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COMPARISON OF EFFICACY OF ATRACURIUM AND CISATRACURIUM IN PATIENTS UNDERGOING ABDOMINAL SURGERIES UNDER GENERAL ANESTHESIA.

Anaesthesiology

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ABSTRACT

Background: The present study was done to test the efficacy of cisatracurium at a higher dose of 0.3mg/kg when compared to the recommended intubating dose of atracurium of 0.5mg/kg.

Materials and methods: This study was done in the Department of Anaesthesia, Alluri Sita Rama raju Academy Of Medical Sciences, Eluru. Study was done for a period from June 2017 to October 2018. Double blind randomized study was conducted after obtaining approval from ethical committee.An informed consent was taken from all patients. Group A (30 patients) received Atracurium 0.5mg/kg IV and Group C (30 patients) received Cisatracurium 0.3mg/kg IV.

Results: Duration of action of Cisatracurium (0.3 mg/kg) is significantly high compared to Atracurium (0.5mg/kg) with $p<0.001$. 83% of patients treated with Cisatracurium had excellent intubating conditions as compared to 47% with Atracurium which was significant. Hemodynamic changes in either of them were clinically insignificant. Signs of histamine release was seen in two patients in Atracurium group whereas none in Cisatracurium group.

Conclusion: Cisatracurium at a higher dose of 0.3mg/kg as compared to Atracurium 0.5mg/kg provided more effective and rapid neuromuscular blockade with excellent intubating conditions, longer duration of action, stable hemodynamics and no associated signs of histamine release clinically.

KEYWORDS

Atracurium, Cisatracurium, Neuromuscular Monitoring

INTRODUCTION:

Neuromuscular blocking drugs are to provide skeletal muscle relaxation for facilitating tracheal intubation and to improve surgical working conditions during general anesthesia.Cisatracurium is a new non-depolarizing, benzylisoquinolinium NMBD with intermediate duration of action.Atracurium is more effective than cisatracurium at same dose of 0.1mg/kg. Increasing the dose of cisatracurium to (0.2mg/kg) and (0.3mg/kg) provided more effective neuromuscular blockade and excellent cardiovascular stability with no marked histamine release clinically.

AIM: This study was designed to compare the efficacy of atracurium and cisatracurium regarding onset time, condition of intubation, duration of action, hemodynamic effects, and signs of histamine release.

MATERIALS AND METHODS:

Double blind randomized study was conducted after obtaining approval from ethical committee. An informed consent was taken from all patients. Sixty patients of ASA Grade I &II aged 20 to 65 years of both sexes who are posted for abdominal surgeries were included. Patients with cardiovascular, hepatic, renal or neuromuscular system disorders, patients with airway problems suggesting difficultintubation, patients receiving drugs known to interact with neuromuscular blocking agents were excluded from the study.

Group A (30 patients) received Atracurium 0.5mg/kg IV and Group C (30 patients) received Cisatracurium 0.3mg/kgIV.

PROCEDURE:

A thorough pre-anesthetic evaluation, appropriate baseline investigations were done. An informed consent was taken. IV line was secured and the patients were premedicated with Inj. Glycopyrrolate 0.01mg/kg IV, Inj. Midazolam 0.05mg/kg IV 10 min preoperatively. On the operation table, patients were connected to non-invasive monitoring with ECG, pulse oximetry and sphygmomanometer.

One forearm was immobilized in splint and ulnar nerve at wrist (1cm proximal to wrist crease) was selected for neuromuscular monitoring using Nerve Stimulator NS-100 neuromuscular monitor. The ulnar nerve was stimulated with a supramaximal current (mA) The force of contraction of adductor pollicis muscle was noted by visual and tactile means in form of index finger flexion and thumb adduction.TOF impulses at 2 Hz frequency were applied at 0.5sec interval with a minimum gap of 12 seconds between two stimulation patterns. Preoperative BP and HR were recorded. Patients were preoxygenated with 100% oxygen for 3 minutes. Induction in all patients with IV Inj. Fentanyl (2 mcg/kg), Inj.Propofol (2 mg/kg). Anesthesia dose of either Inj. Atracurium 0.5mg/kg IV or Inj. Cisatracurium 0.3mg/kg IV injected within 5-10 seconds by an anesthesiologist who was aware of the drug given. Endotracheal intubation was done with appropriate size endotracheal tube. BP, HR, SpO2 recorded at regular timed intervals after injecting the muscle relaxant (1, 2, & 5min) and during the surgery. Duration of action was taken as the time from injection of loading dose of muscle relaxation to return of train of four count to 1.

