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COMPARISON OF CONTINUOUS INFUSION OF VECURONIUM AND ATRACURIUM IN LAPAROTOMIES AT SMCH, GHAZIABAD, U.P.

Anaesthesiology

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ABSTRACT

Sixty adult patients of either sex, 25 – 45 years of age, belonging to ASA physical status I or II, who were scheduled for midline and paramedian laparotomies under general anaesthesia lasting for up to two hours were recruited for a prospective randomized controlled study intended to compare vecuronium and atracurium when the drugs were used as a continuous infusion. The drugs were compared with respect to recovery from neuromuscular blockade on stopping the infusion and cardiovascular performance. The study was approved by the Institutional Ethics Committee and all patients enrolled provided written informed consent. Patients were randomly allocated into two equal groups and received either vecuronium (Group I) or atracurium (Group II) in intravenous infusion for maintenance of muscle relaxation. Fentanyl was used as analgesic and inductions were done with thiopental and intubation with vecuronium (0.1 mg/kg body weight) in Group I patients and atracurium (0.5 mg/kg body weight) in Group II patients. Anesthesia was maintained with 33% oxygen in nitrous oxide and incremental doses of fentanyl and propofol infusion at a rate of 2-4 mg /kg/hour. Intravenous infusions of muscle relaxants were adjusted to maintain 90% of neuromuscular blockade monitored by stimulating ulnar nerve at the wrist by a peripheral nerve stimulator throughout surgery. At the end of the procedure, at 25% recovery of twitch height, neuromuscular blockade was reversed with neostigmine and glycopyrrolate.

KEYWORDS

INTRODUCTION

Anaesthesia involves administration of drugs to produce analgesia, amnesia, hypnosis and muscle relaxation. Inhalational anaesthetics, regional nerve blocks or neuromuscular junction blocking agents can produce skeletal muscle relaxation component of anaesthesia.

The use of muscle relaxants in clinical practice can be traced back to the finding of Benjamin Brodie in 1811-12, that animals poisoned by the drug curare could be kept alive by artificial ventilation. In the landmark experiment of Grifith and Johnson in the year 1942, in Montreal, purified curare was used to obtain adequate muscle relaxation. This was one of the milestones in the history of specialty. The use of neuromuscular blockers has been important in the evolution of anaesthesia and surgery and is a common practice in present day operating rooms. Muscle relaxants, by providing immobility and thus ease for a surgeon's operation, not only revolutionized the practice of anaesthesia in the modern era but have also led to explosive developments in cardiothoracic, neurologic and organ transplantation surgery. They are now used routinely to facilitate endotracheal intubation and are commonly used to maintain anaesthesia in different surgical procedures. Drugs named, anticholinesterases, can easily reverse their effect. They provide a relaxed and immobile patient without the need for large doses of hypnotics and opioids. The latter thus minimizes the risk of hemodynamic instability and residual postoperative effect causing respiratory depression. But several catastrophes have occurred with the use of d-tubocurarine in the past due to the lack of adequate knowledge about its pharmacology and lack of antagonists.[1,2]

So, alternatives were looked for. In 1967 Baird and Reid, first reported the administration of a synthetic aminosteroid muscle relaxant, pancuronium.[3] Pancuronium and other longer acting drugs are mainly excreted through kidneys with minimum metabolism. They are used during anaesthesia in intermittent boluses on observation of reversal from their effects. However, bolus administration leads to variations in the degree of relaxation and also hemodynamics, making it difficult to maintain uniformly relaxed state and stable hemodynamics to facilitate uneventful anaesthesia and surgery. So, the concept of continuous infusion of muscle relaxants came into existence. However, longer acting agents can't be used as continuous infusions for maintenance of anaesthesia because they have a tendency to accumulate, leading to prolonged residual effect.

An ideal muscle relaxant that can be used as a continuous infusion should have low potency, rapid onset, and a short duration of action, without any cumulative effect and their action should be easily reversible with proper antagonists. Vecuronium, an aminosteroid and atracurium, a benzylisoquinolinium compound, are two muscle relaxants that come close to fulfilling most of the above criteria. Lack of cumulative effect and rapid recovery index make them suitable for this mode of administration. They have similar duration of action and both have been used to maintain neuromuscular blockade by repeated boluses and by infusion. The potential advantages of continuous infusion include a more consistent degree of paralysis, the scope for individualizing relaxant input and minimizing drug requirements in comparison to repeated bolus injections. There is little evidence of delayed recovery when an infusion system is used to administer these drugs in healthy patients. Use of neuromuscular monitoring makes such continuous infusions more feasible.

