COMPARISON OF INTRAOPERATIVE MUSCLE RELAXATION AND NEUROMUSCULAR RECOVERY FROM CONTINUOUS INFUSION OF VECURONIUM AND ATRACURIUM USING TRAIN-OF-FOUR

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ABSTRACT

BACKGROUND

Not only analgesia, muscle relaxation is also part of balanced anaesthesia. An ideal muscle relaxant for continuous infusion should have low potency, rapid onset, short duration of action, without any cumulative effect and, should be easily reversible with proper antagonists. Vecuronium and Atracurium are two muscle relaxants that come close to fulfil most of the above criteria. Neuromuscular monitoring reduces the incidence of residual block and should be part of standard monitoring equipment. The train-of-four (TOF) count appears to be the method of choice. We wanted to compare intraoperative muscle relaxation and neuromuscular recovery after continuous infusion of vecuronium and atracurium using train-of-four.

METHODS

The comparative study was done in 40 patients aged 18-60 years undergoing craniotomies with ASA Grade I and II. 40 patients were divided into two groups, 20 in each group. Group V received Vecuronium with loading dose of 0.1 mg/kg and after appearance of TOF COUNT 1, infusion started at a rate 0.8 mcg/kg/min. Group A received Atracurium loading dose of 0.5 mg/kg and infusion started at a rate of 412 mcg/kg/min. After stopping the infusion at the end of surgery, time for TOF COUNT 3 was noted.

RESULTS

Intra operative haemodynamics were stable for Vecuronium compared to Atracurium. Mean Recovery Time for a duration of infusion of about 3-4 hrs were noted for both groups. Then for Vecuronium, the mean recovery time was 62.63 ± 23.6 min and for Atracurium, it was only 26.8 ± 10.8 min., respectively.

CONCLUSIONS

Time for intubation did not show significant difference between the two groups. The rate of infusion was more for the Atracurium group as compared to Vecuronium group because of quicker spontaneous recovery. Combination of Continuous Infusion of Atracurium or Vecuronium, monitored by TOF count, use of anticholinesterase drugs, permits safe and successful recovery. It was concluded that Vecuronium produced more haemodynamic stability compared to Atracurium but there is slower spontaneous recovery of residual neuromuscular blockade than with Atracurium.

KEY WORDS

Muscle Relaxation, Continuous Infusion, Vecuronium, Atracurium, Neuromuscular recovery, TOF

HOW TO CITE THIS ARTICLE: Ganesh GV, Rani PU, Tirumala A. Comparison of intraoperative muscle relaxation and neuromuscular recovery from continuous infusion of vecuronium and atracurium using train-of-four. J. Evolution Med. Dent. Sci. 2019;8(23):1848-1851, DOI: 10.14260/jemds/2019/406

BACKGROUND

Muscle relaxation forms part of balanced anaesthesia along with analgesia, suppression of reflexes and hypnosis. In 1942, Griffeth and Johnson used purified curare to obtain adequate muscle relaxation.[1] But several catastrophes have occurred with the use of d-tubocurarine in the past.

For most of the anaesthetists until recently, the routine method of administration of Non depolarizing neuromuscular blocking agents is loading dose based on the patient's weight, followed by re-injections of one-third to one-fifth of the loading dose.

'Financial or Other Competing Interest': None.
Submission 30-11-2019, Peer Review 24-05-2019,
Acceptance 01-06-2019, Published 10-06-2019.
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DOI: 10.14260/jemds/2019/406

But bolus administration leads to variations in the degree of relaxation and also haemodynamics, making it difficult to maintain uniformly relaxed state and stable haemodynamics to facilitate uneventful anaesthesia and surgery.

So, the concept of Continuous Infusion of muscle relaxants came into existence. However, longer acting agents cannot be used as continuous infusions, because of tendency to accumulate, leading to prolonged residual effect.

An ideal muscle relaxant for continuous infusion should have low potency, rapid onset, short duration of action, without any cumulative effect and, should be easily reversible with proper antagonists. Vecuronium and Atracurium are two muscle relaxants that come close to fulfil most of the above criteria.

Adequate recovery of postoperative neuromuscular function cannot be guaranteed without objective neuromuscular monitoring. Neuromuscular monitoring reduces the incidence of residual block and should be part of standard monitoring equipment.

The train-of-four (TOF) count appears to be the method of choice (Hunter, Jones and Utting, 1982a; Viby-Mogensen et

al., 1983).[2] With proper and optimal monitoring of the depth of neuromuscular blockade, continuous infusions are safe to use and give a stable and easily reversible neuromuscular block. L. S. Chaudhari et al.[3] Compared Vecuronium and Atracurium infusions, by using either clinical criteria or subjective monitoring of neuromuscular blockade with peripheral nerve stimulator. In the present study. Objective TOF monitoring with Accelerograph was used.

