Original Research Article

Comparison between Magnesium Sulphate and Esmolol in Attenuating Haemodynamic Responses to Laryngoscopy and Endotracheal Intubation

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Abstract

During induction of general anaesthesia, the act of laryngoscopy and tracheal intubation stimulates the sympathetic nervous system resulting in an increase in blood pressure and heart rate which may be harmful especially in elderly patients with pre-existing ischaemic heart disease. Several drugs have therefore been used to obtund this increase including esmolol, nicardipine, magnesium sulphate and lignocaine. This prospective, double blind randomised clinical trial compared the efficacy of magnesium sulphate and esmolol in attenuating haemodynamic responses to laryngoscopy and tracheal intubation. One hundred and twenty six ASA I-II patients scheduled for elective surgery requiring general anaesthesia with tracheal intubation were enrolled and randomised into two groups: Group 1 (n = 67) received MgSO$_4$ 40 mg/kg diluted in 100 ml normal saline administered over ten minutes, whereas Group 2 (n = 59) received a bolus of esmolol 1.0 mg/kg diluted to 10 ml. Systolic and diastolic blood pressures and heart rate were recorded every minute for subsequent 10 minutes following laryngoscopy and tracheal intubation. Attenuation of the mean systolic and diastolic blood pressures following laryngoscopy and tracheal intubation was significantly larger in Group 2 compared to Group 1. Patients in Group 2 had significantly better suppression of heart rate response compared to Group 1 during the first four minutes after laryngoscopy and tracheal intubation (p<0.05). Attenuation of the haemodynamic response to laryngoscopy and tracheal intubation by esmolol 1.0 mg/kg was more pronounced compared to MgSO$_4$ 40 mg/kg in normotensive patients undergoing general anaesthesia for elective surgery.

Keywords: Anaesthesia, blood pressure, esmolol, heart rate, laryngoscopy, magnesium sulphate

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Introduction

The act of laryngoscopy and tracheal intubation associated with an increase in blood pressure (BP) and heart rate (HR) and possibly dysrhythmias greatly increase the risk of myocardial ischemia / infarction or stroke especially in the elderly age group (1,2). Haemodynamic changes that occur are due to sympathoadrenal activity. Laryngoscopy increases the BP and HR, achieving a peak in 1 or 2 minutes but normalises 5 minutes thereafter (3). Many pharmacological agents have been shown to be effective in controlling these haemodynamic responses which include esmolol (4), nicardipine (5), magnesium sulphate (MgSO$_4$) (6) and lignocaine (7).

MgSO$_4$ is known to have an anti-adrenergic effect whereby it inhibits catecholamine release from adrenergic nerve terminals and from adrenal medulla which makes it a suitable agent as an adjuvant in anaesthetic practice (8-11). MgSO$_4$ when given intravenously has a moderate large volume of distribution close to the volume of the extracellular space and therefore would require a large initial dose

(40-60 mg/kg) in order to achieve therapeutic serum magnesium levels. However, when administered as intravenous bolus, it can cause flushing due to vasodilation and therefore should be given via infusion (12).

Many studies have been done to assess the role of intravenous MgSO$_4$ in obtunding the haemodynamic responses of laryngoscopy and tracheal intubation (13,14). James et al. investigated the use of intravenous MgSO$_4$ to inhibit catecholamine release associated with tracheal intubation and found that MgSO$_4$ significantly attenuated the release of catecholamines at the time of tracheal intubation and thus reduce the severity of haemodynamic response (15).

Esmolol, an ultra-short acting β_1-adrenoreceptor antagonist, has been used to control the haemodynamic responses due to laryngoscopy and tracheal intubation. It has a very short diffusion and elimination half-life (9 minutes) reaching a peak effect of 1-2 minutes after a bolus injection (16). Clinically, the use of esmolol is for controlling perioperative hypertension and tachycardia including supraventricular tachyarrhythmias in order to decrease myocardial oxygen consumption and myocardial ischaemia (17). Helfman et al. demonstrated the efficacy of 150 mg bolus of esmolol which provided a consistent and reliable protection against increases in both HR and systolic BP (SBP) following laryngoscopy and tracheal intubation as compared with fentanyl 200 mcg or 200 mg lignocaine (18).

