Original article

Comparative evaluation of the effect of magnesium sulphate with lignocaine on the haemodynamic response to orotracheal intubation

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Abstract

Introduction: Magnesium sulphate inhibits the release of catecholamines from adrenal medulla whereas lignocaine blocks conduction of nerve impulses. Both these drugs may suppress adverse haemodynamic responses to laryngoscopy and intubation. **Aim:** The purpose of the study was to evaluate the effect and safety of an intravenous bolus dose of 2%lignocaine (1.5 mg/kg) or 50%magnesium sulphate (40 mg/kg) on the haemodynamic response to laryngoscopy and intubation in anaesthetised and paralysed adults. **Patients and Methods:** This was a prospective, randomised, double-blind study. Sixty four adults, belonging to ASA PS 1 and 2, were randomised to one of two groups: Group M and Group L. Heart rate, systolic, diastolic and mean arterial blood pressures were recorded every minute from injection of study drug upto 5 minutes post-intubation. Serum magnesium levels were measured before and after giving magnesium in Group M patients. **Results:** Heart rate was significantly higher and diastolic blood pressure significantly lower at 30 seconds in magnesium group whereas systolic and mean arterial pressures were comparable in both groups at all time intervals. Total muscle relaxation time was highly significant in magnesium group as compared to lignocaine. Post-study magnesium levels in Group M were statistically significant but not clinically significant as all values were within normal therapeutic range. **Conclusion:** Intravenous bolus dose of magnesium sulphate (40 mg/kg) can be used safely as a substitute for lignocaine for attenuation of haemodynamic responses to laryngoscopy and orotracheal intubation.

Keywords: Laryngoscopy, Lignocaine, Magnesium sulphate, Orotracheal intubation

Introduction

Laryngoscopy and endotracheal intubation are associated with an increase in heart rate, blood pressure, pulmonary arterial pressure and capillary wedge pressures.[1] The methods to reduce intubation related stress response include the use of lignocaine topically or intravenously,[2] beta-blockers,[3] opioids[4]and vasodilators. However, none of these methods are consistent and effective in attenuating these adverse effects and none are without complications. Hence, the search for a consistent, effective and safe alternative continues. Magnesium sulphate, could produce a consistent and effective suppression of this adverse haemodynamic response.[5,6] At the same time, slow administration of the drug would minimise the incidence of adverse events such as hypotension, bradycardia and arrhythmia.

The main objective of the study was to compare the effectiveness of an intravenous bolus dose of magnesium sulphate 50% (40 mg/kg) with lignocaine 2% (1.5 mg/kg) and also to evaluate the safety of intravenous bolus dose of magnesium sulphate (40 mg/kg) as determined by postintubation serum magnesium levels.

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Patients and methods

After obtaining Ethics Committee clearance and written informed consent, 64 patients fulfilling selection criteria were randomised into two groups, with 32 patients in each group, based on draw of lots.

Patients in the age group 18–60 years, of either gender, belonging to ASA PS I and II requiring orotracheal intubation, scheduled for elective noncardiac surgery were included in the study. The patients with baseline heart rate less than 50 beats per minute, hepatic, respiratory or cardiac dysfunction, heart block of any degree, renal failure, oliguria, electrolyte imbalances, pregnant patient, prior treatment with calcium channel blockers, β blockers, antiarrhythmics and antihypertensive medications, known allergy to study drugs, anticipated or known difficult airway, patients planned for rapid sequence induction, neuromuscular disease, diabetic neuropathy were excluded from the study. Peripheral venous blood sample for serum magnesium levels were sent on the morning of surgery for all the patients.

Study drugs were prepared in 10 mL syringes, each made up to a volume of 10 mL with normal saline in addition to the study drug. Study drug contained either magnesium sulphate 40 mg/kg or lignocaine 1.5 mg/kg depending on the group to which the patient was randomised. Each study drug was administered over a period of 30 seconds. Electrocardiogram lead II and V, pulse oximeter, automated noninvasive blood pressure in the upper limb (opposite to planned site for intravenous access), capnograph and peripheral nerve stimulator with "train of four" mode were connected. Two monitoring consoles were used for the study: DatexOhmeda (DatexOhmeda Inc., USA) or Marquette Solar 8000 (Marquette Electronics Inc., UK).

