

Effect of atracurium and cisatracurium as nondepolarising neuromuscular blocking agents: A comparative study

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Abstract

Introduction: General anesthesia, for a surgical procedure is normally done with the help of endotracheal intubation. The non-depolarizing muscle relaxant, or the non depolarising muscular blocking (NMBA) agents are known to inhibit the action of acetylcholine, while differing in the onset and the duration of action, potency, metabolic route and side effects. The main aim of this study was to compare the neuromuscular blockade of atracurium and Cisatracurium and the recovery characteristics.

Materials and Methods: 60 patients, between 18-60 years of age and of ASA Class I or II who had come to the Department of Surgery and required procedure under General anaesthesia were divided randomly into two groups using computerized randomization code. Group I received 2 x ED₉₅ 0.5mg/kg IV Inj. Atracurium and Group II received 2xED₉₅ 0.2mg/kg IV Inj Cisatracurium.

Results: The time of onset of anesthesia was 3.59 ± 0.83 mins in Group I and 2.88 ± 1.36 in Group II, which was highly significant. The duration of anesthesia was also more in Group II where it was 46.45 ± 9.61 mins, while in group I it was 39.74 ± 8.35 mins/the recovery index in both the groups was comparable. The hemodynamic parameters were stable in the cisatracurium group, with minimal histamine release.

Conclusion: Cisatracurium is a more effective and potent drug than atracurium. It has a shorter onset time, longer duration and lesser hemodynamic changes.

Keywords: Cisatracurium, atracurium, non depolarising neuromuscular blocking agents

Introduction

General anesthesia, for a surgical procedure is normally done with the help of endotracheal intubation. In 1952, succinylcholine was introduced for the first time by Thesleff *et al.* and was considered to be one of the most effective depolarizing muscle relaxant having a rapid action onset and short duration ^[1]. It is still considered as a relaxant of choice for endotracheal intubation. However, succinylcholine has many side effects including fasciculations, dysrhythmias, bradycardia, intracranial tension, increased ocular pressure, intragastric pressure, post-operative myalgia, malignant hyperthermia. These side effects are due depolarization of succinylcholine. Thus, there is a need for a reliable non depolarizing muscle relaxant which also has a rapid action with excellent intubation conditions ^[2-6]. The non-depolarizing muscle relaxant, or the nondepolarising muscular blocking (NMBA)

agents are known to inhibit the action of acetylcholine, while differing in the onset and the duration of action, potency, metabolic route and side effects [7-9]. These NMBA's bind to the alpha subunit of the acetylcholine receptors present at the neuromuscular junctions thereby producing paralysis of the muscles [10].

Since 1980s, atracurium, a bis benzyl tetrahydroisoquinoline has been in use as an NMBA [11]. It is spontaneous in degradation without depending on an organ for its elimination, therefore is the drug of choice over other NMBA's. Its limiting factors are haemodynamic instability and histamine release [12, 13]. Cisatracurium, discovered in 1995 is one of the 10 isomers of atracurium. It has a low propensity for histamine release and high stability. It is capable of producing 3 to 4 times more potent block than atracurium [14].

After the administration of a neuromuscular blocking drug, monitoring of the neuromuscular junction is very important. It helps the anesthesiologist to administer the correct dose and the recovery from these drugs is also adequate from the residual effects of the drug. Since the peripheral nerves are involved, monitoring helps in the evaluation of the response such as contraction or twitch of the muscle involved [15, 16].

The main aim of this study was to compare the neuromuscular blockade of artacurium and Cisatracurium and the recovery characteristics.

Materials and Methods

This randomized prospective comparative study was conducted by the Department of Anaesthesiology at Mamata Medical College, Khammam over a period of 12 months (March 2018 to March 2019). 60 patients who were scheduled for surgery under general anaesthesia with intubation were included into the study. After attaining clearance from our Institutional Ethical Committee, the nature of the study, its risks, were explained to all the participants and their relatives and informed consent was taken from all of them.

60 patients, between 18-60 years of age and of ASA Class I or II who had come to the Department of Surgery and required procedure under General anaesthesia were divided randomly into two groups using computerized randomization code. Group I received 2 x ED95 0.5mg/kg IV Inj. Atracurium and Group II received 2xED95 0.1mg/kg IV Inj Cisatracurium.

All the patients underwent a thorough clinical examination before admission and demographic details were noted from all of them. One day prior to the surgery, all the patients were given Tab. Alprazolam 0.25mg and 150mg of Tab. Ranitidine and the same was given even in the morning of the surgery. At the operation theatre, 18 gauge IV line was inserted for the regular fluids and drugs and another 20 gauge IV line was secured for the study drug.

