NEUROMUSCULAR BLOCKING EFFECT OF CONTINUOUS INFUSION OF VECURONIUM BROMIDE AND INTERMITTENT ADMINISTRATION OF PANCURONIUM BROMIDE AND VECURONIUM BROMIDE- A CLINICAL COMPARATIVE STUDY

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ABSTRACT

Aim and Objectives: To compare the continuous infusion of vecuronium bromide with intermittent incremental administration of vecuronium bromide and pancuronium bromide in terms of the quality of neuromuscular blockade, haemodynamic stability, recovery profiles and complications.

Method: Total 60 patients were enrolled and randomly divided into three equal groups. Group A received injection pancuronium bromide 0.075mg/kg as bolus dose followed by 0.015mg/kg of maintenance dose. Group B received injection vecuronium bromide 0.075mg/kg as bolus dose followed by 0.015 mg/kg of maintenance dose. Group C patients received injection vecuronium bromide 0.075mg/kg as bolus dose followed by an infusion of vecuronium delivering at the rate of 0.075 mg/kg/hr.

Results: Mean time of onset for neuromuscular blockage was 5.05±3.4, 3.15±2.6 and 3±1.6 min in group A, B and C respectively. The clinical duration of bolus dose was 51.75min in group A and 27.65min in group B. Duration of action of maintenance dose was 30±18.4min and 17.8±6.7min in group A and B respectively. The recovery time was 36.3±4.73min in group A, 16.3±3.24min in group B and 16.95±3.13 min in group C. The mean level of block was 88.9±14.2 in group A, 88.05±9.8 in group B and 91.3±7.6 in group C. Group A showed significant rise in pulse rate at 15 min (97.5±16.5bpm) and 30 min (96.55±9.5bpm) while group B and C showed significant decreased in pulse rate at 180 min of intraoperative period from baseline value.

Conclusion: Infusion of vecuronium is a safer alternative to intermittent incremental doses if adequate facilities for neuromuscular monitoring are available.

Keywords: Neuromuscular blockade; Vecuronium; Pancuronium; Bromide; Haemodynamic stability; Bolus dose; Maintenance dose; Recovery time

INTRODUCTION

Neuromuscular blocking drugs are used primarily to facilitate tracheal intubation, decrease the potential for injury to vocal cords from laryngoscopy, and improve surgical conditions. However, neuromuscular blockers are not the sole determinant in achieving acceptable intubating conditions or preventing intraoperative movement of anesthetized patients. Guidelines are also needed regarding appropriate administration of

anesthetic induction agents and titration of these agents intraoperatively to ensure an optimal plane of general anesthesia [1].

Vecuronium is a non-depolarizing neuromuscular blocking agent which has been introduced to clinical practice in 1984. Although closely related chemically to its bisquatemary analogue, pancuronium, it has a considerably shorter duration of action and lacks the occasional undesirable cardiovascular side-effects of pancuronium [2,3]. These differences in clinical characterstics might confer some advantage in combining the two drugs in clinical practice: the alternate administration of neuromuscular blockers with different durations of action might enable the anaesthetist to regulate to a finer degree the depth and duration of neuromuscular blockade during surgery, according to the stage of an operation and the clinical requirements [4].

Having demonstrated previously that, during prolonged surgical procedures, bolus injections of vecuronium were required as frequently as every 10 min [5], suggested that the continuous infusion of this drug would be a more appropriate technique with which to maintain a consistent degree of neuromuscular blockade. This mode of administration' has been studied and compared the quality of neuromuscular blockade, recovery profiles and haemodynamic changes during continuous infusion with that of intermittent incremental doses.

MATERIALS AND METHODS

The study comprised of sixty patients of ASA grade I and II belongs to age group of 20-60 years drawn from various surgical specialties and undergoing elective surgery under general anaesthesia. Paediatric patients, pregnant women, ASA grade III and IV patients, patients with deranged hepatic and renal function, patients suffering from neuromuscular diseases and medications known to affect the pharmacodynamics of neuromuscular blocking drugs were excluded from the study.

A thorough preanaesthetic checkup was done and informed consent for surgery and general anaesthesia was obtained. Investigations including routine blood test (Hb, TLC, DLC, and ESR) were done. All patients were pre-medicated with injection atropine 0.6 mg IV and injection pentazocine 30 mg IV. After preoxygenation for 3 minutes, general anaesthesia was induced in all patients with injection thiopentone sodium 5mg/kg followed by injection succinylcholine chloride 2mg/kg. The patients were randomly divided into three groups. Group A patients received injection pancuronium bromide 0.075mg/kg as bolus dose followed by 0.015mg/kg of maintenance dose. Group B patients received injection vecuronium bromide 0.075mg/kg as bolus dose followed by 0.015 mg/kg of maintenance dose. Group C patients received injection vecuronium bromide 0.075mg/kg as bolus dose followed by an infusion of vecuronium delivering at the rate of 0.075 mg/kg/hr. Neuromuscular monitoring was done by observing Train of four (TOF). The NMB was assessed as follows-

1. Fourth stimulus disappears i.e. 75% block

2. Fourth stimulus disappears i.e. 80% block
3. Fourth stimulus disappears i.e. 90% block
4. Fourth stimulus disappears i.e. 100% block

In Group A and B, maintenance dose was given whenever second twitch of TOF felt. The onset time, duration of action of bolus and maintenance dose, the recovery time, adverse effects were recorded. Level of neuromuscular blockade, pulse rate and blood pressure were recorded at every 15 minutes during intraoperative period. Pulse rate and blood pressure were also measured for 2 hours postoperatively at an interval of 15 minutes. Anaesthesia was maintained with 60% nitrous oxide in oxygen and 0.5%-1.0% halothane. After completion of surgery reversal was done with injection atropine sulphate 0.02 mg/kg IV and injection neostigmine 0.05 mg/kg IV. Results were analyzed statistically by X^2 test and p value <0.05 was considered statistically significant.

