

Effect of Magnesium Sulphate on the Speed of Onset and Duration of Neuromuscular Block Produced by Rocuronium Bromide

Dr. Barun Ram¹, Dr. Bharati², Dr (Prof.) Usha Suwalka³

^{1,2}Senior Resident, ³Professor & HOD Department Of Anesthesiology
Rajendra Institute Of Medical Sciences, Ranchi, Jharkhand

Abstract

Background: Rocuronium bromide is said to be devoid of the adverse effects that are seen with suxamethonium. Its mechanism of action is competitive non-depolarizing neuromuscular block with high degree of selectivity for post-nicotinic cholinergic receptors of skeletal muscle. The most important advantages of rocuronium are the rapid onset and good to excellent intubating conditions within 60-90 seconds after administration of 0.6 mg/kg dose. The speeds of onset of neuromuscular blocking drug are increased by prior administration of magnesium sulphate. MgSO₄ administered before intubation provides better intubating conditions and intraoperative haemodynamic stability.

Methods: A total of 50 patients were selected randomly from the routine operation lists for the study. All patients were ASA grade - I & II between age group of 18 to 60 years of either sex. The patients were divided in to two groups of twenty five each. Group I (MgSO₄ Group)- Patients were given MgSO₄ 60 mg/kg diluted in normal saline making it total 100 ml as an intravenous infusion. Group II (Control Group)- Patients were given 100 ml normal saline as an intravenous infusion.

Results: Results demonstrated that onset time in group - I was 85.84 ± 17.83 seconds (mean \pm S.D) and in group - II it was 89.2 ± 20.70 seconds. The differences in mean onset time between groups were not statistically significant ($P=0.5415$, $P > 0.05$). Furthermore, clinical duration in group - I was 45.92 ± 8.80 minutes and in group II it was 25.36 ± 4.28 minutes. The differences in mean clinical duration between groups were statistically highly significant ($P=0.0001$, $P < 0.05$). Mean clinical duration was significantly prolonged in group I than in group II. Thus, prior administration of MgSO₄ (60 mg/kg) did not increase speed of onset, but prolonged duration of action of rocuronium induced (0.6 mg/kg) neuromuscular block.

Conclusion: MgSO₄ did not increase the speed of onset time, but prolonged the clinical duration of rocuronium-induced neuromuscular block. Also, MgSO₄ administered before intubation provides better intubating conditions and intraoperative haemodynamic stability.

Keywords: Rocuronium bromide, Magnesium sulphate, Neuromuscular block

I. Introduction

The action of non-depolarizing neuromuscular blockers is potentiated by magnesium sulphate (MgSO₄)¹ and the speeds of onset of pancuronium, atracurium and vecuronium are increased by prior administration of MgSO₄.²⁻⁴ The aims of this study were to determine the effects of prior administration of MgSO₄ 60 mg/kg i.v. on the onset and duration of rocuronium-induced neuromuscular block, and intraoperative haemodynamic stability. Good intubating conditions minimize the risk of trauma associated with tracheal intubations. Intubating conditions (muscle tone, vocal cords position, reaction to laryngoscopy and tube positioning) depend on anaesthetic depth and kind of anaesthetics used. Neuromuscular blocking agents has revolutionized the anaesthetic practice completely. These agents are used to attain tracheal intubation, proper muscle relaxation during surgical operations. A good surgical anaesthesia comprises of unconsciousness, analgesia and muscle relaxation to facilitate good operating conditions. An important fundamental principle of anaesthesia is the provision of adequate reflex suppression.

According to Booji and Crul [1983]⁵, ideal neuromuscular blocking agent should have non-depolarizing mechanisms of action, a rapid onset of action, high potency, rapid recovery completely reversible by cholinesterase inhibitors, should not release histamine, should have good hemodynamic stability, pharmacologically inactive metabolites and effects should be non-cumulative. The most important advantages of rocuronium are the rapid onset and good to excellent intubating conditions within 60-90 seconds after administration of 0.6 mg/kg dose. It has intermediate duration of action with good hemodynamic stability as demonstrated by Eamon P. McCoy et al. (1993)⁶ and Mark E. Hudson et al. (1998)⁷. Also Levy and Jerold H. et al. (1994)⁸ demonstrated no increases in plasma histamine levels at 1, 3 and 5 mm after the rapid IV bolus doses of 0.6, 0.9, 1.2 mg/kg rocuronium-i bromide as determined by a new radio-immunoassay with a sensitivity for

histamine quantification of 0.05 ng/ml. Thus, no clinical evidence of histamine release in wide variety of patients.

