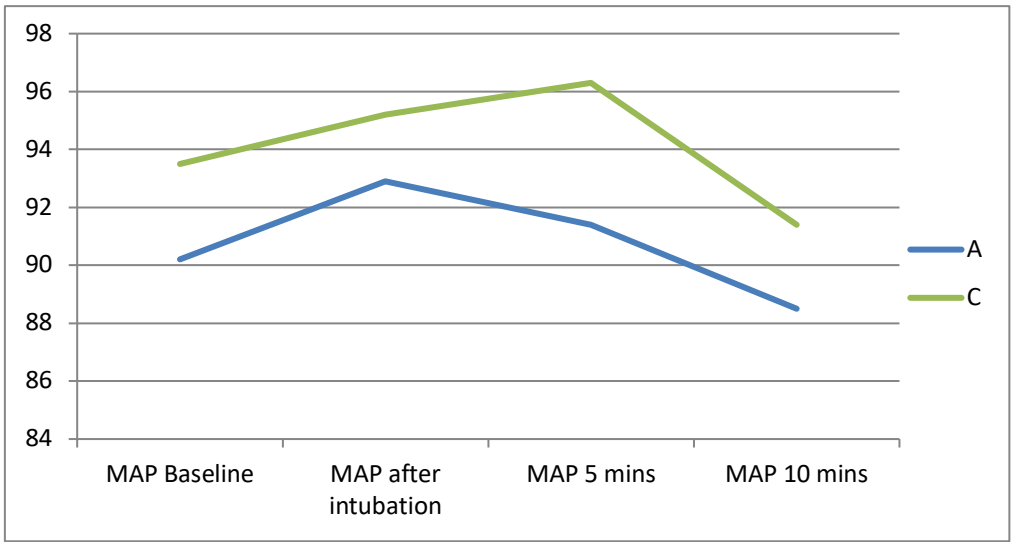

Figure 2: Mean arterial pressure changes before and after administration of atracurium and cisatracurium

The mean and standard deviation of baseline MAP, MAP after intubation and at different time intervals at 5 and 10mins among two groups were compared. The results obtained from the analysis shows that there was an increase in MAP compared to baseline in both groups after intubation and at 5 mins which gradually returned to baseline at 10mins but there was no statistical significant difference. The results obtained from the analysis shows that there is no statistically significant difference with MAP changes ($p>0.05$). (Fig 2)

The onset time in the Group C was significantly short in comparison to Group A ($p<0.05$). (Fig 3)

