Original Research Article

A comparative study of the efficacy of I.V. esmolol and megnesium sulphate in attenuating haemodynamic response to laryngoscopy and tracheal intubation

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Abstract

Problem Statement: The tracheal intubation is a powerful noxious stimulus. During laryngoscopy and tracheal intubation these is cardiovascular stress response. It occurs frequently and results in increased serum concentration of catecholamine's. This adrenergic response may result in transient but intense increase in blood pressure by 40% - 50% and heart rate by 20%, which in turn increases cardiac work load and thereby myocardial oxygen demand. As a result, perioperative myocardial ischaemia, acute heart failure, and arrhythmia may develop in susceptible individuals. Cardia arrhythmia which may follow endotracheal intubation are due to either vagal release following the escape of anaesthetic agent from the lungs or to atrial asphyxia as a result of bronchospasm precipitated by the insertion of tube into inadequately anaesthetized patients. **Methods:** 90 normotensive patients of either sex belonging to ASA physical status I and II, in age group 15-65 ears, weighing 30-80 kg, undergoing general anesthesia for various elective non-cardiac surgical procedures, were taken for this study. **Results:** The tracheal intubation is well known to invoke cardiovascular responses partly as a result of reflex sympatho-adrenal discharge char-acterised by increase in arterial blood pressure, change in heart rate and disturbance in the cardiac rhythm. The heniodynamic changes as a result of tracheal intubation might produce adeleterious effect in a patient wi compromised cardiac function. Several attempts have been made to blun the haemodynamic responses to tracheal intubation. So, in the view of above finding the present clinical study was undertaken to evaluate the effect of two drugs esmolol and magnesium sulphate on hemodynamic response to laryngoscopy and tracheal intubation. Study was done in 3 groups in. group 1 patients received normal saline as placebo. In group I patients received magnesium sulphate 60mgkg^{-1} and in group III patients received esmolol 2 mgkg^{-1}. Findings of each groups are discussed in comparison with their pre-operative values and with control group with at different time interval with regard to heart rate, systolic blood pressure, diastolic blood pressure and other complications. **Conclusion:** The esmolol in bolus dose of 2 mgkg^{-1-} body weight, more effectively attenuates the haemodynamic response to laryngoscopy and tracheal intubation than magnesium sulphate. Esmolol also shortens the time interval needed for the heart rate, blood pressure and rate-pressure product to come down to the normal or base line value more effectively than magnesium. However, the rise in blood pressure was suppressed and not prevented after intubation by this dose of esmolol. Complications found were insignificant. Thus use of esmolol is quite safe, reliable and free of side effects.

Key Words: Laryngoscopy, Tracheal intubation Myocardial Ischaemia, Heart failure, Esmolol, Magnesium sulphate.

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This potentially adverse haemodynamic response can be blunted by varying degree of success of the general anaesthesia, with Ether (King *et al.* 1951)[104], ganglion blocking agent intravenous or topical lidocaine, vasodilator eg. Sodium nitroprusside and nitroglycerine (Stolting 1979)[1], analgesics eg. Morphine and phentanyl and long acting beta adrenergic blockers eg. Propranolol, metoprolol, (Kaplan *et al*; 1975, Jones *et al*; 1976, Safwal *et al*; 1981)[2] Each technique has some disadvantages; he most obviously is effect of preventive intravenous often considerably outlast stressful adrenergic response.