The objective of this study was to compare the efficacy of intravenous MgSO$_4$ and esmolol in attenuating the haemodynamic responses to laryngoscopy and tracheal intubation in normotensive patients undergoing general anaesthesia for elective surgery.

Materials and Methods

This was a prospective, double-blind, randomised clinical trial which compared the efficacy of MgSO$_4$ and esmolol in attenuating the haemodynamic response to laryngoscopy and tracheal intubation. Prior approval was obtained from the Dissertation Committee of the Department of Anaesthesiology and Intensive Care and the Research Ethics Committee of Universiti Kebangsaan Malaysia Medical Centre (Approval Project Code: FF-211-2013).

After obtaining written informed consent, a total of 144 ASA I and II normotensive patients aged 18-50 years old scheduled for elective surgery requiring laryngoscopy and tracheal intubation were recruited in this study. Those excluded were patients with ischaemic heart disease, anticipated difficult airway, known allergy or contraindicated to the medications used in this study, increased risk of aspiration including obstetric patients, BMI > 35 kg/m^2 and a baseline HR of less than 60 beats per minute. Patients were then randomised into two groups using Table of Random Numbers that were computer-generated. The test drugs were prepared by a separate anaesthetic medical officer who was not involved with the conduct of anaesthesia and data collection in this study.

The patients were fasted overnight and received oral midazolam 7.5 mg on the eve and morning of operation. Standard monitoring with continuous ECG, non-invasive blood pressure and pulse oximetry were established before induction of anaesthesia. Baseline values of the systolic and diastolic blood pressure (SBP and DBP) and HR were recorded. Patients in Group 1 received 40 mg/kg of MgSO$_4$ diluted in 100 ml normal saline while patients in Group 2 received normal saline 100 ml, given over 10 minutes. Immediately after the administration of the study drug, standard general anaesthesia was administered which comprised of IV fentanyl 1.0-2.0 mcg/kg followed by propofol 1-2 mg/kg and rocuronium 0.6 mg/kg to produce neuromuscular blockade. Anaesthesia was maintained using oxygen / air / sevoflurane regime with 5 L/min fresh gas flow to achieve MAC of 1.0 and end-tidal carbon dioxide (EtCO$_2$) at 30-40 mmHg. One minute following this, patients in Group 1 were then given 10 ml normal saline while those in Group 2 received 1.0 mg/kg esmolol diluted to 10 ml. Laryngoscopy and tracheal intubation was then performed one minute after this. Duration of laryngoscopy and tracheal intubation was defined as the time from introduction of the laryngoscope blade until its removal from the oral cavity. Patients who had unsuccessful intubation at first attempt or duration of laryngoscopy which exceeded 20 seconds were excluded.

Haemodynamic variables (SBP, DBP and HR) were recorded every minute for the next 10 minutes. Hypotension (defined as drop in systolic blood pressure $\geq$ 20% baseline) and bradycardia (HR<60 bpm) were managed accordingly by the anaesthetists conducting the case and were excluded from the study. No other stimulus was allowed during the study and observation period.

Statistical Analysis

Sample size calculation was done using software "PS –Power and Sample Size Calculation" from http://biostat.mc.vanderbilt.edu/wiki/Main/PowerSamp

leSize (19). The sample size calculation was based on the data from a previous study (20) and 120 patients were required for a desired α value of 0.05 and a power of 0.8. Allowing a dropout rate of 20%, the total sample size required was 144 patients. Data analysis was performed using SPSS for Windows version 20.0, Chicago, IL. Parametric and non-parametric data were analyzed using Student t-test and Chi-square respectively. Data were expressed in mean ± SD and number (percentage) wherever appropriate. A p value of less than 0.05 was considered as statistically significant.