Blood Pressure, ECG, SpO2 readings were all noted for the baseline parameter and was continued to be monitored throughout the surgery. Tactile evaluation of the patient for adductor pollicis response to Train of four (TOF) was done for neostigmine induced reversal of neuromuscular block as per the given guidelines [17]. For this 2 electrodes were placed on the surface over the ulnar nerve at the wrist, one near the distal crease of the nerve and the other, along the course of the nerve, 2cm proximal to the first. The proximal electrode was connected to the positive lead and the distal, to the negative.

After 100% preoxygenation, 1 mg IV Inj Butorphanol and 0.03mg/kg IV Inj Midazolam were given followed by 2mcg/kg IV Inj. Fentanyl and 2mg/kg IV Inj Propofol. The ulnar nerve was stimulated with supramaximal stimulus with 50mA after the patient completely lost Consciousness. The appropriate muscle relaxant was added according to the group adding required volume of saline and making the total volume of the solution 5ml.

After the muscle relaxant was given, the TOF was monitored every 30 seconds till the TOF became 0. The interval from the muscle relaxant administration to the maximal suppression of T1 % was noted as the onset time. After this, endotracheal intubation was done using

appropriate polyvinyl chloride endotracheal tube.

Statistical analysis was done using Microsoft Excel and SPSS software, version 22. Qualitative data was depicted using charts and tables and comparative tests were done using Chi Square test.

Results

The mean age of the patients in Group I was 37.82 ± 9.47 years and in Group II, 39.81 ± 8.44 years. The number of males were 14 and 18 in Group I and II respectively a 16 and 12 in Group II respectively. 19 patients in Group I belonged to the ASA Class I and 11 belonged to the ASA Class II while in Group II, 18 belonged to Class I and 12 belonged to Class II (Table: 1).

There was no significant difference among the age, gender, ASA class and BMI of the patients in Group I and Group II

Table 1: Demographic details of the patients

Variables	Group I	Group II	Significance
Age (mean \pm SD) in years	37.82 ± 9.47	39.81 ± 8.44	NS
Gender			
Males	14	18	NS
Females	16	12	
ASA			
Class I	19	18	
Class II	11	12	
BMI Kg/m ²	23.84 ± 5.22	24.53 ± 4.92	NS

The time of onset of anaesthesia was 3.59 ± 0.83 mins in Group I and 2.88 ± 1.36 in Group II, which was highly significant. The duration of anesthesia was also more in Group II where it was 46.45 ± 9.61 mins, while in group I it was 39.74 ± 8.35 mins/ The recovery index in both the groups was comparable, with 14.62 ± 4.21 in Group I and 15.03 ± 4.10 in Group II. (Table: 2)

Table 2: Details of sensory blockade

Variable	Group I	Group II	P value
Time of onset of anesthesia (in mins)	3.59 ± 0.83	2.88 ± 1.36	<0.05
Duration	39.74 ± 8.35	46.45 ± 9.61	<0.05
Recovery Index	14.62 ± 4.21	15.03 ± 4.10	>0.05

There was minimal histamine release among the patients belonging to Group II, while in group I nearly 50% of the patients had Flush, erythema, wheal and bronchospasms, all of which are signs and symptoms of histamine release (Table: 3).

Table 3: Histamine release

Signs of histamine release	Group I	Group II	P value
Flush	14 (46.67%)	4 (13.3%)	<0.05
Erythema	14 (46.67%)	3 (10%)	<0.05
Wheal	14 (46.67%)	3 (10%)	<0.05
Bronchospasms	14 (46.67%)	1 (3.3%)	<0.05

The mean heart rate among the Group I patients was 90 at base line and increased to 101

during the first 1 minute, fell to around 95 at 10 minutes and then maintained a steady rate, while in Group II, the mean heart rate was continuously maintained around 85 - 90 beats per minute throughout the surgery (Fig: 1).

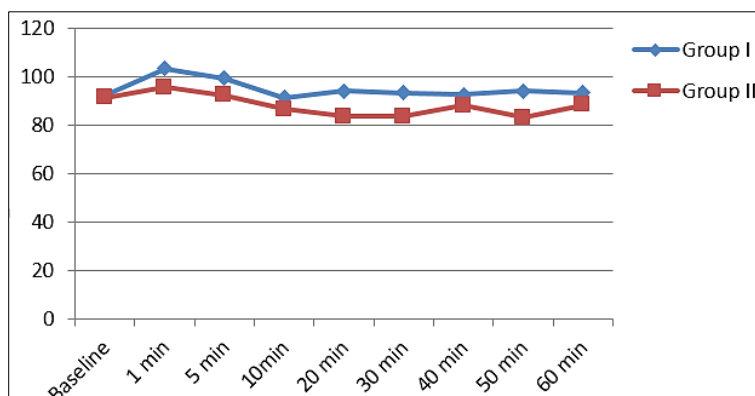


Fig 1: Mean heart rate

The mean arterial pressure in the group I rose immediately within 5 minutes after the onset of anesthesia to around 103.8 and maintained their throughout the surgery, while in Group II, the heart rate was maintained around 98 (Fig: 2).