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Recently, the importance of magnesium sulphate in anaesthetic practice has been highlighted. It is suggested that magnesium has potential to treat and prevent pain by acting as an antagonist of N-methyl D-aspartate (NMDA) receptors. In animal, magnesium sulphate has suppressed NMDA induce behavior reaction and hypersensitivity resulting from nerve injury. In a clinical study the role of magnesium sulphate in reducing analgesic requirement during post operative period has been demonstrated. (Fawcett Wjet *et al*; 1999, Dube Laurent *et al*; 2003)[3] At the beginning of last century magnesium sulphate was reported as general anaesthetic. Although magnesium was regarded as a central nervous system depressant, its anaesthetic effect was shown to result from cerebral hypoxia after progressive respiratory and cardiac depression. Recently, Koining and colleagues (1988)[4.] reported that magnesium administration lead to a significant reduction in fentanyl consumption in peri and post-operative period. The stress of intubation is associated with catecholamine release, magnesium reduces its release from adrenal medulla and adrenergic nerve endings. The plasma concentration of epinephrine and norepinephrine were markedly lower after intubation in the magnesium treated patients. There was no increase in arterial pressure or heart rate and moderate decrease in plasma catecholamine concentration after intubation. There is a need for rapid onset sort acting cardio selective beta-blockers. The effect of which can be rapidly controlled if an adverse event occur, Esmolol is only available short acting selective beta-adrenergic blocking agent. Its dose can be easily titrated providing minute by minute control of blood pressure and heart rate and there is substantial attenuation of haemodynamic disturbances during laryngoscopy and tracheal intubation. Esmolol when administered by infusion has been found to be effective in blunting haemodynamic effects of laryngoscopy and tracheal intubation (Menkhaus *et al*; 1985)[5]. Main drawback is that while the infusions are easy to setup, they require additional equipment and time. Bolus doses of esmolol may circumvent these problems. Recent studies were investigated for the use of bolus doses of esmolol for prevention of post intubation tachycardia and hypertension. Moreover, there is a lot of discrepancy regarding appropriate dose of esmolol and optimal time for its administration to attenuate the pressure responses. A comparative study performed by Dr. Mishra M. N. *et al* (2003)[6] proved esmolol is most effective in attenuating haemodynamic response during laryngoscopy and tracheal intubation as compared to diltiazem and magnesium sulphate. Therefore, the present study has been undertaken to make comparative study of both drugs esmolol and magnesium sulphate in attenuating the haemodynamic changes during laryngoscopy and tracheal intubation.

MATERIAL AND METHODS

The anaesthetic technique was identifical in each group. The patients were pre-oxygenated with 100 percent oxygen for 3 minutes and were given placebo or required dose of the study drugs (Esmolol 2mg kg^1 body weight I.V. or magnesium sulphate 60 mg kg. 1 body weight I.V.) over a period of 1 minute. After waiting for 30 seconds thiopentone sodium 2.5 percent solution in a dose of 4-6 mg kg^1 was given over a period of 15 seconds immediately followed by succinylcholine 2mg kg^1 body weight. When apnoea set in, the performed and proper size cuff endotracheal tube was inserted at 1 minute after giving the magnesium sulphate and 2 minutes after giving the esmolol. Patients in whom laryngoscopy and intubation took more than 30 seconds were excluded from the study. Maintenance of anaesthesia was done with intermittent positive pressure vertilation with 33 percent oxygen, 66 percent nitrous oxide and vecuronium bromide. Intravenous Pentazocine (0.5 mg Kg^1 bod weight) was given but 1` minute before the surgical incision was given.

RESULTS

The present study comprised of 90 patients belonging to ASA Grade I and II of both sexes, requiring general anesthesia for various surgical procedures. These patients were allocated randomly in to 3 groups of 30 patients each on the basis of study drug given. The study groups of include the patients receiving magnesium sulphate 60 mg kg^{-1} in group II or smolol 2 mg kg^{-1} in group III. While the control group comprised of the patient receiving normal saline (placebo) in group I as a part of the induction technique. The distribution of cases according to the demographic characteristics is shown in table 1. The mean age was 37.63 $\pm$ 11.3 (19 - 62) in group 1 37.63 $\pm$ 11.3 (15-60) in group II, 36.73 $\pm$ 11.3 (19 – 60) years in group III. The mean weight of patients varied between 35 and 65 kg (53.033 $\pm$ 7.29) in group I. 40 – 70 kg (56.93 $\pm$ 9.1) in group II, 40 and 60 kg (55.9 $\pm$ 6.5) in group II. However, on statistical analysis, all the 3 stud groups were found to be comport able in respect of age and weight (P> 0.05) as shown in table 2. Observation were made for the following hemodynamic changes in various group.

1. Hearty rate (beats/minute)
2. Systolic blood pressure (mmHg)
3. Diastolic blood pressure (mmHg)

In the present study, drug was given from 0 to q minute in case of esmolol and 1 to 2 minute in case of magnesium sulphate. Laryngoscopy and intubation was done 2

minute after the injection of esmolol and 1 minute after injection of magnesium sulphate and completed within 30 seconds.