Results

A total of 144 patients were recruited but only 126 patients were included in the analysis. Five patients from Group 1 and one from Group 2 had duration of laryngoscopy and tracheal intubation exceeding 20 seconds and were excluded from the study. Another 12 patients from Group 2 who developed hypotension requiring rescue with IV ephedrine boluses were also excluded from analysis.

There were no statistically significant differences in terms of patient characteristics, surgical or anaesthetic data (Table 1). Patients in Group 2 had significantly lower SBP, DBP and HR at one minute after intubation, compared to Group 1 as shown in Table 2. The SBP was noted to decrease after induction of anaesthesia but increased within one minute following laryngoscopy and tracheal intubation in both the groups when compared to their respective baseline values as shown in Figure 1. The attenuation of SBP following laryngoscopy and tracheal intubation was significantly bigger in Group 2 compared to Group 1. Further analysis of SBP showed that in almost all measurements except at baseline and just before intubation, there was significantly lower SBP values noted in Group 2 compared to Group 1. Suppression of DBP was more pronounced in Group 2 compared to Group 1, as evidenced by a significantly lower DBP values in Group 2 during the first nine minutes after laryngoscopy and tracheal intubation (Fig. 2). Intergroup comparison showed that patients in Group 2 had significantly more suppression of HR response as compared to Group 1 during the first four minutes after laryngoscopy and tracheal intubation. Differences in mean HR between the 2 groups during the rest of the study period were not statistically significant (Fig. 3).

Discussion

It has been well established that haemodynamic response to laryngoscopy and tracheal intubation

Table 1: Demographic, surgical and anaesthetic data. Values expressed as Mean ± SD or number (%) where appropriate.

	Group 1 (n = 67)	Group 2 (n = 59)	*p*-value
Age (years)	36.2 ± 9.3	33.6 ± 8.6	0.11
Gender			
Male	21 (31.3)	23 (39.0)	0.37
Female	46 (68.7)	36 (61.0)	
Race			
Malay	47 (70.1)	38 (64.4)	0.73
Chinese	11 (16.4)	14 (23.7)	
Indian	4 (6.0)	4 (6.7)	
Others	5 (7.5)	3 (5.2)	
BMI (kg/m²)	23.9 ± 3.2	23.4 ± 3.5	0.41
Type of surgery			
Orthopaedic	13 (19.4)	12 (20.3)	0.62
General surgery	19 (28.4)	21 (35.6)	
Others	35 (52.2)	26 (44.1)	
Duration of laryngoscopy (sec)	18.3 ± 2.9	18.0 ± 2.6	0.55

induces marked increases in BP and HR which results in an imbalance between the supply and demand of myocardial oxygenation (21). The response of haemodynamic changes to laryngeal stimulation varies with factors such as duration and the degree of difficulty during laryngoscopy and intubation. Besides that, age of the patient, presence of other pre-existing co-morbidities such as diabetes mellitus or cardiovascular diseases plays a major role too (22).

Our study demonstrated that the attenuation of the increase in both the BP and HR was more pronounced with esmolol compared to MgSO₄. This is in agreement with an earlier study by Sharma et al. who compared MgSO₄ 40 mg/kg with a higher dose of esmolol 1.5 mg/kg in controlled hypertensive patients (20). Esmolol, when combined with anaesthetic induction agents caused marked hypotension requiring rescue with IV boluses of ephedrine. This was observed in our study as twelve patients from Group 2 had to be excluded. This adverse effect was however not reported by Sharma et al. possibly due to the fact that their study was done on hypertensive patients.

Table 2: Haemodynamic changes 1 minute after intubation compared with values just before intubation. Values expressed as Mean ± SD.

