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COMPARISON OF NEUROMUSCULAR BLOCKING EFFECT AND RECOVERY PROFILE OF CISATRACURIUM AND ATRACURIUM IN ELECTIVE SURGICAL PATIENTS - A PROSPECTIVE RANDOMIZED CONTROL TRIAL.

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ABSTRACT

BACKGROUND: Neuromuscular blocking agents form an integral part of administering smooth and safe general anaesthesia to patients. This study was designed to compare the two drugs atracurium and cisatracurium with the use of neuromuscular monitoring.

Under anaesthesia and during recovery from anaesthesia, assessment of neuromuscular function can be done by clinical tests and to the response of muscle to nerve stimulation. The Clinical tests for neuromuscular function are muscle tone, head lift, eye opening, tongue protrusion, hand grip, tidal volume, peak inspiratory pressure etc. When monitoring of Neuromuscular function is not performed, and clinical criteria alone are used, up to 42% of the patients are inadequately reversed upon arrival to the recovery room.(1). Residual NM block is a main risk factor for many critical events in the immediate postoperative period such as ventilatory insufficiency, hypoxemia and pulmonary infection(2). The short acting Neuromuscular blockers and wide spread use of perioperative Neuromuscular junction monitoring was useful in reducing these complications (3)

METHODS: A Prospective randomized control trial was designed at government villupuram medical college with 64 patients into two groups of 32 each receiving atracurium (A) and cisatracurium(C) respectively with neuromuscular monitoring. The hemodynamic effects, intubating conditions and recovery profile were analysed using SPSS 16 statistical software.

RESULTS : There was no statistical significance between the mean age of patients, gender, weight, intubating conditions, mean onset of block. Intra operative hemodynamic monitoring showed no significant difference in mean heart rate, mean systolic blood pressure, mean diastolic blood pressure between the two groups. But the mean duration of block and mean time for complete recovery were statistically significant for cis atracurium group (C) both being slightly prolonged in cisatracurium group (C) compared to atracurium group (A)

CONCLUSION: Cisatracurium besylate was more potent, had equal onset time, longer duration of action, more predictable recovery profile with better hemodynamic stability compared to atracurium. Also use of intraoperative neuromuscular monitoring helps to have a safe and predictable recovery profile

AIM OF STUDY

To compare the Neuromuscular Blocking Effects using neuromuscular monitoring, Hemodynamic Effects, Intubating conditions and Recovery profile of Cisatracurium and Atracurium in Adult Elective Surgical Patients.

Primary objective:

To compare Onset of action, Duration of action and Duration of recovery of Cisatracurium and Atracurium

Secondary objective:

To assess Intubating condition between groups, To look for signs of histamine release and Haemodynamic changes

MATERIALS AND METHOD

STUDY DESIGN: A Randomized controlled Trial.

STUDY CENTRE: Govt villupuram Medical college and Hospital, Villupuram.

DURATION OF STUDY: 3 Months

SAMPLE SIZE: 64 patients divided into 32 patients each in atracurium (A) and cisatracurium group (C)

The minimum sample size calculated is 64. 32 in Group(A) and 32 in Group(C).

After approval from the institutional ethical committee and written informed consent n = 64 patients will be selected for the study based on inclusion and exclusion criteria.

INCLUSION CRITERIA:

1. All consented adult patients aged between 16-65 years
2. ASA PS-I and ASA PS-II
3. Elective surgery requiring general anaesthesia
4. MPC I and MPC II
5. Both sexes

EXCLUSION CRITERIA:

1. Expected difficult intubation
2. Pregnant and lactating women.
3. Patient with medications known to interact with neuromuscular blocking drugs.
4. Drugs that prolong or alter neuromuscular blocking agents.

METHODOLOGY:

Written informed consent was obtained from the patient the day before surgery 64 Adult patients in the age group of 16 - 65 years of age randomized into 2 groups of 32 each. Group 1: Atracurium for 32 patients with initial dose of 0.5 mg/kg. 2x ED 95 dose. Group 2: Cis atracurium for 32 patients with initial dose for 0.2 mg/kg. 4x ED 95 dose.

Pre-anaesthestic assessment was done.