Table 1: Demographic characteristics (Mean ± S.E.) Of the 3 study groups

Parameter	Study groups		
	I (Placebo)	II (Magnesium sulphate)	III. Esmolol
Sample Size	30	30	30
Sex (M.F.)	11:19	8:22	15:15
Age (Yrs)	37.63 ± 11.3 (19-62)	37.1 ± 11.76 (25-50)	38.1 ± 1.78 (25-50)
Weight (Kgs)	53.85 ± 3.49 (55-56)	56.7 ± 1.43 (40-70)	55.15 ± 1.4 (40-60)

Table 2: Statistical comparison of the mean heart rate in the 3 groups at the stated time interval (within groups)

Time-interval	Study Groups Compared (t-values)		
	I (Placebo)	II (Magnesium sulphate) 60 mg kg[1]	III Esmolol 2 mg kg[1]
Basal value	-------	-------	-------
Pre-operative	3.463 P-0020**	-2.650 P0.013*	.0.091 P.0.928
After giving the Study drug	-4.745 P000***	-2.320 P0.028*	.3.695 P.001***
Immediately after intubation	-10.251 -000***	-8.167 P0.000***	-7.886 0.000***
At 1 minute after intubation	-10.085 P-000***	-5.600 P.0.000***	-7.069 0.000***
At 3 minute after intubation	-6.002 P.000***	-3.334 P0.002**	-5.095 0.000***
At 5 minute after intubation	-3.011 P0.005**	-1.608 P0.119	-1.687 0.102

Table 3: Mean of percentage changesin the heart rate at different time interval

Time-interval	Study Groups		
	Group - I	Group - II	Group - III
Baseline value	-------	-------	-------
Pre-operative	1.08 ±4.06	5.47 ±11.44	5.74 ± 5.73
After giving the Study drug	6.32 ± 7.31	6.67 ± 14.60	6.17 ± 9.10
Immediately after intubation	28.50 ± 15.12	18.36 ± 12.38	16.95 ± 13.08
At 1 minute after intubation	23.69 ± 12.79	13.45 ± 12.99	14.47 ± 10.44
At 3 minute after intubation	12.35 ± 11.15	6.60 ± 10.65	-6.18 ± 6.87
At 5 minute after intubation	4.72 ± 8.38	3.78 ± 11.47	1.72 ± 5.38

Table 4: Statistical comparison of the mean systolic blood pressure in the 3 group at the stated time interval (within groups)

Time-interval	Study Groups Compared (t – values)		
	I	II	III
Baseline	----	----	----
Pre-operative	2.165*	-7.339**	-1.939
After giving the Study drug	2.902**	3.883***	3.950***
Immediately after intubation	38.287***	-15.465***	-10.411***
At 1 minute after intubation	-21.058***	-4.358***	-8.460***
At 3 minute after intubation	-14.193***	-0.803***	-0.0569***
At 5 minute after intubation	-3.643***	1.708*	2.799**

Table 5: Statistical comparison of the mean systolic blood pressure in the 3 groups at the stated time interval (within groups)

Time-interval	Study Groups Compared (t – values)		
	I	II	III
Baseline	----	----	----
Pre-operative	2.165* P0.039	-1.646** .111	-1.939** P.000
After giving the Study drug	2.902** P.007	3.883*** .001	3.950*** P.000
Immediately after intubation	-38.287***	-15.565*** P0.000	-10.411*** P.000
At 1 minute after intubation	-21.058*** P0.000	-4.358*** P0.000	-8.460*** P.000
At 3 minute after intubation	-14.193*** P0.000	-0.803*** P.428	-0.569*** P.573
At 5 minute after intubation	-3.643*** P0.001	.708*** P0.098	2.799*** P0.009+

Table 6: Statistical comparison of Rate-pressure product (within group) at different time – intervals.