AIMS AND OBJECTIVES

1. To assess the recovery from neuromuscular blockade on stopping the infusion of vecuronium and atracurium.
2. To assess the cardiovascular performance during the perioperative period.

MATERIAL AND METHODS

This study was carried out in the Department of Anaesthesiology at Santosh Medical College & Hospital, Ghaziabad, U.P between February 2018 and September 2019.

Sixty adult patients of American Society of Anesthesiology (ASA) physical status I and II, scheduled for median and paramedian laparotomies under general anaesthesia, were included in the study. Informed consent was obtained from each patient prior to including him/her for the study.

STUDY DESIGN

Patients were randomly allocated to two equal groups (n = 30 in each group) using computer generated random number list. Group I comprised patients who received vecuronium bromide and group II comprised those who received atracurium besylate. The study was prospective, parallel group, single blind and controlled.

CRITERIA FOR SELECTION OF PATIENTS
INCLUSION CRITERIA

1) Adult patients of both sexes aged between 25-45 years.
2) ASA physical status I and II
3) Scheduled for elective median and paramedian laparotomies

EXCLUSION CRITERIA

1) Bronchial asthma
2) Diabetes
3) History of seizure
4) Known neuromuscular disorder like myasthenia gravis
5) Hepatic failure
6) Patient receiving aminoglycoside antibiotics, lithium, antiep ileptic drugs, frusemide
7) Anticipated difficult intubation

PRE OPERATIVE INVESTIGATIONS

Routine investigations were carried in all patients. These included:

1) Total RBC count and haemoglobin percentage
2) Total and differential WBC counts
5) Routine urine analysis
4) Estimation of blood glucose, urea and creatinine
5) Chest X-ray (PA view)
6) ECG (in patients above 40 years of age or with specific complaints)

PRE OPERATIVE VISIT AND CLINICAL EXAMINATION

The day before surgery, each patient was attended to and examined properly for preoperative counseling and anaesthetic check up. This was done under the following headings:

A) History: A detailed history was obtained from every patient regarding any symptom of breathlessness, asthmatic attack, bleeding disorder, drug allergy, any muscle weakness, seizure, diabetes, jaundice, previous history of surgery and anaesthesia, unconsciousness or prolonged drug treatment if any.
B) Physical examination: Anaemia, jaundice, cyanosis, clubbing, pulse rate and blood pressure were noted. Assessment of the airway was done to anticipate any difficulty in intubation.
C) Systemic examination: Thorough examination of the cardiov ascular and respiratory system was done in all patients. Examination of the other systems was carried out as well. The body weights of all patients were also recorded.
D) Preoperative fasting: All patients were instructed not to consume solid food after midnight on the day of surgery, but clear fluids were permitted till four hours prior to scheduled time of operation.

ANAESTHETIC TECHNIQUE

Intravenous access with two 3-way connections was secured in all patients in their left hand. Proper checking of the anaesthesia machine and equipment was carried out beforehand and full range of drugs and equipment, including appropriate sized laryngoscope blades and handles, airways, endotracheal tubes and resuscitation equipment were kept at hand. Ten milligram of vecuronium was diluted in 10 ml of 5% dextrose. This reconstituted vecuronium was used for intravenous bolus for intubation. Then for infusion, 10 mg vecuronium was diluted in 5% dextrose in 50 ml syringe. Atracurium 50 mg was diluted in 50 ml of 5% dextrose for continuous infusion in 50 ml syringe. Twenty milligram of propofol was taken in another syringe and it was also set in a syringe pump with extension tube. Before induction two syringe pumps containing muscle relaxant and propofol were connected to the 3-way connections.

Monitoring devices like blood pressure cuff, ECG leads, finger probe of pulse oximeter and surface electrodes on the wrist were applied to monitor blood pressure, heart rate, oxygen saturation neuromuscular blockade respectively.