Anesthesia was maintained with a mixture of 67% N2O, 33% O2, isoflurane (0.8-1MAC) and intermittent bolus doses of muscle relaxant Group A: Atracurium 0.125mg/kg IV Group C: Cisatracurium 0.025mg/kg IV. Patients were monitored for any signs of histamine release clinically through skin changes graded as flush, erythema, or wheals and presence of any hemodynamic changes or bronchospasm.

Reversal was achieved at the end of surgery Inj. Neostigmine 0.05mg/kg IV and Inj. Glycopyrrolate 0.01mg/kg IV and the patients were extubated.At the end of operation with 25% recovery of T1%, reversal (induced recovery) was achieved by administration of neostigmine and atropine mixture (2.5 mg neostigmine: 1 mg atropine) through slow IV injection. TOF-ratio>0.9 was sufficient for safe extubation of the trachea.

RESULTS:

Table 1: Onset time

Onset time	Atracurium		Cisatracurium	
	No.	%	No.	%
110-150	2	6.7	30	100.0
160-200	28	93.3	0	0.0
Total	30	100.0	30	100.0
Mean ±SD	174.00±13.02		122.33±13.82	

Table 2: Duration of action of loading dose (min)

Duration	Atracurium		Cisatracurium	
	No.	%	No.	%
35-40	21	70.0	0	0.0
41-50	9	30.0	0	0.0

51-60	0	0.0	30	100.0
Total	30	100.0	30	100.0
Mean±SD	38.60±2.90		70.21±3.86	

Table 3: Intubating Condition

Intubation	No.	Atracurium %	No.	Cisatracurium %
Poor	1	3.3	0	0.0
Good	15	50.0	5	16.7
Excellent	14	46.7	25	83.3
Total	30	100.0	30	100.0

Onset time taken for maximal depression of twitch response in train of four stimulus was found to be significantly lower with higher doses of cisatracurium (0.3mg/kg) than with atracurium (0.5mg/kg. Regarding the duration of action, higher doses of cisatracurium (0.3mg/kg) showed statistically significant longer duration of action than lower doses of cisatracurium and the atracurium (0.5mg/kg).

Excellent intubating conditions were observed in 46.7% and 83.3% of patients in Group A and C respectively. Good intubating conditions were observed in 50% and 16.7% of patients in Group A and C respectively. Poor intubating conditions were observed in one patient in Group A and none in Group C.

Heart rate changes were statistically insignificant between two groups. MAP was gradually decreased from preoperative values after 5 min of giving Atracurium. But this change was not observed with Cisatracurium. No signs of histamine release were noted with cisatracurium, whereas it was noted with atracurium in 2 cases.

STATISTICAL METHODS:

Descriptive and inferential statistical analysis has been carried out in the present study. Results are presented on Mean ± SD. Student t test, Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two groups. P value <0.05 is taken as significant.

Study design: Two groups were considered, group A (Atracurium, group C (Cisatracurium) consisting of 30 patients each.

DISCUSSION:

Cisatracurium is a new stereoisomer of atracurium with a potency of approximately 3 to 4 times greater than that of atracurium and is associated with stable hemodynamics without histamine release even at doses of up to 0.4mg/kg. The recommended intubating dose is 0.15mg/kg & higher.

In the present study, clinical comparison was made Atracurium besylate and Cisatracurium besylate. Initial (bolus) doses of the muscle relaxants administered were Atracurium (0.5mg/kg) and Cisatracurium (0.3mg/kg). All patients were assessed for hemodynamic state (heart rate, blood pressure), onset time, duration of action, and signs of histamine release clinically and intubating conditions. The neuromuscular monitoring is done to assess the onset time and duration of action.