Time-interval	Study Groups Compared (t – values)		
	I	II	III
Baseline	----	----	----
Pre-operative	-.535	-2.951**	-1.958
After giving the Study drug	-2.415*	0.824***	2.250*
Immediately after intubation	-17.034***	12.815***	-11.055***
At 1 minute after intubation	-16.163***	-6.924***	-11.015***
At 3 minute after intubation	-10.083***	-2.702***	-3.731***
At 5 minute after intubation	-4.251***	-.003***	1.228***

Table 7: Incidence of adverse effects in the 3 study groups

Adverse effect	Study Groups		
	Group - I	Group - II	Group - III
Hypotension	0	0	0
Bradycardia	0	0	0
Cardiac arrest	0	0	0
Nausea	0	0	0
Vomiting	0	0	1
Convulsion	0	0	0

DISCUSSION

Heart rate: Our study demonstrated highly significant rise in heart rate in control group immediately after intubation (P<0.001), at 1 minute (P<0.001) and at 3 minutes after tracheal intubation, while significant rise (P<0.01) at 5 minutes after intubation. It gradually returned to near normal levels in 10-15 (1951)[104], who found a rise of heart rate by 23 beats minute $^{-1}$ but rise of 13 beats minute^{-1} as anaesthesia deepened and then gradual return to pre-laryngoscopy level in 10-15 minutes. Findings in esmolol group (III) when compared with their pre-operative value (Table 3a) showed significant rise (P<0.001) in heart rate immediately after intubation, at 1 minute and at 3 minute after intubation. It showed a consistent decrease from 3 minutes after intubation and at 5 minutes after intubation it comes to less than the preoperative value (<0.001). While comparing the esmolol group with control group there is significantly less rise in heart rate immediately after intubation (P<0.001) at 1 minute (P<0.001) at 3 minutes (P<0.001), and at 5 minutes (P<0.01) after intubation. These findings resemble with that of Meankhaus *et al*; (1985)[131], Mishra M.N. *et al* (2003)[6], who found that esmolol given by continuous/ bolus infusion attenuated heart rate responses 1, 3 and 5 minutes after laryngoscopy and tracheal intubation. However, failed to demonstrate a decrease in heart rate with 100mg as well as 200mg of bolus dose of esmolol the probable explanation may that insufficient time was allowed for the drug to produce its effect. A study by Sheppard *et al* ; 1990 using placebo, 100mg and 200mg of esmolol 90 seconds prior to intubation demonstrated a significant decreases in the heart rate and blood pressure. One can infer from these observations that esmolol immediately prior to intubation could not effectively prevent the haemodynamic changes in response to laryngoscopy and tracheal intubation. Thus administration of esmolol should be a least 90 seconds or 2 minutes prior to intubation, that has been taken in consideration in our study. However, the haemodynamicchanges as evidenced by increased in heart rate, Blood pressure ad rate pressure product following larngoscopy and intubation could not be abolished completely but can be attenuated to some extent using esmolol. Magnesium sulphate in group II on comparison with its pre-operative value (Table 3a) showed significant (P<0.01) rise in heart rate after laryngoscopy and intubation till 5 minutes. While in control group there was significantly more rise after intubation. These findings are in agreement with that of James FM 1989, Yap L.C. *et al* 1994, Vandenberg *et al*; 1997, Mishra M.N. *et al* 2003)[6.]

Systolic and diastolic blood pressure: Our study showed an average rise in mean systolic blood pressure 29.96 ± 4.28 mmHg (24.98 ±3.96 percent) in group I (Control group), 19.76 ± 7.00 mmHg (16.92 ± 6.64 percent) in group II (magnesium sulphate group), and 15.60 ± 8.20 mmHg (13.49 ±7.72 percent) in group III (esmolol group) immediately after intubation from baseline value. The average rise in mean diastolic blood pressure is 19.4 ± 7.86 mmHg (24.48 ± 10.50 percent) in group I 12.33 ± 6.64 mmHg (15.88 ± 9.41percent) in group II and 11.3 ± 7.28 mmHg (14.47 ± 9.95 percent) in group III immediately after intubation (Tables 4d,4e,5d,5e). from above data it is quue obvious that rise in mean systolic and diastolic blood pressure in quite less in group III patients i.e. esmolol group. Esmolol group showed significant fall in systolic and diastolic blood pressure after giving the study drug and also there was significantly less rise in both systolic and diastolic blood pressure soon after intubation and at 1 minute after intubation. At 3 minutes after intubation. These findings are in agreement with study of Menkhaus *et al* ; (1985)[5.] The systolic and diastolic blood pressure did not come to base line value in both group I and group II even after 3 minute of laryngoscopy and intubation. The systolic blood pressure in magnesium sulphate group (II) and esmolol group III when compared to the pre-operative values showed that after giving the drug there is significant fall. The findings are in similar to that of Jones MF *et al* ; (1989)[7], Mishra M.N. *et al*; (2003)[6].