Magnesium sulphate (MgSO₄) has long been used in the treatment of pre-eclampsia and hypertension^{9, 10}. Recently the appreciation of the multiple actions of magnesium within the cell, has led to marked increase in its use in clinical practice.

MgSO₄ has been shown to produce dose related inhibition of neuromuscular transmission by competition with Ca²⁺ for membrane channels on the presynaptic terminals leading to a decrease in acetylcholine release at motor nerve terminals, consequently it may enhance the effect of neuromuscular blockers¹¹. Thus, the potential exists for possible interaction between Mg²⁺ and muscle relaxants used during anaesthesia or for mechanically ventilated patients in intensive care units¹². MgSO₄ decreases the onset time and prolongs the clinical duration of non-depolarizing neuromuscular blocking agents, we are presuming that administration of magnesium sulphate before rocuronium will decrease the onset time and prolong the duration of neuromuscular block.

II. Methods

Following approval from our institutional Ethical Committee, informed written consent was obtained from all patients. Fifty patients of aged between 18 and 60 yr, ASA grade I&II, selected. After confirming inclusion and exclusion criteria, 50 Patients were randomly divided into two groups of 25 each. The present study was conducted at RIMS, Ranchi.

Group I:(MgSO₄ Group)- Patients were given MgSO₄ 60 mg/kg diluted in normal saline making it total 100 ml as an intravenous infusion over ten minutes before induction of general anaesthesia.

Group II:(Control Group)- Patients were given 100 ml normal saline as an intravenous infusion ten minutes before induction of general anaesthesia.

Preoperative preparation:All the patients were seen one day before surgery. They were explained about the procedure of anaesthesia to allay anxiety and apprehension. All the patients were asked to take a light meal in the previous night and kept nil orally thereafter. They were given 0.5 mg Alprazolam orally at the bed time on the previous night of surgery.

Premedication: On the morning of surgery in the operation theatre, an intravenous line was secured with appropriate size IV cannula to give i.v fluids and drugs. All the patients were premedicated with Glycopyrrolate 0.01mg/kg intramuscular 1 hour prior to induction and Midazolam 0.03 mg/kg, Ranitidine 50mg, Metoclopramide 10mg intravenously just prior to induction. For analgesia, all patients were given Butorphanol 0.03 mg/kg intravenously before induction.

Monitors included non-invasive blood pressure monitor, electrocardiogram pulse oximeter and neuromuscular monitor - TOF Watch. Neuromuscular transmission was assessed by electromyography (EMG)(Relax graph). The ulnar nerve was used for stimulation. Surface electrodes were applied over the volar aspect of the wrist after adequate preparation of the area. The negative electrode was placed about 1 cm proximal to the proximal wrist crease. The other electrode was placed 3-4 cm proximal to the first one. The patient's hand was fixed carefully in a splint to minimize movement induced changes in twitch response and the arm was wrapped with a cotton blanket to maintain skin temperature.

The response of the first dorsal interosseous muscle of the hand after stimulation of the ulnar nerve at the wrist with supramaximal stimuli of 0.2 ms duration in a train of four (TOF) mode at 2 Hz every 20 seconds. The first of the four evoked responses was considered the twitch height Ti. Measurements commenced after induction of anaesthesia.

III. Induction And Maintenance Of Anaesthesia

Pre-anaesthetic pulse rate and blood pressure were taken. Ten minutes before induction of general anaesthesia, group

I - patients received MgSO₄ 60 mg/kg diluted in saline as an i.v infusion over ten minutes and group

II- patients received the same volume of saline only.

All the patients in the study group were pre-oxygenated with 100% oxygen for about 3 minutes before induction. Propofol 2mg/kg was injected intravenously as an induction agent. Neuromuscular transmission was assessed by electromyography (EMG) (Relaxograph). After this, Rocuronium 0.6 mg/kg was given i.v over 5 seconds. Patients were intubated 2 minutes after administration of Rocuronium and maintenance was done with 0.5% isoflurane and 66% nitrous oxide in oxygen. Adequate relaxation was maintained with intermittent bolus doses 0.15 mg/kg of Rocuronium. The following parameters were noted:

- Onset time: Time from the end of injection of Rocuronium till maximum neuromuscular blockade (complete disappearance of TOF response).