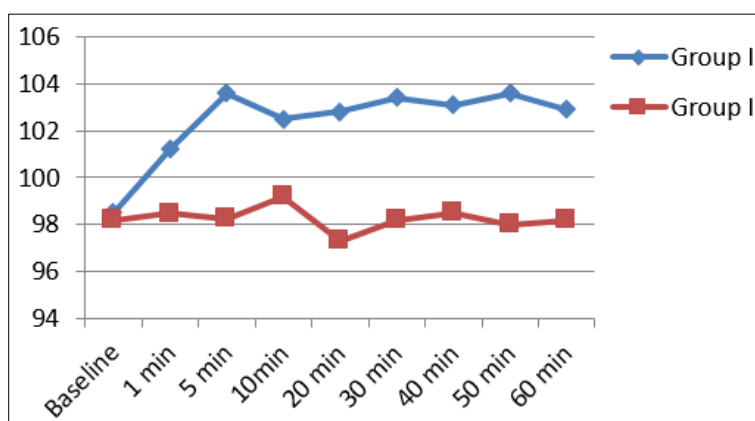


Fig 2: Mean Heart rate of the patients in both Groups

Discussion

Endotracheal intubation is one of the very important procedures to be done prior to a surgery, which is done under general anaesthesia. For this, neuromuscular blocking drugs are used which help to provide a complete skeletal relaxation to facilitate the intubation. Cisatracurium is a non-depolarizing, benzyl-isoquinolinium with intermediate action at 0.1 mg/kg, when increased to 0.2 mg/kg, it is a more potent blockade agent than atracurium.

There was no significant difference among the age, gender, ASA class and BMI of the patients in Group I and Group II. Similar age grouping, gender and ASA class was seen in a similar study by Shah and Chalekar and as in our study, they found no significant difference in these variables in both the groups ^[18].

The time of onset of anaesthesia was significantly lower in patients given cisatracurium rather than those given atracurium, as was the duration of anaesthesia, which was also higher in Group II than in Group I. However the recovery index in both the groups was comparable. A study by Niranjana *et al.* also found the onset time of cisatracurium to be far shorter than atracurium and the duration of the drug to be longer, corroborating our study ^[19]. Although

we did not compare the different doses of cisatracurium, Niranjana *et al.* compared the efficacy of the increasing dose of cisatracurium and found that the onset is indirectly proportional and the duration is directly proportional to the increase in the dosage^[19]. Similar results were found by El-Kasaby *et al.*^[20]. Mandal P, also concluded that a higher dose of cisatracurium produces excellent intubation conditions^[21]. A study by Shrey Shruti and Amol reported that the onset of anaesthesia was longer and duration was shorter in 0.5mg/kg atracurium group when compared to the cisatracurium group, in accordance to our study^[22]. In contrast to our study, a study by Harpreet kaur *et al.* reported a shorter onset time in atracurium Group when compared to the cisatracurium group. This was due to the fact that they had taken equipotent doses of the two neuromuscular blockers. A higher dose of cisatracurium was more potent with shorter onset time and longer duration^[23].

The histamine release was far higher in the patients of Group I, while in Group II only 10-13% of the patients had any side effects due to the histamine release. This difference was highly significant. Niranjana *et al.* also found similar results, with cisatracurium being devoid of histamine release effects^[19]. A study by Athaluri *et al.* found no evidence of histamine release among the patients in the cisatracurium group compared to the atracurium group and suggested the reason to be stereospecific^[24].

The hemodynamic changes, i.e the mean arterial pressure and the heart rate during the surgery was constant in cisatracurium in comparison to the atracurium group in the present study. This was in accordance to a study by Shruthi and Amol, where they observed good intraoperative hemodynamic parameters in the cisatracurium group rather than in the atracurium group^[22]. No statistical significance was seen in the hemodynamic changes in a study by Shah and Chelkar in a similar study^[18]. A study by Harpreet Kaur *et al.* found no significant difference in the hemodynamic changes in the two groups, which was in contrast to our study^[23].

Conclusion

Cisatracurium is a more effective and potent drug than atracurium. It has a shorter onset time, longer duration and lesser hemodynamic changes. There is minimal histamine release in cisatracurium, which further reduces the complications in the patient.

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