Intra venous line secured. Monitors attached and baseline parameters HR, NIBP, ECG, Spo2 were recorded/

Pre-medication: inj. Glycopyrrolate 5mcg/kg, inj. Midazolam 30-40 mcg/kg inj. Fentanyl 2 mcg/kg.

Supramaximal stimuli is determined at ulnar nerve by contraction of adductor pollicis muscle

Preoxygenation: 100% o2 for 3 minutes.

Induction: inj. Thiopentone sodium 5 mg/kg inj. Atracurium 0.5 mg/kg or cis atracurium 0.2 mg/kg. Anaesthesia is maintained with mixture of 50% N2O in O2 and sevoflurane 1%.

From the time of injection of Neuromuscular blocking agent, patients Pulse rate and blood pressure are monitored for each minute for next 10 minutes and then every 10 minutes throughout the surgery.

Onset time: administration of Neuromuscular blocking agent to complete suppression of single twitch Mean duration from the last dose of Neuromuscular blocking agent to appearance of third twitch in TOF.

Recovery: from the last dose of Neuromuscular blocking agent to 25% recovery of TOF.

THE EASE OF INTUBATION GRADING:

Excellent: easy passage of 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 slight coughing and or bucking. Vocal cords moderately adducted.

Not possible: vocal cords not relaxed, tightly adducted

DATA ANALYSIS PLAN: Values were presented as mean values, standard deviation (mean ± SD) and percentages. Statistical significance was set at $P < 0.05$. Data was analysed with independent sample ± test, Fisher's exact and chi squared test. Analysis was carried out by using SPSS - 16 statistical software.

OBSERVATION AND RESULTS The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data, descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference in the Independent groups the Unpaired sample t-test was used. To find the significance in categorical data Chi-Square test was used similarly, if the expected cell frequency is less than 5 in 2×2 tables then the Fisher's Exact was used. In all the above statistical tools the probability value .05 is considered as significant level.

AGE DISTRIBUTION: Mean age of both groups was 36. P value of 0.931 was statistically insignificant

GENDER 43.8% and 56.3% were male in Atracurium group and 56.3% and 43.8% were female in cisatracurium group P value was insignificant.

WEIGHT Mean weight was 61.8 in atracurium and 64.6 in cisatracurium which was statistically insignificant

INTUBATING CONDITION 90.6 % was excellent and 9.4% was good in atracurium group. In cisatracurium excellent conditions were present in 96.9% and good in 3.1%, but statistically insignificant.

MEAN TIME OF ONSET OF BLOCK

Mean onset of atracurium was 3.7 and cisatracurium 3.8. P Value was significant

MEAN DURATION OF BLOCK

Atracurium has mean duration of action 41.6 min p value of 0.000 and for cisatracurium 57.8 min and p value of 0.005 which was statistically significant.

MEAN DURATION FOR COMPLETE RECOVERY

For atracurium it is 25.9 with p value 0.000 and cisatracurium 37.7 with p value of 0.005 which was statistically significant

HEMODYNAMIC CHANGES

On observing the hemodynamic changes, there was no statistical significance between the two groups regarding the mean heart rate, mean systolic pressure and mean diastolic pressure

SIGNS OF HISTAMINE RELEASE

9.4% of patients developed wheel reaction in atracurium group which was secondary to histamine release.

DISCUSSION

D tubocurrine was the first nondepolarising neuromucular blocker which was synthesized and soon it was followed by the synthesis of several non depolarizing neromuclular blocking drugs with their own advantages and disadvantages

In our study, we compared atracurium and its isomer, cisatracurium in various parameters like onset of action, duration of action, recovery time from the last dose, Hemodynamic changes like heart rate, systolic blood pressure and diastolic blood pressure, ease of intubation and signs of histamine release were observed. Hemodynamic changes recorded at various level from baseline to before and after intubation and every 5 minutes for 30 minutes after intubation were recorded. Both groups were comparable as regard age, sex, weight, Mallampatti class, ASA status and the duration of operation. The character of the study population, the mean age for atracurium and cisatracurium groups are same at 36 years. The p value is 0.935. It is not significant. In our study, the character of study group shows the mean 85 weight for atracurium group is 61.8 kg, and for the cisatracurium group 64.6 kg. The p value is 0.413. The mean weight is insignificant.

