Research Paper

Volume : 5 | Issue : 5 | May 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Tracheal Intubation in Patients with Pregnancy Induced Hypertension: Comparative Study between Esmolol, Diltiazem & Magnesium Sulphate

Medical Science

KEYWORDS : Esmolol, Diltiazem, Magnesium Sulphate, Pregnancy Induced Hypertension, Tracheal Intubation

Deepika Shukla — Anaesthesia Consultant, BSES MG Hospital, Department of Anaesthesiology, Padm. Dr. DY Patil Medical College & Hospital

*** Madhuri Dhabarde** — Lecturer, Department of Anaesthesiology, Padm. Dr. DY Patil Medical College & Hospital.
* Corresponding Author:

ABSTRACT

Background: Reflex changes in the cardiovascular system after laryngoscopy and intubation are most marked. They manifest themselves in the form of tachycardia, hypertension and cardiac arrhythmias, ectopics being most common. In patients with pregnancy induced hypertension, these reflex responses are greatly exaggerated. The present study was undertaken to compare the effect of intravenous Esmolol, intravenous Diltiazem and intravenous Magnesium Sulphate on blunting the haemodynamic response to endotracheal intubation in patients with pregnancy induced hypertension.

Materials & Methods: The study was conducted in 120 patients with PIH, coming to emergency and outdoor clinic, for undergoing surgery in a tertiary care centre. All 120 patients were assigned to one of the four groups of 30 each before induction of anaesthesia using a random number table: Group I: Normal Saline (controls), Group II: Inj. Esmolol, Group III: Inj. Diltiazem and; Group IV: Inj. Magnesium Sulphate. Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were recorded at following stages: Preoperative, after giving the study drug, immediately after intubation and at 1 minute, 3 minutes and 5 minutes after intubation. Statistical analysis was done using SPSS ver. 21.

Results: Significant fall in pulse rate in group II, insignificant rise in group III and significant rise ($p<0.01$) in group IV was observed after giving the study drug. Only in group II (esmolol), there was no significant rise in heart rate at any time interval. In group I (control) and III (diltiazem) there is significant increase in heart rate upto 3 minutes after intubation. In group IV (Mgso4), pulse rate is significantly higher at all time intervals. After giving the study drug, there is significant fall in mean arterial pressure in group II & III and insignificant fall in group IV. There is significant increase in mean arterial pressure in group I, II and III immediately after intubation and 1 minute after intubation while in control group, upto 3 minutes after intubation. In group IV there is insignificant difference at all the time intervals (all the values are below basal values in MgSO4 group).

Conclusion: Esmolol due to its rapid onset and short duration of action is a suitable drug for the attenuation of the haemodynamic response to laryngoscopy and intubation.

INTRODUCTION

Laryngoscopy and intubation violate the patient's protective airway reflexes and leads to physiological changes involving various systems of the body. Reflex changes in the cardiovascular system after laryngoscopy and intubation are most marked. They manifest themselves in the form of tachycardia, hypertension and cardiac arrhythmias, ectopics being most common. In patients with pregnancy induced hypertension (PIH), these reflex responses are greatly exaggerated and can precipitate complications such as intracranial haemorrhage, myocardial ischemia, cardiac arrhythmias, pulmonary oedema and cardiac failure [1].

Hence, to overcome this undesired response, the quest for an effective blockade of these responses has included the use of [2]: Premedication, topical and systemic lidocaine, vasodilators, ACE inhibitors, opiates, Inhaled anaesthetic agents and thoracic epidural block.

None of these above mentioned approaches have been proved entirely satisfactory. Hence, the search for an ideal agent to attenuate the hemodynamic responses is still continuing. Hence the present study was undertaken to compare the effect of intravenous Esmolol, intravenous Diltiazem and intravenous Magnesium Sulphate on blunting the haemodynamic response to endotracheal intubation in patients with pregnancy induced hypertension.

MATERIALS AND METHODS

After the approval of hospital ethical committee and informed consent, the study was conducted in 120 patients with PIH, coming to emergency and outdoor clinic, for undergoing surgery in a tertiary care centre.

Inclusion Criteria

- ASA grade II – III Patients
- Age between 20-35 years suffering from PIH undergoing lower segment caesarean under general anaesthesia

Exclusion Criteria

- Pre-operative Heart Rate < 70/min
- Pre-operative systolic blood pressure < 100 mmHg
- Presence of cardiac disease like heart block or chronic hypertension
- Significant hepatic, renal or respiratory dysfunction
- Morbid obesity
- History of convulsions
- Exposure to β-adrenergic agonists in the last 24 hrs
- Patients requiring multiple attempts at laryngoscopy and intubation

Grouping of cases

All 120 patients were assigned to one of the four groups of 30 each before induction of anaesthesia using a random number table.