	Group 1 (n = 67)	Group 2 (n = 59)	*p*-value
Mean SBP (mmHg)			
Baseline	118.4 ± 10.2	114.9 ± 10.1	0.06
Just before intubation	100.9 ± 8.6	98.0 ± 8.5	0.06
1 minute after intubation	117.6 ± 13.8	101.9 ± 11.1	0.001*
Mean DBP (mmHg)			
Baseline	70.4 ± 9.0	69.0 ± 7.8	0.06
Just before intubation	57.7 ± 7.7	56.2 ± 7.6	0.27
1 minute after intubation	70.0 ± 10.9	59.7 ± 8.3	0.001*
Mean HR (bpm)			
Baseline	77.8 ± 9.6	76.3 ± 9.7	0.39
Just before intubation	68.7 ± 11.2	67.9 ± 12.0	0.71
1 minute after intubation	78.4 ± 13.5	69.5 ± 13.1	0.001*

The mean values of SBP and DBP in Group 1 and 2 decreased to the lowest point (just before intubation) compared to their baseline values by 14.8 vs 14.7% and 18.0 vs 18.6% respectively. At this point in time, the values were comparable for both groups. In Group 1, following laryngoscopy and tracheal intubation, we observed a significant rise in both the mean SBP and DBP values from the lowest point, almost reaching its baseline values in the first minute. However, in Group 2, the rise in the SBP and DBP at one minute was not significant from the lowest point (Fig. 2 and 3). When intergroup comparison was made at one minute after intubation, there was a significant attenuation in the SBP and DBP values in Group 2. This clearly showed that esmolol 1.0 mg/kg exerted a more profound effect on the haemodynamic response during laryngoscopy and tracheal intubation, when compared to MgSO$_4$ 40 mg/kg. A similar finding was reported by Bostan et al. when comparing fentanyl 1.0 mcg/kg, esmolol 1.0 mg/kg and lignocaine 1.0 mg/kg to prevent haemodynamic response to tracheal intubation. They found that esmolol was more effective in preventing the rise in SBP and DBP values compared to the other study drugs (23). Louizos et al. shared similar finding
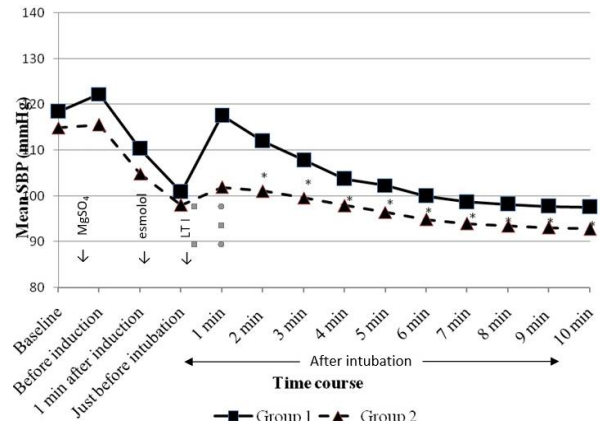

Figure 1: Changes of mean SBP (mmHg) over time (mins). (LTI- laryngoscopy & tracheal intubation, *p < 0.05 when intergroup comparison was made).
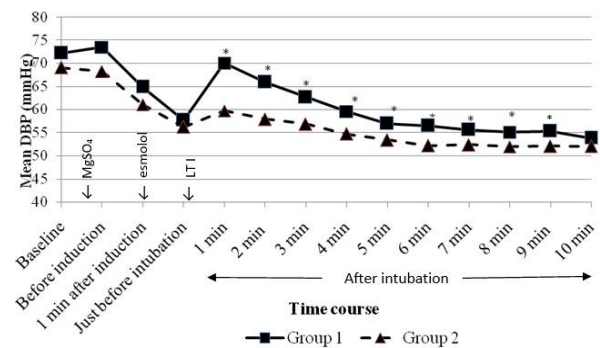

Figure 2: Haemodynamic changes one minute after intubation compared with values just before intubation. Values expressed as Mean ± SD. (*p < 0.05)
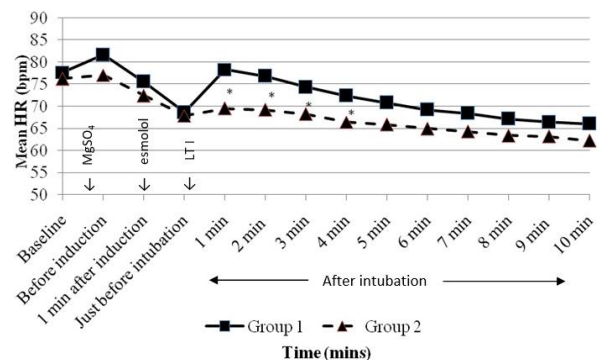