Rate-pressure product: The rate – pressure product is the sensitive index of MVO_2 (Globel *et al*; 1978)[8]. However, the esmolol as well as placebo and magnesium sulphate failed to attenuate the response to laryngoscopy in terms of rate pressure product as almost all patients showed rate pressure product > 12,000. A highly significant increase (P<0.001) in rate pressure product was found at immediately after intubation and at 1 minute after intubation in all the groups from the baseline value. This rise persisted at 3 minutes in group III whereas it persisted for longer duration in group I and group II. The incidence of patients showing rate pressure product of > 12,000 was also less in group III as compared to group I and II. However, none of the patients in group III showed the rate- pressure product above 15,000. Whereas in, all patients in group I and group II rate-pressure product increased above 15,000 at immediately after laryngoscopy and intubation. The rate-pressure product

greater than 15,000 is considered undesirable in patients with compromised cardiac function e.g. coronary ischaemic disease (vacevic *et al*; 1992)[9].In present study none of the patients in group II showed rate pressure product >15,000 as compared and observed by vucevic *et al* ; (1992)[9] using continuous infusion of esmolol. Thus it appears that esmolol when used as bolus more effectively controls the cardiovascular response of laryngoscopy and intubation than the continuous infusion. The use of esmolol is mandatory in order to prevent cardiovascular responses to laryngoscopy and intubation especially in patients with compromised cardiovascular function. Thus, from above it is clear that the heart rate, blood pressure and rate-pressure product showed a significant increase (P<0.001) following laryngoscopy and tracheal intubation in all the patients irrespective of the drug used and remain increased for a variable period. However, in patients with placebo group, the haemodynamics changes didn't come to base line even after 10-12 minutes. Whereas in both magnesium sulphate (group II) and esmolol (group III) rie in blood pressure and heart rate is comparative and there is not much significant increase at various duration post intubation. There is significant fall in heart rate in esmolol (group III) as compared to magnesium sulphate (group II) after 3 minutes' post intubation. Thus the use of esmolol not only attenuate the haemodynamic changes in response to laryngoscopy and intubation, but also shorten the time of interval needed for the heart rate, blood pressure and rate-pressure product to come down to the normal or base line value more effectively than magnesium sulphate.

CONCLUSION

Heart rate was better controlled in patients group receiving esmolol 2 $mgkg^{-1}$ body weight. Following tracheal intubation patients in each group demonstrated an increase in the mean heart rate. However, rise in heart rate in esmolol group were (P<0.05) Moreover, the increase in heart rate was transient in esmolol group III and magnesium sulphate group II but persisted for longer duration in control group I. Though patients in all the 3 groups showed a significant decrease (P<0.001) in the blood pressure preoperatively, there was a highly significant rise (P<0.001) in the blood pressure in all the 3 groups, immediately after intubation. Here also the rise was transient of lower grade in group III as compared to group I and group II, where rise in blood pressure was higher and lasted for quite longer duration. In general, diastolic blood pressure showed parallel changes as systolic blood pressure throughout the study period. A highly significant increase (P<0.001) in rate pressure product was found immediately after intubation in all the groups from baseline value. This rise persisted for longer duration in group I and group II compared to group III. Incidence of patients showing rate- pressure product of > 12,000 was also less in groups III as compared to group I and II. However, none of the groups III as compared to group III showed the rate pressure product above 15,000 whereas, all patients in group I and group II showed rate pressure product above 15,000 at immediately after intubation. No abnormality in E.C.G. was seen in any of the patients. No adverse effect was seen in group I and group II. 1 episode of vomiting was seen in group III after recovery from anaesthesia.

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