So the present study was to compare the Time to Recovery following, - Continuous IV infusions of Atracurium and Vecuronium for Craniotomies using train -of-four.

METHODS

A comparative study was conducted on 40 adult patients undergoing Craniotomy under general anaesthesia at King George Hospital, Visakhapatnam during the period August to November 2018. After obtaining the approval from Institutional Ethics Committee and written informed consent from the patients who participated in the study 40 patients were divided into two groups of 20 each, .Group V and Group A.

Inclusion Criteria

Include ASA physical status I and II, Age between 18 -60 years and patients undergoing Craniotomies.

Exclusion Criteria

Include Patients having Asthma. Diabetes, 20% deviation from normal weight, known neuromuscular disorder, hepatic failure and those receiving medications which have known interaction with neuromuscular blocking drugs.

Premedication

Patients were pre medicated with glycopyrrolate 0.2 mg, midazolam 1 mg and fentanyl 2 µg/kg. Monitored with NIBP, Pulse-oximeter, 5 lead ECG, Surface electrodes and Mindray NMT Monitor [Acceleromyography] were connected. Preoxygenated for 3 minutes. Induced with Inj. thiopental sodium (4-6 mg/kg body wt.) intravenously till the loss of eye lash reflex. Then calibration of NMT MONITOR was done in single twitch mode. Group V patients were given Vecuronium (0.1 mg/ kg) bolus dose and Group A patients were given Atracurium (0.5 mg/kg) bolus dose. Now the mode was changed to TOF. Intubation was done with cuffed flexo-metallic endotracheal tube of appropriate size when there was no response to train -of-four stimuli. i.e. [TOF 0]

Anaesthesia was maintained with Isoflurane 0 – 1 % w/v, 66% nitrous oxide in oxygen and Fentanyl and Propofol were given as and when required. After intubation, train-of-four responses at regular intervals were recorded. [20 sec .When the TOF count 1 appeared, Continuous infusion of the muscle relaxants were started.

Group V were given infusion dose of Vecuronium (1 µg/kg/min) and Group A were given Atracurium (10 µg/kg/min). Infusion stopped at the time of closure of dura matter [Near the ending of surgery].Time of appearance of TOF Count 3 was noted and finally reversal was given.

Neuromuscular blockade was reversed with injection neostigmine (0.05 mg/kg) and injection glycopyrrolate (0.01 mg/kg) intravenously. Adequate reversal of neuromuscular blockade was confirmed with the help of Double Burst Stimulation (DBS) mode.

RESULTS

Time (Min.)	Group V	Group A	p Value
After bolus dose To TOF ' 0'	4.2 ± 0.9	4.3 ± 0.8	0.712
After bolus dose To TOF '1'	53.8± 9.8	38.7 ± 6.8	<.0001**
After starting infusion to TOF '0'	12.6 ±2.9	16.1 ± 3.1	<0.0007*
After stopping infusion to TOF 3	62.2± 17.7	27.9 ± 6.7	< 0.0001**

Table 1. Comparison of time taken (in minutes) to reach TOF 0 and also recovery to reach TOF 3 after bolus infusion of Vecuronium and Atracurium

* p value < 0.05 is significant, ** highly significant

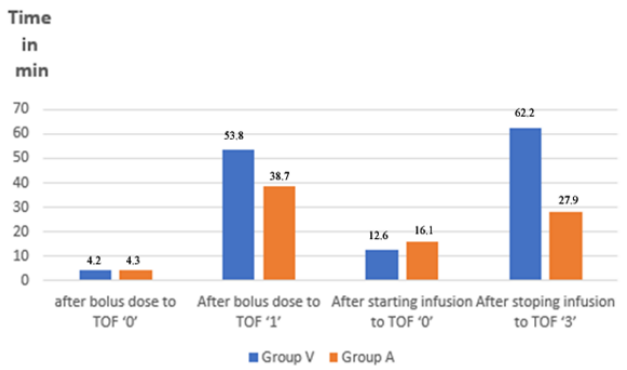

Figure 1. Comparison of time in minutes to achieve required TOF among vecuronium and atracurium groups after equipotant doses