- Clinical duration: Time from injection of Rocuronium until the twitch tension recovery to 25% of the control (Ti).

Reversal:

At the end of surgery, patients were reversed with 0.05 mg/kg of neostigmine + 0.2 mg of glycopyrrolate per mg of neostigmine intravenously. After proper oral suctioning, patients were extubated. Patients were oxygenated with 100% oxygen after extubation by face mask for 5-10 minutes.

IV. Observation And Results

A total of 50 patients were selected randomly from the routine operation lists for the study. All patients were adults (ASA grade - I &II) between age group of 18 to 60 years of either sex.

Table - 1

Weight (in Kilograms)	Group I (MgSO ₄ Group) (n=25)		Group II (Control Group) (n=25)	
	No. of Patients	%	No. of patients	%
Excellent	17	68	14	56
Good	8	32	10	40
Poor	0	0	1	4

Table1. shows intubation scores in Group I and Group II patients. Intubating conditions were excellent in 17 patients (68 %) in group - I while they were excellent in 14 patients (56 %) in group - II. The intubating conditions were good in 8 patients (32 %) in group - I while they were good in 10 patients (40 %) in group - II. No patient showed poor intubating conditions in group - I whereas 1 patient showed poor intubating conditions in group - II.

Table - 2

Groups	Onset time (in seconds)			
	Mean ± S.D	Range	p-value	t-value
Group I (MgSO ₄ Group) (n=25)	85.84 ± 17.83	60-120	0.5415	0.6149
Group II (Control Group) (n=25)	89.2±20.70	60-132		

Table 2.shows mean onset time (in seconds) in group I and II patients. Onset time in group - I was 85.84 ± 17.83 seconds (mean ± S.D) and in group - II it was 89.2 ± 20.70 seconds (mean ± S.D). The differences in mean onset time between groups were not statistically significant (F> 0.05).

Table - 3

Groups	Clinical duration (in minutes)			
	Mean±S.D	Range	p-value	t-value
Group I (MgSO ₄ Group) (n=25)	45.92±8.80	30-63	0.0001	10.5052
Group II (Control Group) (n=25)	25.36±4.25	18.35		

Table3. shows mean clinical duration (in minutes) of patients in group I and II. Clinical duration in group - I was 45.92 ± 8.80 minutes (mean ± S.D) and in group - II it was 25.36 ± 4.28 minutes (mean ± S.D). The differences in mean clinical duration between groups were statistically highly significant (P< 0.05). Mean clinical duration was significantly prolonged in group I than in group II.

V. Discussion

The current study was done to demonstrate the effects of magnesium sulphate on the speed of onset and duration of neuromuscular blockade produced by rocuroniumbromide. In our study, the effects of prior i.v administration of MgSO₄ 60 mg/kg on the neuromuscular blocking effects of rocuronium 0.6 mg/kg during isoflurane anaesthesia was studied. Neuromuscular function was measured electromyographically (Relaxograph) in 50 adult patients who received either MgSO₄ 60 mg/kg or normal saline. Results demonstrated that onset time in group - I was 85.84 ± 17.83 seconds and in group - II it was 89.2 ± 20.70 seconds (mean ± S.D). The differences in mean onset time between groups were not statistically significant (P=0.5415, P> 0.05). Mean onset times were almost similar in both the groups. Furthermore, clinical duration in group - I was 45.92 ± 8.80 minutes and in group II it was 25.36 ± 4.28 minutes. The differences in mean clinical duration between groups were statistically highly significant (P=0.0001, P< 0.05). Mean clinical duration was significantly prolonged in group I than in group II. Thus, prior administration of MgSO₄ (60 mg/kg) did not