In this study onset time was observed by time taken from injection of loading dose of muscle relaxant to maximal suppression of twitch response in train of four stimulation. Onset time was found to be significantly shorter for Cisatracurium 0.3mg/kg when compared to Atracurium 0.5mg/kg which is highly significant. (p<0.001**)

A,N,El-Kasaby, H M Atefet al[2] studied Cisatracurium in different doses versus Atracurium during general anaesthesia for abdominal surgeries. They found that longer duration &onset time was shorter with increasing doses of cisatracurium 0.2mg/kg and 0.3mg/kg than atracurium 0.5mg/kg which correlated with our study. **Bluestein S Linda et al**[6] conducted a study where they compared Atracurium and Cisatracurium for tracheal intubation and concluded that the shorter onset of action of cisatracurium as compared to atracurium at equipotent doses is probably due to its greater potency.Duration of action of muscle relaxant was noted as the time from injection of loading dose of the drug to return of Train of Four Count to 1.The observed difference between the two groups was statistically highly significant (p<0.001) with Cisatracurium having a longer duration of action compared to atracurium. **Prakash Jammar et al**[4] has done a clinical comparative study of two intubating doses of cisatracurium during general anesthesia for gynecological study and they reported that the mean duration of action of Cisatracurium was longer at higher doses than Atracurium.Intubating conditions were assessed andrecorded.Excellent intubating conditions were observed in 46.7% and 83.3% of patients in Group A and C respectively. Good intubating conditions were observed in 50% and 16.7% of patients in Group A and C respectively. In group A, one patient had poor intubating condition.

Intubating condition is excellent in Cisatracurium with p=0.006.**Mandal P et al**[9] concluded that excellent to good intubating conditions could be achieved on administration of 0.2mg/kg at 90 sec and 0.25mg/kg at 75sec suggesting a higher dose of Cisatracurium provides excellent intubating conditions faster. In our study excellent intubating conditions were achieved in 83.3% of patients receiving 0.3mg/kg Cisatracurium in 70 sec. **Schmautz E, Deriaz H et al**[7], concluded that doses of 0.15mg/kg and 0.2mg/kg of cisatracurium, may produce generally excellent or good intubating conditions in 2min and 1.5min respectively. In our study excellent intubating conditions were seen in 83.3% of patients receiving 0.3mg/kg dose of Cisatracurium in 1.2 min and 46.7% of patients receiving 0.5mg/kg dose of Atracurium.Atracurium and Cisatracurium tend to cause histamine release, which can result in facial flushing and hemodynamic aberrations. The cardiovascular effects are decrease in mean arterial pressure and a compensatory increase in heart rate. These responses normally are transient and are related to the dose of the relaxant administered and the time course over which the relaxant is given.Administration of large doses of these relaxants over 30-60 seconds, rather than over 5 seconds, will attenuate the hemodynamic changes associated with their rapid administration.The circulatory changes occur seconds after administration of Atracurium and disappearing within 5 minutes. Cisatracurium is devoid of histamine-releasing effects, In our study, patients were monitored for any signs of histamine release clinically through skin changes graded as flushing (if redness lasted >120 seconds), erythema, or wheals and presence of any hemodynamic changes or bronchospasm.Only two patients who received Atracurium showed signs of histamine release in the form of flushing at the site of injection in the forearm, whereas no patients in Cisatracurium group showed signs of histamine release. The difference was however statistically insignificant.None of the patients in both groups had hemodynamic instability or bronchospasm as we have injected the loading dose of muscle relaxants slowly IV .**A.M.ElKasaby, H.M.Atef, et al**[2] compared cisatracurium in different doses and atracurium during general anaesthesia in abdominal surgery for signs of histamine release. The results showed 6.5% of the patients who received 0.5mg/kg dose of Atracurium showed signs of histamine release(flush,erythema). Patients receiving doses of 0.1mg/kg,0.2mg/kg and 0.3mg/kg of Cisatracurium showed no signs of histamine release. In a study done by **Cynthia A Lien, Matthew R Belmontet al**[1] it was, stated that no cutaneous flushing was noted after rapid injection of doses up to 0.4mg/kg Cisatracurium.

CONCLUSION:

Cisatracurium at a higher dose of 0.3mg/kg as compared to Atracurium 0.5mg/kg provided more effective, more rapid neuromuscular blockade with excellent intubating conditions, longer duration of action, stable hemodynamic status without clinical significant changes in HR and MAP, and no associated signs of histamine release clinically. Hence Cisatracurium, though more costly, is more effective and a better isomer of Atracurium.

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