OBSERVATIONS AND RESULTS

Total 60 patients were enrolled in the study and were divided into three groups of 20 patients in each group. In group A equal distribution of sex was observed while in group B and C there were female predominance. In all three groups, there was not statistically significant difference observed in regards to demographic profile of the patients (p>0.05) as shown in table 1.

The level of block was found to higher in group C and in this group, 50% of patients fall in the range of 91-95% of block. Comparison of neuromuscular blocking effect in all three groups is depicted in 2.

DISCUSSION

In operations of more than 1 h duration the administration of pancuronium by repeated i.v. injection provided adequate neuromuscular blockade: the disadvantages were related to an extremely variable duration of action and slow recovery. In contrast, the duration of action of equieffective doses of vecuronium was more predictable, and the final recovery of neuromuscular transmission occurred much more rapidly. However, the need for frequent injections was inconvenient from a practical point of view. The most satisfactory results were obtained with a continuous infusion of vecuronium, which provided adequate surgical relaxation for any desired period of time without evidence of cumulation. However, after the infusion of vecuronium, recovery of neuromuscular transmission was slower than after repeated bolus injections of the same drug. D' Hollander and colleagues[6] studied the effects of an infusion of vecuronium started 10 min after the injection i.v. of a 0.07-mg kg"1 loading dose and readjusted every 10 min for stable 90% twitch depression.

In present study, the time of onset for neuromuscular blockage was 5.05 min, 3.15 min and 3 min in group A, B and C respectively, which is similar to study conducted by Noeldge et al[7]. Duration of action means time from end of injection of

muscle relaxant to 25% recovery of control twitch height. The clinical duration of bolus dose was 51.75 min in group A and 27.65 min in group B. This finding is comparable with the study done by Noeldge et al[7] and Rorvic et al [8]. Duration of action of maintenance dose (Dur rep_{25}) define as time from end of injection of maintenance dose to 25% recovery of control twitch height. The Dur rep_{25} was 30 min and 17.8 min in group A and B respectively which is correlated with the study conducted by Noeldge et al [7]. Recovery time define as time from 25% to 75% recovery of control twitch height. The recovery time in group A was significantly longer (36.3 min) than group B (16.3 min) and group C (16.95 min) which was similar to Noeldge et al [7]. Thus the recovery time was found to be shorter in group B and longer in group A. The difference in recovery time in group B and group C was not statistically significant. The level of block was found to be higher in group C, and in this group 50% patient's fall in the range of 91-95% of block. In group B and group C, higher numbers of patients were seen in the range of 85-90% of block. The mean level of block was 88.9 in group A, 88.05 in group B and 91.3 in group C which was similar to Noeldge et al study [7].

Group A showed significant rise in pulse rate at 15 min (97.5±16.5bpm) and 30 min (96.55±9.5bpm) of intraoperative period from the baseline value (84.3±11 bpm). This may be because of vagolytic action of pancuronium bromide. Group B showed significant decreased in pulse rate at 180 min (66±0 bpm) of intraoperative period from baseline value (88.45±11.9 bpm) and also group C showed significant decreased in pulse rate at 180 min (68±0 bpm) of intraoperative period from baseline value (92.6±16.7 bpm). However, there was no significant change in mean arterial pressure was observed in any of the three groups. Similar findings are reported in Rorvik et al [8]. Two patients in group B and one patient in group C needed Inj. Atropine to treat bradycardia. In group A, two patients showed tachycardia (pulse rate >120 bpm).

The infusion of vecuronium gave more consistent and better quality of muscle relaxation with stable haemodynamic parameters. The recovery time was similar to that seen with intermittent doses of vecuronium. It did not have delayed recovery as seen with pancuronium and peaks and valleys in the level of neuromuscular blockade as seen with incremental doses of pancuronium and vecuronium.

CONCLUSION

Based on results obtained, it can be concluded that infusion of vecuronium is a safer alternative to intermittent incremental doses if adequate facilities for neuromuscular monitoring are available. However, it does not seem justifiable to use a fix infusion dose as individual variation is seen at the level of neuromuscular blockade during the study. Therefore the infusion rate should be titrated according to need of patient during intra-operative period to maintain a constant level of neuromuscular blockade with the aid of a neuromuscular monitor.

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Table 1: Demographic data of the patients

Demographic data	Group A	Group B	Group C
Age (years)	37.45±15.3	37.35±15.01	35.6±13.8
Male/Female	10 (50%)/10 (50%)	11 (55%)/ 12 (60%)	11 (55%)/ 12 (60%)
Weight (kgs)	49.1±8.71	48.3±7.6	48.1±9.0

Table 2: Comparison of neuromuscular blocking effect among three groups

Parameters	Group A	Group B	Group C
Onset time (min)	5.05±3.4	3.15±2.6	3.0±1.6
Duration of action of bolus dose (min)	51.75±33.2	27.65±12	-
Duration of action of maintenance dose (min)	30±18.4	17.8±6.7	-
Recovery time (min)	36.3±4.73	16.3±3.24	16.95±3.13
Neuromuscular blockade	88.9±14.2	88.05±9.8	91.3±7.6