increase speed of onset, but prolonged duration of action of rocuronium induced (0.6 mg/kg) neuromuscular block. Azer et al (2002)¹³ studied the effect of intraoperative MgSO₄ infusion on the course of neuromuscular blockade of atracurium and found that patients who received intraoperative MgSO₄ infusion with atracurium had better intubating conditions and haemodynamic stability, also MgSO₄ potentiated the action of atracurium induced neuromuscular blockade with significant increase in the time of onset, clinical duration and reversal time after neostigmine. Kussman et al (1997)¹⁴ and Czametzki et al (2008)¹⁵ studied the interaction of MgSO₄ with rocuronium. Their results were inconclusive about the onset time but both found that prior administration of magnesium sulphate before rocuronium prolonged the duration of neuromuscular block. Ghoneim et al (1970)¹⁶ found that magnesium potentiated the neuromuscular blockade produced by non-depolarizing neuromuscular blocking agents and, to a lesser extent, enhances the neuromuscular block as was reported by Giesecke and colleagues (1968)¹⁴. Sinatra et al (1985)¹⁷ found prolonged neuromuscular block with magnesium sulphate and vecuronium.

Fuchs-Buder et al (1995)¹⁸ studied the interaction between magnesium sulphate and vecuronium. He studied 125 adult patients ASA I and II who received either MgSO₄ 40 mg/kg or normal saline i.v before vecuronium 100µg/kg. Neuromuscular function was measured electromyographically (Relaxograph). The ED₅₀ and ED₉₀ of vecuronium were reduced by 25% in MgSO₄ group. Mean onset time was nearly halved and recovery time, recovery index and duration to 75% recovery nearly doubled in patients pre-treated with MgSO₄. He found that the neuromuscular potency of vecuronium was increased by pre-treatment with MgSO₄. Kwan et al (1996)¹⁹ reported a case report showing that therapeutic serum magnesium levels in a woman with severe pre-eclampsia prolong the effect of 1 mg of vecuronium to 4 hours. Our study demonstrated that the use of MgSO₄ produced a higher incidence of excellent intubating conditions (68%) than control group (52%) but did not shorten the onset time. Thus, MgSO₄ affords favourable intubating conditions. There was rise in mean heart rate and blood pressure between groups before induction, after induction, after intubation and 2 minutes after intubation. But, the differences in heart rate and blood pressure between the MgSO₄ and control groups were clinically significant only just after intubation. Thus, MgSO₄ provides haemodynamic stability. The ability of Mg²⁺ to inhibit the release of catecholamine from adrenergic nerve terminals and from the adrenal medulla, supports its use to control the hypertensive response to intubation and surgical stimulation as observed by James et al. (1992)²⁰.

VI. Summary

In our study, the effects of prior administration of magnesium sulphate on the speed of onset and duration of rocuronium-induced neuromuscular blockade were done. Pre-anaesthetic pulse rate and blood pressure were taken. All the patients were pre-medicated, for analgesia, Butorphanol 0.03 mg/kg given intravenously. Ten minutes before induction of general anaesthesia, group I - patients received MgSO₄ 60 mg/kg diluted in saline as an i.v infusion over ten minutes and group II- patients received the same volume of saline only. A standard and uniform general anaesthesia procedure was followed for all patients. Onset time in group - I was 85.84 ± 17.83 seconds and in group - II it was 89.2 ± 20.70 seconds. The differences in mean onset time between groups were not statistically significant (P=0.5415, F> 0.05). Clinical duration in group - I was 45.92 ± 8.80 minutes and in group - II it was 25.36 ± 4.28 minutes (mean ± S.D). The differences in mean clinical duration between groups were statistically highly significant (P=0.0001, P< 0.05). Thus, mean clinical duration was significantly prolonged in group I than in group II. Use of MgSO₄ produced a higher incidence of excellent intubating conditions (68%) than control group (52%). Thus, MgSO₄ affords favourable intubating conditions. There was rise in mean heart rate and blood pressure between groups before induction, after induction, after intubation and 2 minutes after intubation. But, the differences in heart rate and blood pressure between the MgSO₄ and control groups were clinically significant only just after intubation.

VII. Conclusion

MgSO₄ did not increase the speed of onset time, but prolonged the clinical duration of rocuronium-induced neuromuscular block. Also, MgSO₄ administered before intubation provides better intubating conditions and intraoperative haemodynamic stability. Thus, MgSO₄ has many advantageous effects during the course of anaesthesia. However, adequate neuromuscular blockade monitoring is necessary in patients pre-treated with MgSO₄ because an unanticipated prolonged neuromuscular block could result which is potentially harmful.

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