Original Article

Comparison of different doses of atracurium for quality of muscle relaxation during modified rapid sequence induction in emergency laparotomy: A prospective randomised double blind study

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Submitted: 24-Mar-2022
Revised: 23-Nov-2022
Accepted: 05-Dec-2022
Published: 20-Dec-2022

Access this article online
Website: www.ijaweb.org
DOI: 10.4103/ija.ija_285_22
Quick response code

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ABSTRACT

Background and Aims: In emergency and non-fasting patients posted for laparotomy under general anaesthesia, rapid sequence induction (RSI) is preferred, and it is routinely done by using succinylcholine or rocuronium. Using higher doses of atracurium [i.e. 3-4 times the 95% effective dose (ED95)] can provide acceptable intubating conditions in a short time. The primary objective of our study was to compare two different higher doses of atracurium to achieve good intubating conditions for RSI without using a priming dose. The secondary objective was to compare the duration of muscle relaxation using neuromuscular monitoring and haemodynamic responses during and after intubation. **Methods:** Sixty patients were enroled and randomly assigned into two groups:-, group A1 (atracurium: 0.75 mg/kg) and group A2 (atracurium: 1 mg/kg). After premedication, anaesthesia was induced with propofol 2-2.5 mg/kg and atracurium injections, followed by intubation within a minute by trained anaesthesiologists. Meanwhile, intubating conditions, neuromuscular monitoring using train-of-four (TOF) measurements and post-tetanic-count and haemodynamics were recorded. Data were analysed statistically by using the Chi-square test and Student's t-test. **Results:** Excellent intubation conditions (without coughing or bucking) were attained in 56.7% of cases in group A2 and in 13.3% in group A1 ($P < 0.001$). Duration of muscle relaxation, measured by time until TOF is two, was more prolonged in group A2 (79.2 ± 9.2 min) than in group A1 (60.13 ± 8.7 min, $P < 0.001$). **Conclusion:** Acceptable intubating conditions can be achieved in a minute with the use of a high dose of atracurium (1 mg/kg) during RSI. Hence, atracurium can be used as an alternative drug for RSI.

Key words: Atracurium, muscle relaxation, rapid sequence induction and intubation

INTRODUCTION

For intubation in emergency and full stomach patients, rapid sequence induction (RSI) plays an important role in avoiding the risk of aspiration of gastric contents. To achieve this RSI, drugs like succinylcholine and rocuronium are commonly used because of their fast onset of action.

Succinylcholine, the most commonly used drug for RSI, has various side effects and is contraindicated in certain conditions like hyperkalaemia, cardiac arrhythmias, raised intracranial pressure (ICP) and intraocular pressure (IOP).[1] Rocuronium is primarily metabolised in the liver and is excreted by the bile, and hence is avoided in patients with hepatic diseases and

How to cite this article: Holkunde R, Masur S, Patil BA, Patil C, Naik D, Lamani S. Comparison of different doses of atracurium for quality of muscle relaxation during modified rapid sequence induction in emergency laparotomy: A prospective randomised double blind study. Indian J Anaesth 2022;66:849-53.

with deranged liver enzyme profiles.[2] Atracurium, a benzylisoquinolinium compound, is a depolarising neuromuscular agent with intermediate action and is considered to be a safe drug for use in hepatic and renal disease patients because of its Hofmann's elimination. Atracurium, when given in higher doses, that is 3-4 times of 95% effective dose (ED95), has been proven to facilitate good and comparable endotracheal intubating conditions as high doses of rocuronium.[3,4]

The priming technique is most commonly used to enhance the process of rapid intubation in RSI. However, it also increases the risk of gastric aspiration. Our study involved patients posted for emergency laparotomy as study subjects, and hence, we avoided using the priming technique.[5] As such, as per our knowledge, there are currently no studies evaluating the usage of high doses of atracurium for RSI without priming in emergency laparotomies. Hence, we designed our study with the primary objective of comparing intubating conditions using two different doses of atracurium. The secondary objective was to assess the duration of muscle relaxation using neuromuscular monitoring and comparing the haemodynamics.