Intravenous access was secured after recording the baseline vitals. Observer 1 examined all patients and ensured that they met all the inclusion criteria and did not have any exclusion criteria. Observer 2 recorded the haemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure) at significant time intervals in the course of the study. Observer 3 performed the laryngoscopy and intubation. Anaesthesia was induced with titrating doses 4-6 mg/kg of thiopentone. After confirming ability to mask ventilate, they were paralysed with 0.1 mg/kg of vecuronium bromide. Patients were mask-ventilated with 1.5% isoflurane in oxygen till train-of-four count on peripheral nerve stimulator was zero. This was followed by administration of study drug over 30 seconds. All patients were intubated 90 seconds after giving study drug. Laryngoscopy and intubation were performed and confirmation of tube position established by auscultation and presence of a square wave capnogram. Anaesthesia was maintained with isoflurane in a mixture of 40% oxygen and 60% nitrous oxide maintaining a MAC of 1.0 for the next 5 minutes *via* controlled ventilation with 8-10 ml/kg of tidal volume, respiratory rate adjusted to maintain end-tidal carbon dioxide at 35-40 mmHg. Intravenous fluids were given at the rate of 5 ml/kg/h in both the groups. Patients were left undisturbed for the next 5 minutes following intubation until the end of study period. Peripheral venous blood for serum magnesium levels was sent 5 minutes post-intubation for all patients in Group M. All patients were followed up till the end of surgery to note any delayed emergence or recovery time from anaesthesia.

Any deviation in haemodynamic parameters, more than 25% from the baseline was considered significant. Appropriate treatment was instituted as decided by Observer 3 if there was any drop from baseline in heart rate to < 50 beats per minute or mean arterial pressure to < 60 mm Hg. Any other complication was noted and treated as necessary. Any requirement for deepening of anaesthesia or any other additional drug therapy was noted. Intubation time was defined as the time from insertion of laryngoscope to the time the laryngoscope is removed from the oral cavity after intubation.Total muscle relaxation time was defined as time from the disappearance of all four twitches to the appearance of first twitch on train-of-four mode of peripheral nerve stimulator. Any patient requiring more than one attempt or oesophageal intubation was excluded from the study and the randomisation chit for such a patient was utilised for the next patient fulfilling the selection criteria.

Results

The sample size of this study was calculated, based on assuming a power of 85% with 95% confidence levels,to be 64 patients, 32 patients in each group. Statistical analysis of the data obtained was done using SPSS version 11.5 for Windows (copyright SPSS Inc., Chicago, U.S.A.). For all tests in the study, $P < 0.05$ was considered significant, $P < 0.005$ was considered highly significant and $P > 0.05$ was considered insignificant.

Both the groups were comparable in terms of age, weight and sex distribution. All patients were intubated in the first attempt and there was no significant difference in the mean duration of intubation among the two groups.

Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) showed a normal distribution. Percentage change in heart rate from the baseline was also compared between the groups apart from the inter-group analysis of mean heart rate at significant time periods *(Figure 1)*.

The increase in heart rate was significantly higher at 30 seconds after study drug in magnesium group as compared to lignocaine group. There was a significant increase in the percentage change in the heart rate from baseline at 30 seconds in magnesium (5%) group as compared to lignocaine group (-2%).

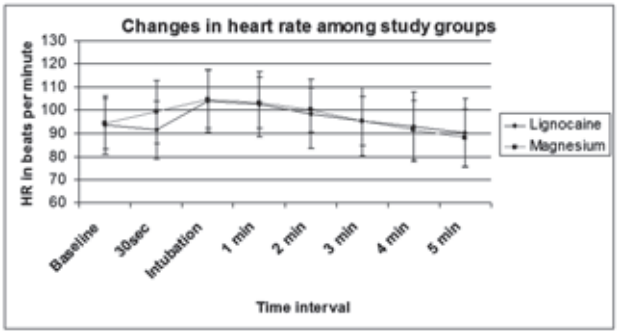

Figure 1: Percentage change in heart rate with pretreatment with lignocaine and magnesium

On further analysis of patients with 25% change in heart rate from baseline, both the groups were comparable at all time intervals.Twenty five per cent increase in heart rate from baseline was seen in a significant number of patients at time of intubation. Two patients in Group L and 5 patients in Group M showed a 25 % increase in heart rate. Such increase in heart rate occurred mainly at intubation and first minute post-intubation.

The percentage change in systolic blood pressure from baseline at all time intervals were comparable in both the groups as observed in *Figure 2*. Twelve patients in each group showed more than 25% rise in systolic blood pressure at the time of intubation which were comparable in both the groups at all time points.