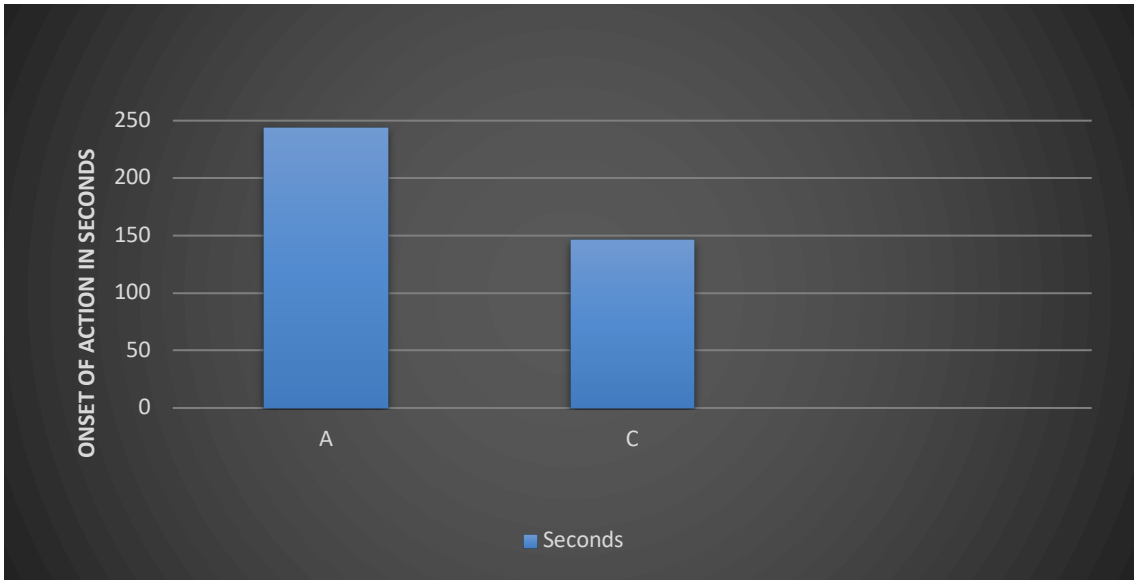

Figure 3: Onset of action of atracurium and cisatracurium

Table1: Intubating conditions in both groups

Group	Excellent	Good	Poor	Not Possible
Group A	16 (53%)	14(47%)	0	0
Group C	20(66%)	10(34%)	0	0

Intubating conditions are described as: Excellent: Easy passage of the tube without coughing. Vocal cords relaxed and abducted. Good: Passage of tube with slight coughing and/or bucking. Vocal cords relaxed and abducted. Poor: Passage of tube with moderate coughing and/or bucking. Vocal cords moderately adducted.Intubating conditions were either excellent or good in all the groups and had no fair or poor intubating condition. Intubating conditions were excellent in 53% cases and good in 47% cases in group A.

In group C 66% had excellent intubating conditions and 34% had good intubating conditions. (Table 1)

Table 2: Signs of histamine release in both groups

Group	No of patients (%)
Group A	3(10%)
Group C	0

Only 3 patients out of 30 who were administered atracurium showed signs of histamine release like facial flushing. Patients administered cisatracurium had no signs of histamine release. (Table 2)

Discussion

Ideal neuromuscular agents for tracheal intubation is an agent with a fast onset of action, optimal intubating conditions, better hemodynamic stability, and good spontaneous reversal.[9]

Succinylcholine may be an ideal agent but hyperkalemia is a major risk factor when used in conditions like burn. Cisatracurium possess most of these properties of an "ideal" muscle relaxant. It is similar in structure and properties to atracurium but has the added advantage of rapid onset of action, no signs of histamine release, less laudanosine production on metabolism.[10] In the present study, we have compared atracurium (0.5 mg/kg) and cisatracurium (0.2 mg/kg). All patients were assessed for hemodynamic data (heart rate, blood pressure), onset time, duration of action, and signs of histamine release clinically, condition of intubations, and vocal cords assessment. Signs of histamine release were shown in 6 patient in this study in the form of transient facial flushing after the administration of atracurium; however, this patient did not experience hypotension or tachycardia.

In our study we used neuromuscular monitoring by Train of four because the response of neuromuscular blocking drugs is not predictable in all patients so the monitoring of neuromuscular function provides more predictable and rational approach to the use of muscle relaxants and better and faster recovery of the patients by optimizing the doses, hence provide better patient care.[11] In the present study the onset of action was considered as the time taken from Injection of muscle relaxant to abolition of all four responses to train of four stimuli. Onset of action in group C was rapid compared to A group. The present study concurs with the findings of the studies of, Bluestein et al[12]who have also reported the onset time similar to our present study. Intubating conditions were either excellent or good in all the groups in our study. Intubating conditions with atracurium were excellent in 53% and good in 47% patients while in the cisatracurium group, intubating condition were excellent in 66% and good in 34% patients. Lien et al.[13] concluded that the maximal MABP and HR changes of patients receiving cisatracurium were small and similar to those observed in patients receiving two times the ED95 of atracurium. Yazdanian et al.[14] reported comparable hemodynamic effects in atracurium and cisatracurium but found that cost-benefit was observed with atracurium. Even with the higher doses of cisatracurium (8 × ED95), there was no histamine-release sign because of its stereospecific property.[15]Our study was similar to study by Ranjan et al[16] who found that cisatracurium in a dose of 0.15 mg/kg had a faster onset and duration of action than atracurium 0.5 mg/kg. At this dose, cisatracurium provides optimal intubating condition, rapid neuromuscular blocking with longer duration of action, stable hemodynamic status, no signs of histamine release clinically, and without any residual muscle paralysis compared to atracurium.

Conclusion

In patients posted for burn surgeries cisatracurium provides optimal intubating condition, rapid neuromuscular blocking with longer duration of action and stable hemodynamic without any histamine release compared to atracurium.

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