In all patients, after 3 minutes of pre-oxygenation, injection fentanyl 2 g/kg was given and general anaesthesia was induced with injection thiopental sodium (4-6 mg/kg body weight) intravenously till loss of eyelash reflex was observed. Injection vecuronium (0.1 mg/kg) or atracurium (0.5 mg/kg) were used in group I and group II respectively to achieve muscle relaxation for endotracheal intubation. Propofol infusion was started at a rate of 2-4 mg/kg/hr and patients ventilated by facemask with nitrous oxide (66%) in oxygen as inhalational agent. Intubation was done with cuffed endotracheal tube of appropriate size when there was no response to train of four stimuli. After intubation and inflation of cuff, correct placement of endotracheal tube was confirmed by auscultation and capnography. Anaesthesia was maintained with infusion propofol, 66% nitrous oxide in oxygen and fentanyl as and when required. After intubation train of four responses were studied at regular intervals. As soon as the first response to train of four stimuli appeared, intravenous infusion of vecuronium (0.8-1 g/kg/min) or atracurium (4-12 g/kg/min) was started at a rate that was appropriate for that patient. Dose of infusion of relaxants was adjusted in such a way that first response of train of four was spared but second response remained suppressed. Time taken to achieve this steady state of block from the time of starting the infusion was noted. The infusion was also titrated by resistance to ventilation, surgical relaxation and haemodynamic changes. The patients were also monitored for spontaneous respiration, movements of limbs and signs of histamine release like flushing of the face, hypotension, bronchospasm and changes in pulse rate.

The surgical team also assessed quality of muscle relaxation. It involved estimating the degree of difficulty in retracting the abdominal wall and closing the muscle layer. Immediately after muscle layers were approximated, infusion was stopped and spontaneous recovery monitored using peripheral nerve stimulator and clinical criteria. Time of appearance of three responses to train of four stimuli was noted; residual 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 of peripheral nerve stimulator. When patients were fully awake, 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 was used to assess the degree of neuromuscular blockade – absence of any twitch response indicating 100% block and appearance of 1, 2 or 3 response indicating 90%, 80% or 75% block respectively. The INNERVATOR 272 model manufactured by M/s Fisher and Paykel Healthcare International (NewZealand) was the instrument used.

Hemodynamic parameters like pulse rate, systolic BP and diastolic BP were measured at different time points. These included baseline preoperative values, 2 minutes and 10 minutes after bolus dose administration, 2 minutes and 10 minutes after starting infusion and postoperatively. Measurements 2 minutes after bolus dose (that is before laryngoscopy and intubation) indicated bolus dose effect on haemodymnamics. This was repeated at 10 minutes because the effect of laryngoscopy and intubation is considered to wear off at that time point. Parameters measured 2 minutes and 10 minutes after starting infusion indicated hemodynamic performance during the infusion. Postoperative values were used to compare with other values measured pre- and intra-operatively and to assess the adequacy of analgesia.

STATISTICALANALYSIS

For the purpose of sample size calculation, pulse rate was taken to be the hemodynamic parameter of prime interest. It was calculated that 29 subjects would be required per group in order to detect a difference of 3 beats per minute in pulse rate with 80% power and 5% probability of Type I error. This calculation assumed a standard deviation of 4 with respect to this parameter.

For statistical analysis, raw data was entered into a MS Excel spreadsheet and analyzed by SPSS version 13.0 (SPSS Inc.; Chicago, Illinois, USA; 2004) and Statistica version 6.0 (Statsoft Inc.; Tulsa, Oklahoma, USA; 2001). Sample size calculation was done with the latter software.

Hemodynamic variables were compared between groups by Mann-Whitney U test, making no assumptions as to the distribution of the variables in the population. Unpaired Student's t test was used to compare normally distributed numerical variables such as age and body weight. Categorical variables were compared using Chi-square test or Fisher's exact test, as appropriate. All analysis was two-tailed and $p < 0.05$ was taken to be statistically significant.

RESULTS

The two study groups were comparable in terms of demographic parameters, body weight, duration and type of surgery. Majority of the subjects were young adults of average body weight. The median time and inter quartile range which is taken from intravenous bolus dose to

10% recovery is less in vecuronium group (23±2 min) than atracurium group (25±2 min). Vecuronium (median 15.5 ± 3 min) took less time to achieve steady state of block after starting infusion than atracurium (median 18 ± 3 min).

Twenty five percent recovery after stopping infusion was earlier in vecuronium (median 538.5 ± 7.5 sec.) group than atracurium (593.5 ± 17 sec.) group.

Patients who received vecuronium recovered early from relaxant effect with more stable hemodynamics. There was no incidence of bronchospasm, cutaneous flushing or any other sign of histamine release in any of the groups.

CONCLUSIONS

1. Time that is taken from intravenous bolus dose to 10% recovery is less in vecuronium group.
2. Vecuronium took less time to achieve steady state of block after starting infusion
3. Twenty five percent recovery after stopping infusion was earlier in vecuronium group.
4. Vecuronium maintained more stable hemodynamics than atracurium when used in continuous infusion

Thus vecuronium can be considered as a safe and effective alternative to atracurium as a muscle relaxant when using in continuous infusion in ASA grade I and II patients posted for median and paramedian elective laparotomies.

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