A.M. ElKasaby et al.(8) in 2017 compared 3 groups of cisatracurium 2 x ED 95, 4 x ED 95, 6 x ED 95 dose with 2 x ED95 dose of atracurium. They observed, the same dose (2 x ED 95) atracurium is more effective neuromuscular blocking agent than cisatracurium.

Based on this result, we selected 4 x ED 95 dose of cisatracurium with 2 x ED 95 dose of atracurium. In our study, the mean onset of action is 3.7 ± 0.4 minutes for atracurium and 3.8 + 0.3 minutes for cisatracurium, which is almost equal for both the drugs. Based on the onset of block time, the 4x ED 95dose of the cisatracurium doesn't have any advantage over atracurium. This could be possibly explained due to failure of cold chain maintenance The mean duration of block in cisatracurium group is 16 minutes more than the atracurium group. The mean duration of action of intubating dose is 41.6 ±2.03 minutes for atracurium and 57.8 ± 0.98 minutes for cisatracurium. This indicates that the cisatracurium group has a greater duration of block compared to 86 atracurium group. The mean duration of recovery for atracurium group and cisatracurium group are 25.86 ± 1.48 minutes and 37.72 ± 0.87 minutes respectively. The mean difference is 11.8 minutes, which is significant. The cisatracurium group are longer duration of recovery from the last dose than atracurium group.

Dr Rochana G Bakhshi et al,(4) also had similar observations in their study. The mean duration of action for first dose in cisatracurium group 61.50 minutes which was significantly more as compared to 38.57 minutes in atracurium group. The recovery from last dose in cisatracurium group was 48.73 minutes and 33.63 minutes in atracurium group and the difference was statistically significant.

Similar observation was obtained by A.M. El kasaby (8) et al in his study while comparing 3 different doses of cisatracurium (2 x ED 95, 4x ED 95, 6x ED 95 dose) with one group of atracurium 2x ED 95 dose. They observed higher doses of cisatracurium had longer duration of action than the atracurium.

Bluestein et al (9) in their study observed that increasing dose of cisatracurium (2xED 95, 4xED 95, 6xED 95 dose) increases the mean time of duration (45 to 55 and 61) minutes

respectively. In our study, the intubation condition were excellent in both groups with marginally better with cisatracurium. However the p value is 0.613, the association is statistically not significant.

In our study, the atracurium group showed wheal in three patients (9.4%). There was no sign of histamine reaction observed in cisatracurium group. The p value is 0.238 which is >0.05, The result is statistically insignificant. Our study report was supported by A M El-Kasaby et al (8) in his study observed similar results, where two cases who received atracurium had signs of histamine release. Also Bevan S J et al (3) reported that atracurium releases histamine when doses of 0.5 mg/kg (2 x ED 95) or more are injected rapidly.

Dr Arun Kumar et al (9) in 2018 compared cisatracurium in different doses with atracurium during thyroid surgery observed cisatracurium is more effective, more rapid onset with longer duration of action and stable haemodynamics without histamine release.

SUMMARY

The duration of block is longer at 57.8 minutes for 4 x ED 95 dose of cisatracurium and the corresponding time is 41.6 minutes for 2 x ED 95 dose of atracurium. The recovery from last dose is 37.7 minutes for cisatracurium and it is 26 minutes for atracurium. The onset of block is 3.7 and 3.8 minutes for atracurium and cisatracurium respectively. No signs of histamine release observed in cisatracurium, whereas 3 patients showed histamine release with atracurium. The intubating condition is excellent in 31 patients and good in 1 patient with cisatracurium. For atracurium, it is excellent in 29 patients and good in 3 patients, which is marginally better for cisatracurium. Hemodynamic changes like Heart rate, systolic Blood pressure and Diastolic Blood Pressure are similar in atracurium and cisatracurium agents.

CONCLUSION

The cisatracurium besylate is a more potent with equal onset time, longer duration of block, more predictable recovery profile with better hemodynamic stability. When compared to atracurium it has a lower propensity to cause histamine release. All these pharmacodynamic properties of cisatracurium makes it an ideal agent in intermediate group of neuromuscular junction blocking agents.

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