METHODS

After obtaining clearance from the institutional ethics committee (SNMC/IECHSR/2019-20/A-80/1.0), the study protocol was registered with the Clinical Trials Registry of India (CTRI/2020/07/026582). The study was conducted between July 2020 and June 2021 in a tertiary care teaching hospital in accordance with the principles of the Declaration of Helsinki. Sixty patients posted for emergency laparotomy were recruited. Written and informed consent was taken from all 60 subjects. Inclusion criteria included patients aged between 20 and 65 years and American Society of Anesthesiologists (ASA) physical status II or III posted for emergency laparotomy. Exclusion criteria were patients with a predicted difficult airway, patient's refusal to participate, any history of severe cardiac disease, history of metabolic or neuromuscular disorders and drug interactions or history of study drug allergy.

Patients were randomised into two study groups of 30 each based on computer-generated random sequence allocation with the allocation being concealed with an opaque sealed envelope technique. Patients and the intubating anaesthesiologist for the study were blinded. Group -A1 (received 0.75 mg/kg of atracurium), which is three times of ED95 (ED95 is the effective dose that decreases the muscle twitch by 95% from baseline) and group -A2 (received 1 mg/kg of atracurium), which is four times the ED95. The two doses of atracurium were prepared in the same volume using syringes of similar size and shape and were coded. The cold chain was maintained till administration of the drug. After pre-anaesthetic evaluation, patients were shifted to the operating room with two 18-gauge intravenous cannulae *in situ*. Standard ASA monitors like pulse oximetry, non-invasive blood pressure and electrocardiogram were attached to the patient. Patients were then pre-oxygenated for 3 min with 100% high flow oxygen, premedicated using injection midazolam 0.02 mg/kg and fentanyl 2 μg/kg intravenously. Modified RSI with injection propofol 2-3 mg/kg and atracurium 0.75 mg/kg (group A1) or 1 mg/kg (group A2) was given to the patients, based on the randomisation. Tracheal intubation was done by trained anaesthesiologists within 60 seconds of the administration of the study drugs. Intubating conditions were assessed by the intubating anaesthesiologist, who was blinded for the dose of the study drug and were graded as;- grade 1-excellent (easy passage of the tube without coughing/bucking), grade 2-good (passage of the tube with slight coughing/bucking), grade 3-fair (passage of the tube with moderate coughing/bucking) and grade 4-poor (not possible to intubate).

After endotracheal intubation and confirmation of bilateral air entry, the tube was fixed and patients were mechanically ventilated with appropriate settings individualised to each patient. At the same time, neuromuscular monitoring and haemodynamics were measured by an anaesthesiologist who was blinded to the drug under study.

Train-of-four (TOF) measurements were done using neuromuscular transmission mechanosensory monitor (GE Healthcare Helsinki, Finland) by placing the transducer along the ulnar nerve and stimulating the adductor pollicis muscle using 50 mA current, and the stimulation was monitored every 12 seconds from the onset of the induction of anaesthesia until the disappearance of all four twitches. Post-tetanic count (PTC) of zero was noted at that particular point of time and the time from induction to PTC of zero was considered as the maximum onset of action of muscle relaxant. TOF stimulation was continued every 5 min till the occurrence of two twitches which indicated

the duration of muscle relaxation. Anaesthesia was maintained with oxygen, nitrous oxide and isoflurane and top-up doses of atracurium were administered for muscle relaxation. Intravenous injections of paracetamol 1 g and tramadol 50 mg were administered for analgesia. Blood pressure, heart rate and peripheral oxygen saturation were recorded every minute for the first 10 min after induction of anaesthesia, followed by every 10 min till the end of surgery. Patients were closely monitored for adverse effects like rashes, cutaneous flushing or bronchospasm during the study period. Hypotension that developed after induction was managed with intravenous bolus of fluids and vasopressor as required.

Sample size estimation was done using OpenEpi Software Version 2.3.1. At 95% confidence level, and 80% power of the study, based on the results of a previous study conducted by Chalermkitpanit P *et al*.,[6] the estimated sample size was 23, which was rounded off to 30 in each group. Study data were entered in Microsoft Excel and later analysed statistically using Statistical Package for Social Sciences for windows, version 19 (International Business Machines Corp, Armonk, N. Y, USA). Mean and standard deviation were calculated for quantitative data like age, weight, neuromuscular monitoring, and Student's t-test was applied. Percentage and number were used to represent qualitative data like gender, ASA physical status, intubating conditions, and Chi-square test was applied. A P value of <0.05 was considered significant.

RESULTS

Sixty-four patients who met the inclusion criteria and were posted for emergency laparotomy were randomised. Four patients refused to participate in the study [Figure 1].