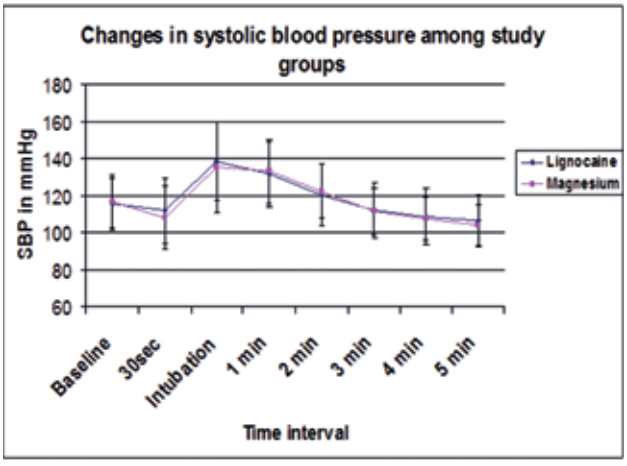

Figure 2: The percentage change in systolic blood pressure from baseline with pretreatment with lignocaine and magnesium

Mean diastolic blood pressure was found to be significantly lower in magnesium group as compared to lignocaine group at 30 seconds, whereas diastolic blood pressure was comparable at other time points in group L and M *(Figure 3)*.

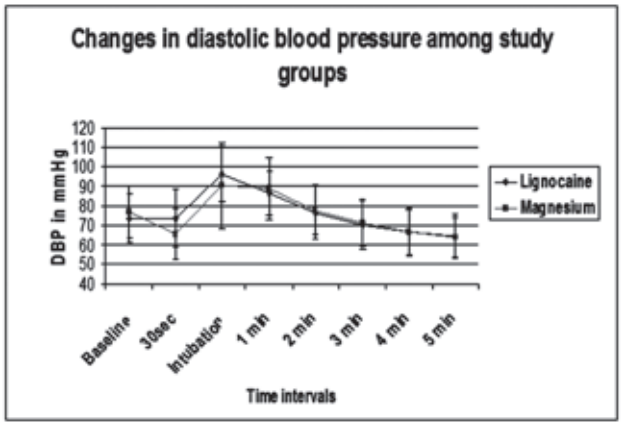

Figure 3: Percentage change in diastolic blood pressure with pretreatment with lignocaine and magnesium

The percentage decrease in diastolic blood pressure from baseline was significantly greater at 30 seconds in group M as compared to group L. There was less increase in diastolic blood pressure at intubation in magnesium group as compared to lignocaine group while at all other time intervals, diastolic blood pressure did not show any appreciable increase after endotracheal intubation in magnesium treated patients compared with those in lignocaine group.

On extrapolating the analysis, sixteen percent of patients in magnesium group and 3% patients in lignocaine group showed decrease in diastolic blood pressure more than 25% from baseline at 30 seconds which were comparable in both the groups. Similarly, 53% patients in group L and only 44% patients in group M showed increase in diastolic blood pressure more than 25% from the baseline at intubation which was statistically not significant.

Mean arterial pressure expressed as percentage change from baseline in *Figure 4*, showed statistically significant drop in mean arterial pressure at 30 seconds in Group M as compared to Group L while comparable values were observed at other intervals.

Nine percent of patients in Group M showed decrease in mean arterial pressure greater than 25% from baseline at 30 seconds which were comparable to Group L and at other time intervals as well.

Three patients in the study had transient hypotension *(Table 1)* with mean arterial pressure < 60 mmHg, one in group L and two patients in group M. Since the hypotension was transient, no treatment was initiated. None of the patients had heart rate below 50 beats/min at any time during the study. Arrhythmias, respiratory depression, drowsiness, delayed emergence or recovery from anaesthesia or bucking were not noticed in any of the patients.

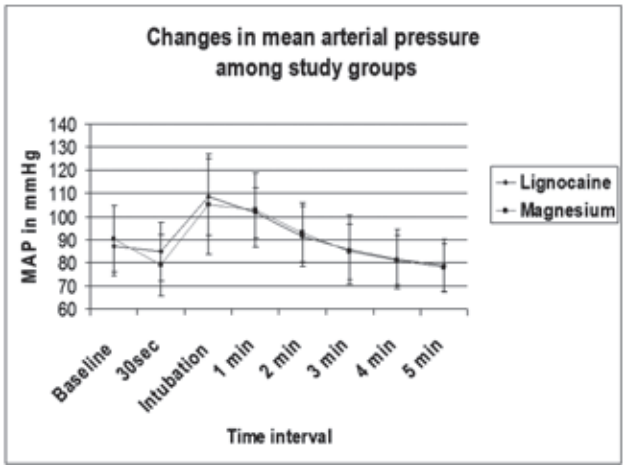

Figure 4: Mean arterial pressure expressed as percentage change from baseline with pretreatment with lignocaine and magnesium

Total muscle relaxation time, was prolonged in group M. This was statistically significant but not clinically as no signs and symptoms of muscle weakness, delayed neuromuscular recovery or emergence from anaesthesia were noted at the end of surgery.