Figure 3: Mean HR (bpm) over time (mins). (LTI- laryngoscopy & tracheal intubation, *p <0.05 when intergroup comparison was made).

when they administered esmolol to cigarette smokers to blunt haemodynamic response during laryngoscopy and tracheal intubation, although in their study, esmolol 2.0 mg/kg was found to be more effective than esmolol 1.0 mg/kg (24). The higher dose required in their study can be attributed to the fact that their

cohort of patients were exposed to nicotine as a result of cigarette smoking causing sympathovagal imbalance which could lead to exaggerated response to laryngoscopy and tracheal intubation, whereas in our study, the lower dose was found to be sufficiently adequate.

The mean values of HR in Group 1 and 2 decreased to the lowest point (just before intubation) compared to their baseline values by 11.7 vs 11.0% respectively, which were comparable for both groups. After laryngoscopy and tracheal intubation, intergroup comparison showed that the patients in Group 1 exhibited a significant rise in HR as compared with Group 2. This finding was similar to a study done by Kumar et al. who compared the effects of MgSO₄ 60 mg/kg with esmolol of 2.0 mg/kg in 190 normotensive patients and concluded that MgSO₄ failed to attenuate the rise in HR when compared with esmolol. Despite higher doses of esmolol used in their study, only one patient developed bradycardia while there was none in our study (25).

The effectiveness of esmolol in attenuating haemodynamic changes following laryngoscopy and tracheal intubation has been shown to be related with the optimum dose and mode of administration. Kindler et al. administered a combination of two different doses of esmolol 1.0 and 2.0 mg/kg and compared them with lignocaine 1.5 mg/kg. They found that esmolol when used alone at either 1.0 or 2.0 mg/kg was effective in attenuating HR but not BP in response to laryngoscopy and tracheal intubation. However, when combined with lignocaine, it significantly lowered SBP following intubation with an accompanying risk of hypotension (26). In our study, we encountered hypotension in twelve patients even with esmolol of 1.0 mg/kg. This could be due to the use of propofol as our induction agent which was known to be associated with a higher incidence of vasodilation and myocardial depression (as opposed to thiopentone in their study). A meta-analysis by Figueredo et al. assessing the effectiveness of esmolol on haemodynamic changes induced by laryngoscopy and tracheal intubation concluded that initial administration with a loading dose of 500 mcg/kg over 4 min and followed by a continuous infusion between a dose of 200 and 300 mcg/kg could reduce the incidence and seriousness of hypotension (27). However, esmolol may also cause atrioventricular block, bradycardia and bronchospasm but these adverse effects were not observed with esmolol 1.0 mg/kg. (28).

MgSO₄ was given as a slow bolus over a ten-minute period before anaesthesia to avoid unpleasant flushing and to achieve a peak effect at the time of laryngoscopy and tracheal intubation (29). Panda et al. investigated different doses of MgSO₄ infusion of 30, 40 and 50 mg/kg to determine the minimal effective dose for attenuation of blood pressure and heart rate during laryngoscopy and tracheal intubation in hypertensive patients. They demonstrated that MgSO₄ 30 mg/kg was the optimum dose for BP control and found that a further increase in the dose of MgSO₄ resulted in significant hypotension requiring intervention (30). In contrast, despite using 40 mg/kg of MgSO₄ infusion in our study (Group 1), none of our patients developed hypotension. This could be due to the fact that propofol infusion was used at the rate of 6–8 mg/kg/hr for maintenance of anaesthesia in their study while our patients were maintained with sevoflurane.

Conclusion

The attenuation of haemodynamic response due to laryngoscopy and tracheal intubation by esmolol at 1.0 mg/kg was more pronounced compared to MgSO₄ at 40 mg/kg in normotensive patients undergoing general anaesthesia for elective surgery.

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