The demographic characteristics of the patients like age, gender, weight and ASA physical status were comparable between the groups [Table 1]. Excellent intubating conditions were achieved in 56.7% of cases in group A2 as compared to group A1 which had excellent intubating conditions in 13.3% ($P < 0.001$) [Table 2]. Good intubating conditions with neuromuscular monitoring were seen in group A2 and also a longer time was required until the TOF count reached two as compared with group A1, which showed statistical significance with $P < 0.001$ [Table 3]. A decrease in the mean arterial

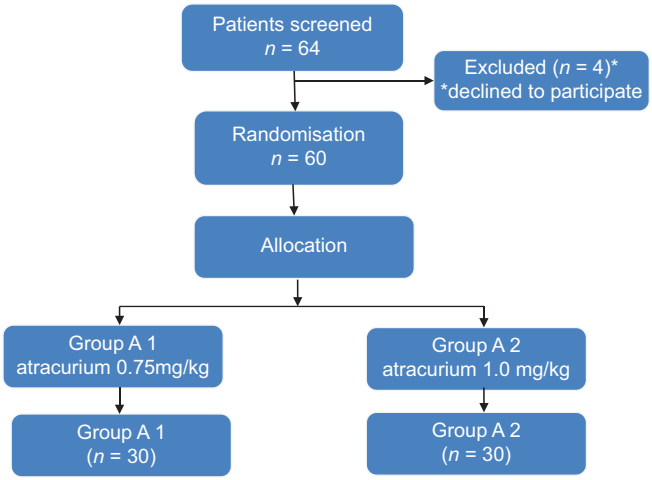

Figure 1: Consolidated Standards of Reporting Trials (CONSORT) diagram

Table 1 Patient demographic characteristics

	Group A1 (*n*=30)	Group A2 (*n*=30)
Age (years)	38.60±14.7	37.2±7.9
Gender		
Male	18 (60)	15 (50)
Female	12 (40)	15 (50)
Weight (kg)	64.97±6.7	66.8±6.3
ASA physical status		
II	16 (53.3)	16 (53.3)
III	14 (46.7)	14 (46.7)

Values presented as mean±Standard deviation, and frequency (%), *n* - number, ASA - American Society of Anesthesiologists

pressure (MAP) after 3 min of induction of general anaesthesia was noted in both groups, among which, group A2 had more fall in MAP than group A1. This fall in MAP was corrected with an intravenous injection of mephentermine 6 mg. No significant changes in heart rate, requiring any intervention, were observed in both groups [Figures 2 and 3]. No other adverse effects were noted, except cutaneous flushing of the face and the arm in which drugs had been injected (10 patients in group -A1 and 12 patients in group A2). This cutaneous flushing resolved on its own within 4-5 min.

DISCUSSION

We evaluated two different doses of atracurium (3–4 times ED95) to achieve RSI and good intubating conditions within a minute. Excellent intubating conditions were achieved in more than half of the patients in group A2 without serious side effects.

In emergency laparotomies, RSI is the method ideally followed for intubation as stomach distension due to air influx during regular bag and mask ventilation

is a common cause of regurgitation. Patients with intestinal obstruction, gastroparesis, full stomach and pregnancy are at a high risk of aspiration.[7] In modified RSI, preoxygenation is done with 100% oxygen for 3 min followed by cricoid pressure until the airway is secured with an endotracheal tube and the cuff is inflated. No bag and mask ventilation is done during this period. Patients remain apnoeic till the airway is secured. Hence, faster-acting muscle relaxant drugs, such as succinylcholine and rocuronium, are generally used for RSI but because of their adverse effects, they are avoided in patients with hyperkalaemia, raised ICP and IOP and also in patients with impaired renal and hepatic functions.

As there is very less literature available on employing atracurium as the sole neuromuscular blocking drug (NMBD) for RSI, we designed this trial in our set up. Atracurium does not play a role in raised ICP or IOP or hyperkalaemia and undergoes Hofmann elimination and hence is safe in renal and hepatic failure patients. Also, the onset time and potency of any NMBD are inversely related, and providing a significant dose of NMBD will accelerate the onset, similar to succinylcholine. When given in large doses, they bind to a large number of nicotinic acetyl-choline receptors, resulting in rapid onset of action.[8-10] Priming technique is believed to enhance this onset of action of NMBDs; However, it has its own disadvantages like, lung aspiration, respiratory weakness and visual disturbances.[11] So, we avoided using the priming technique.