SBP (mmHg) Mean ± SD	Group V	Group A	p Value
Preoperative	130 ±14.9	126.6 ±12.5	0.363
2 min after bolus dose	118.5 ± 15.3	114.4 ± 9.2	0.313
10 min after bolus dose	124.4 ± 11.1	126.1 ±10.8	0.64
2 min after starting infusion	120.15 ± 10.9	115.3 ± 11.6	0.140
10 min after starting infusion	115.1 ± 12.1	117.5 ± 10.9	0.570
2 min after stopping infusion	118 ± 13.5	117.8 ± 10.6	0.786
10 min after stopping infusion	123.4 ± 7.2	118 ± 11.04	0.09

Table 2. Comparison of systolic blood pressure (SBP) in between vecuronium and atracurium groups

P value > 0.05 is not significant

DBP (mmHg) Mean ± SD	Group V	Group A	p Value
Preoperative	86.1 ± 7.8	80.8 ± 9.2	0.22
2 min after bolus dose	78 ± 9.13	67.9 ±7.3	0.0001**
10 min after bolus dose	82.9± 8.6	73 ±7.4	0.0002 **
2 min after starting infusion	78.5 ± 11.4	72 ± 8.8	0.053
10 min after starting infusion	75.650±7.46	74.2 ±7	0.528
2 min after stopping infusion	75.7 ±7.11	79.1 ±10.9	0.249
10 min after stopping infusion	79.8 ± 5.7	79.1± 12.25	0.818

Table 3. Comparison of diastolic blood pressure (DBP) between vecuronium and atracurium groups

p value <0.05 is significant. ** Highly significant

When TOF count reached ≥ 4, ie., patients were fully awake and moving all four limbs to vocal commands with recovery of good muscle tone and power, extubation was done. Subsequently all patients were shifted to the postoperative ward.

Throughout the procedure, train-of-four count was used to assess the degree of neuromuscular blockade. Absence of any twitch response indicate 100% block. Appearance of 1, 2 or 3 response indicate 90%, 80% 75 % block respectively.

At different time points Systolic and Diastolic Blood Pressure were measured. They include Base line preoperatively, 2 minutes and 10 minutes after Bolus dose, 2 minutes and 10 minutes after starting infusion and then postoperatively.

Statistical Methods

Descriptive and inferential statistical analysis was carried out in the present study. Results on continuous measurements were presented on Mean ±SD.

Student t test (Two tailed, independent) was used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters.

P value < 0.05 was considered as statistically significant. SPSS 16 statistics package was used for analysis.

From table 1 it is clear that Time taken to achieve ideal intubating conditions after initial bolus dose that is TOF '0' among vecuronium and atracurium groups was 4.2 ± and 4.3 ± 0.8 min respectively and statistically similar in both the groups and were comparable with a p value =0.712.

Time in minutes for return of TOF '1' after initial bolus dose among vecuronium and atracurium groups was 53.8 ± 9.8 and 38.7 ± 6.8 min respectively and statistically significant with a p value < 0.0001.

After starting the infusion, Group V patients reached TOF 0 in 12.6 ± 2.9 and Group A patients reached TOF 0 in 16.1± 3.1 and P value was< 0.0007 which is significant. But after stopping the infusion Group V Patients took 62.2± 17.7 min whereas Group A patients took only 27.9. ± 6.7 min., and the P value is<0.0001 which is highly significant.

Table 2 shows the descriptive statistics of the systolic blood pressure (SBP) of patients in Group V and Group A at various time points. No significant change was seen in systolic blood pressure between the groups.

Table 3 shows the descriptive statistics of the diastolic blood pressure (DBP) of patients in Group V and A at various points. No significant difference in DBP in between groups preoperatively but the mean diastolic blood pressure in Group A patients was significantly lower than group V 2 and 10 minutes after injection of bolus dose of muscle relaxant ie., (p <0.05). Also, there was no significant change was seen between the groups after starting and stopping the infusion.

DISCUSSION

Muscle relaxants primary objective is to provide ideal conditions for good surgical access. They will also facilitate the intubation of trachea and controlled mechanical ventilation. With the use of these muscle relaxants without increasing the depth of anaesthesia, surgeons function can be facilitated so that major haemodynamic changes associated with increasing depth of anaesthesia can be prevented.

In the present study, infusion dose requirements to maintain deep block with muscle relaxants were studied by maintaining TOF COUNT 0 by using Accelerograph. It was observed that the infusion dose requirements of vecuronium after a dose 0.1 mg/kg averaged 1.02 ± 0.1 µg/kg/min i.e., (0.6 mg/kg/hr) and the dose requirements of atracurium after a bolus dose 0.5 mg/ kg averaged 13.7 1.± 9 µg/kg/min i.e., (0.82 mg/ kg/ hr.) respectively.