Post-study mean magnesium levels in Group M were increased which were statistically significant but not clinically significant as all magnesium values were within normal therapeutic range. The maximum post-study serum levels of magnesium in Group M were 4.90 mg/dL.

Table 1: Incidence of complications

	Lignocaine (n=32)	Magnesium (n=32)	P value*
Hypotension (MAP < 60 mm Hg)	1	2	0.306 NS
Bradycardia (HR < 50/ min)	0	0	-
Arrhythmias	0	0	-
Respiratory depression, drowsiness	0	0	-
Movement / Bucking	0	0	-

MAP- Mean arterial pressure in mmHg, HR- Heart rate in beats/minute
* Independent samples T test, P < 0.05 = Significant, NS = Not significant

Discussion

It is well known that laryngoscopy and tracheal intubation produce marked increase in heart rate and blood pressure.[1] This is associated with the release of catecholamines in large amounts.[7,8] The time interval between injection of slow intravenous bolus dose of magnesium and intubation was maintained strictly at 90 seconds. James *et al* had concluded in his study that intravenous bolus dose of magnesium sulphate produces maximal suppression of plasma epinephrine levels from baseline values at 90 seconds following administration of magnesium and it remained at baseline values upto 2 minutes after intubation.[9] The timing of intravenous bolus dose of lignocaine and intubation was 90 seconds in keeping with the previous studies on this subject and the unique pharmacokinetics of this drug.

We preferred to study the influence of a bolus dose of magnesium than an infusion technique. Although several studies have utilised the latter dosing regimen, the preparation of an infusion and time required for its administration can add a degree of complexity and costs to the induction process.

We found a transient decrease in diastolic blood pressure and mean arterial pressure from baseline at 30 seconds after administration of drug in group M as compared to group L followed by less increase in diastolic blood pressure from baseline at intubation in magnesium group as compared to lignocaine group. These findings were not consistent with those of Puri *et al*, where parenteral magnesium administration resulted in a rapid but transient decrease in systemic vascular resistance and decrease in mean arterial pressure. The arterial pressures did not show any appreciable increase after endotracheal intubation in magnesium treated patients as compared to lignocaine group.[10] The reason for the difference could possibly be due to higher dose of magnesium sulphate 50 mg/kg used in the previous study with no corroboration of serum magnesium levels.

Post-study mean magnesium levels in Group M were increased from the preoperative magnesium values which were statistically significant but not clinically significant as all magnesium values were within normal therapeutic range and no symptoms of muscle weakness were reported by the patients. This is in accordance with the results of Baraka and Yazigi[11] who found that even at slightly higher plasma magnesium concentrations (1.7-2.5 mmol/L), there were no clinical or electromyographic signs of muscle weakness. These data indicate that pretreatment with 40 mg/kg of magnesium sulphate is safe.[12]

There was no significant incidence of side-effects or complications. In circumstances in which complications such as muscle rigidity, bradycardia, hypotension and respiratory depression may be undesirable, magnesium sulphate could be a useful alternative. The clinical duration of action of vecuronium was prolonged in group M as compared to group L which was statistically significant but not clinically. This is in accordance with the study by T. Fuchs-Buder where the duration of vecuronium block was nearly doubled and recovery index (time from 25% to 75% twitch height recovery) was also prolonged after pretreatment with 40 mg/kg of $MgSO_4$.[13]

The clinical consequence of prolonged duration of action of vecuronium and delayed recovery was not observed in our study since long surgical procedures were chosen for the purpose of study and all patients were smoothly extubated without any residual neuromuscular blockade. Clinical assessment in the recovery room showed that patients had normal ventilatory frequency, adequate tidal volumes and normal pupil size.

However, monitoring of neuromuscular function and reduction in dose of vecuronium are required when using magnesium sulphate and vecuronium in combination especially for surgical procedures of short duration.

Conclusion

Both magnesium sulphate 40 mg/kg, and lignocaine 1.5 mg/kg, administered 90 s prior to endotracheal intubation produce inadequate attenuation of increase in systolic and mean arterial pressures. Magnesium attenuates the increase in diastolic pressure significantly more than lignocaine. There

is no significant change in serum magnesium levels with this dose.

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