As per the results of our study, atracurium proved to be effective in achieving good intubating conditions within a minute, and the doses and grading were considered according to the study conducted by Chalermkitpanit P, *et al*.[6]. Also, we could achieve excellent intubating conditions with a success rate of 56.7% with a dose of 1 mg/kg.

In the study conducted by Chalermkitpanit P *et al*.[6] on elective surgical patients under general anaesthesia, the intubating conditions were graded as excellent in 51.4% of patients receiving 1 mg/kg of atracurium, in 43.6% of the patients with 0.75 mg/kg of atracurium and 26.3% patients with 0.6 mg/kg of atracurium ($P < 0.05$). However, unlike their study, we conducted our study only on emergency laparotomies under general anaesthesia using modified RSI. A comparison of the duration of muscle relaxation using neuromuscular monitoring was also made. Group A2 had an early maximum effect indicated by a shorter time until PTC reached zero and a longer duration of action indicated by a longer time until TOF count reached two [Table 3]. The main strengths of our study were the inclusion of patients of ASA grade II and III taken up for emergency laparotomy, the use of modified RSI for intubation, and also the avoidance of

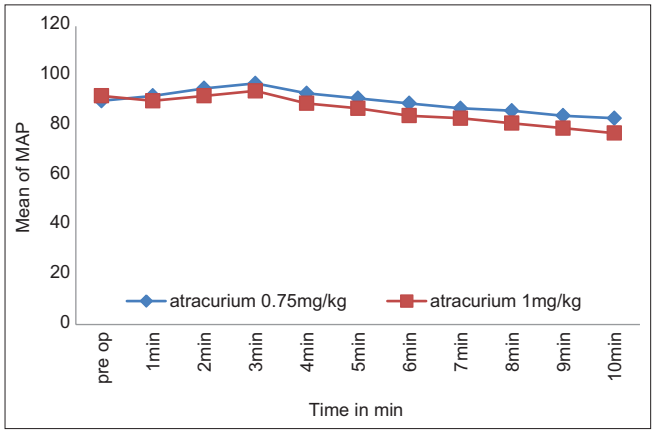

Figure 2: Mean arterial pressure (MAP) values for two doses of atracurium

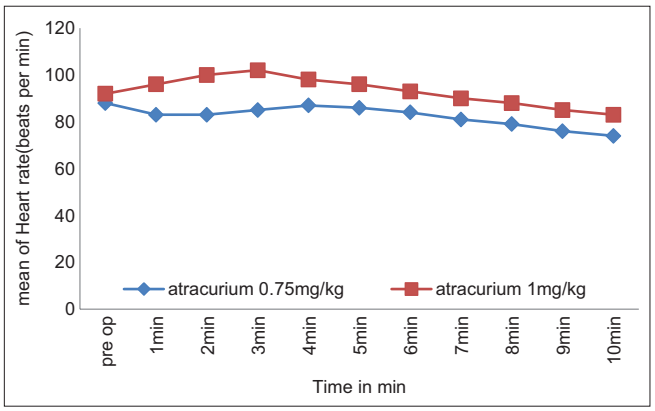

Figure 3: Heart rate (HR) values for two doses of atracurium

Table 2: Intubating conditions

	Atracurium dose 0.75 mg/kg group A1 (*n*=30)	Atracurium dose 1 mg/kg group A2 (*n*=30)
Excellent - easy passage of tube without coughing/bucking	4 (13.3)	17 (56.7)
Good - passage of the tube with slight coughing/bucking	13 (43.3)	13 (43.3)
Fair - passage of the tube with moderate coughing/bucking	13 (43.3)	0 (0)
Poor - not possible to intubate	0 (0)	0 (0)

Values presented as frequency (%), *n* - number

Table 3: Neuromuscular monitoring results

	Group A1 (*n*=30)	Group A2 (*n*=30)
Time until PTC is zero (s)*	214.00±23.9	146.1±33.6
Time until TOF is two (min)*	60.13±8.7	79.2±9.2

Values presented as mean±standard deviation. *t-test P<0.001

priming technique, which otherwise increases the risk of aspiration in such cases.

There is a scope for future studies on this topic in patients undergoing surgeries like craniotomy and caesarean section which require RSI.

CONCLUSION

Atracurium in the dose of 1 mg/kg provides good intubating conditions at 1 min for RSI in emergencies and can be safely used when other drugs are contraindicated.

Acknowledgement

The authors are grateful to Dr Shivanand Hulakund, Professor and Head, Department of Anaesthesia, SN Medical College, Bagalkot for the help given in the conduct of the study.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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