This finding correlates with the Ratul Basu et al study.[4] They found that the infusion dose requirements of Vecuronium was 0.8 – 1 µg/kg/min after a bolus dose of 0.1 mg/kg and for Atracurium was 4.12 µg/kg/min after a bolus dose of 0.5 mg/kg.

In a study by LS Chaudhari et al In midline and paramedian laparotomies noted that, following a bolus dose of 0.5 mg/kg, the mean infusion dose of Atracurium was 478 ± 44.11 µg/kg/hour and that of vecuronium was 63.2 ± 74 µg/kg/hour after a bolus dose of 0.1 mg/kg for adequate muscle relaxation and this dose was similar to the finding in our study.

Raymond et al.[5] found that the infusion rates of Atracurium remained between 4.0±0.7 and 5.0±1.0 µg/kg/m in throughout the study period. But for vecuronium a progressive decrease in the infusion rate of the drug from 1.0 to 0.47± 0.13 µg/kg/min was observed during the study period.

In the present study, Time in minutes to achieve ideal intubating conditions after initial bolus dose ie., TOF 0 among Vecuronium and Atracurium groups was 4.2 ± 0.9 and 4.3 ± 0.8 min respectively and statistically similar in both the groups were comparable.

In a study by Fletcher et al. used electromyography to monitor nerve function, the onset of block times for vecuronium 0.1 mg/kg and atracurium 0.5 mg/kg were 3.5 ± 0.8 minutes and 5.6 ± 2.2 minutes respectively. The actual time to onset more closely parallels the times in this study.

The time interval between initial IV loading dose and the starting of infusion ie., Time in minutes for Return of TOF 1" after initial bolus dose among Vecuronium and Atracurium groups was 53.8 ± 9.8 and 38.7 ± 6.8 min., respectively. Patients in group A recovered faster from initial bolus dose from neuromuscular blockade compared to group V.

In a study by Ratul Basu and Imam Sinha, the duration of action of Vecuronium was significantly less than that of the Atracurium, who used peripheral nerve stimulator. This finding was related to the findings of Gramstad and Associates.[6]

The differences in the duration of Atracurium and Vecuronium after initial bolus dose, with comparison to previous studies could be due to difference in the individual response, and the effect of cold chain maintenance on stability of Atracurium during the storage of the drug, which may also be the reason behind increased mean infusion dose requirements of Atracurium in the present study compared to previous studies.

In the present study, Spontaneous recovery after stopping infusion, return of TOF3 among Vecuronium and Atracurium groups was 62.2 ± 17.7 and 27.9 ±.7 min respectively and statistically significant. Patients in group Atracurium recovered faster compared to Vecuronium group after stopping infusion for a duration of infusion 148 ± 30.4 min in group V and 157 ± 25.5 min in group A respectively.

Chaudhary et al In their study, the recovery was faster with Vecuronium (Mean 540.94 ± SD 72.46 sec) as compared to Atracurium (596.33 ± SD 72.48 sec). But in the present study, Vecuronium and Atracurium infusion rates were kept constant throughout the infusion and allowed for spontaneous recovery till TOF 3, because of differences in the duration of infusion and rate of infusion, which may affect the cumulative nature of Vecuronium over time and the difference in the time of giving reversal, there are difference in the results obtained between the studies.

In the present study, no significant changes were seen in Systolic blood pressure between the groups. No significant changes in Diastolic blood pressure in between groups Preoperatively, but the mean diastolic pressure in group A patients was significantly lower than group V at 2 minutes and 10 minutes of bolus dose of muscle relaxant. And no

significant change was seen between the groups after starting and stopping the infusions.

L. S. Chaudhari et al In their study found that Vecuronium infusion produced more haemodynamic stability then Atracurium infusion. Vecuronium produced lesser change in systolic blood pressure (Mean change 3.46 ± 3.33 %) from baseline values as compared to Atracurium(mean change of 5.81± 3.73 %)from base line values ($p<0.01$) which was statistically significant. The study correlates with my present study.

CONCLUSIONS

Time for intubation did not show significant difference between the two groups. The rate of infusion was more for the Atracurium group as compared to Vecuronium group because of quicker spontaneous recovery. Despite these differences, infusions of both were characterized by their ease of administration, spontaneous recovery even after prolonged infusion. Infusion rate can be precisely controlled with simple monitoring techniques such as TOF count, to allow adjustment of blockade according to surgeon's need combination of continuous infusion of Atracurium or Vecuronium, monitored by TOF count, use of anticholinesterase drugs, permits safe and successful recovery. It was concluded that with Vecuronium produced more haemodynamic stability compared to Atracurium but there is slower spontaneous recovery of residual neuromuscular blockade than with Atracurium.

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