Group I: Normal Saline will be given

Group II: Inj. Esmolol 2 mg/ kg i/v bolus 2 minutes before laryngoscopy and intubation

Group III: Inj. Diltiazem 0.2 mg/ kg i/v bolus 1 minute before laryngoscopy and intubation

Group IV: Inj. Magnesium Sulphate 60 mg/ kg i/v bolus 1 minute before laryngoscopy and intubation

The anaesthetist performing the laryngoscopy and intubation was unaware of the drug being administered.

Technique

Following pre-anaesthetic check-up, all the patients were premedicated with metoclopramide (10 mg) and ranitidine (50 mg) intravenously forty five minutes prior to induction of anaesthesia. Preoperative pulse rate, blood pressure, and foetal heart rate were recorded 30 minutes prior to the induction of anaesthesia.

Patients were shifted to the operation theatre in lateral position and oxygen being administered by hudsons mask. On the operation table, monitoring of heart rate, ECG, automated non-invasive blood pressure and pulse oximetry was instituted.

A standard general anaesthesia technique was followed in all the patients. After denitrogenation with 100% oxygen for 3 mins, a rapid sequence induction was carried out with thiopentone sodium 4mg/kg i/v and succinylcholine 1.5mg/kg i/v was given to facilitate intubation; cricoid pressure was maintained from the time of induction of anaesthesia until airway was secured; i/v vecuronium bromide 0.08mg/kg was given to maintain neuromuscular blockade and incremental doses were given as and when required. Lungs were ventilated with nitrous oxide in Oxygen. Ventilation was adjusted to maintain normocarbia in the intra-operative period. After the delivery of baby, syntocinone 20IU in ringer lactate was administrated by i/v infusion. Residual neuromuscular blockade was reversed with i/v glycopyrollate 0.01mg/kg and neostigmine 0.05mg/kg.

Parameters recorded: Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure. All above mentioned parameters were recorded at following stages: Preoperative, after giving the study drug, immediately after intubation and at 1 minute, 3 minutes and 5 minutes after intubation.

Other information recorded included: Neonatal assessment by Paediatrician, who was blinded to the nature of the drug used (APGAR score at 1, 5 and 10 mins). Complications of various drugs and their management

Statistical Analysis

Analysis of data was done by using SPSS software ver. 21. Data were statistically described in terms of mean (±SD), frequencies (number of cases) and percentages when appropriate. Data were tested first for normal distribution by Klomogorov– Smirnov test. Comparison of quantitative variables between the study groups was done using paired t test if normally distributed. Wilcoxon sign rank test was used for non-normally distributed or ordinal data. A probability value (p value) less than 0.05 was considered statistically significant.

RESULTS

Baseline variables like age, weight and height were comparable among study groups (p> 0.05; table 1). Significant fall in pulse rate in group II, insignificant rise in group III and significant rise (p<0.01) in group IV was observed after giving the study drug. Only in group II (esmolol), there was no significant rise in heart rate at any time interval. In group I (control) and III (diltiazem) there is significant increase in heart rate upto 3 minutes after intubation. In group IV ($Mgso_4$), pulse rate is significantly higher at all time intervals (table 2). After giving the study drug, there is significant fall in mean arterial pressure in group II & III and insignificant fall in group IV. There is significant increase in mean arterial pressure in group I, II and III immediately after intubation and 1 minute after intubation while in control group, upto 3 minutes after intubation. In group IV there is insignificant difference at all the time intervals (all the values are below basal values in $MgSO_4$ group) (table 3). No complication was seen in group I & IV. Bradycardia and hypotension were seen in one patient each in group II & III and hypotension was seen in two patients in group III (table 4). APGAR score of all the 4 groups were comparable and there was no significant effect on the fetal outcome in either of the groups (table 5).

DISCUSSION

Laryngoscopy and intubation are the basis of general anaesthesia. They are recognized as noxious stimuli by the body. Beside the desired achievement of direct visualization of the larynx, there is a complex hemodynamic response both in the normotensive and hypertensive patients. These are usually termed as "Haemodynamic responses to laryngoscopy and intubation". In patients with pregnancy induced hypertension (PIH), these reflex responses are greatly exaggerated and can precipitate complications such as cardiac arrhythmias, pulmonary oedema and cardiac failure as studied by Russell W. J et al. [1]. In the study of Benedetti TJ et al. [3] it was shown that maternal mortality associated with PIH is usually the result of intracranial hemorrhage or cerebral oedema and an exaggerated response to intubation may become one of the major precipitating factors in this group of patients subjected to general anaesthesia. The incidence of intracranial hemorrhage has been stated to be 3-40% in case of severe PIH as shown by Connell J.G. et al. [4]. In an attempt to obtund the response to laryngoscopy and intubation, various agents with various efficacy and results have been used by many workers till date. The present clinical study was undertaken to evaluate the effect of three drugs in patients with PIH, undergoing lower segment caesarean section under general anaesthesia. Study was done in four groups: Controls (gr. 1), esmolol (gr. 2), diltiazem (gr. 3); and magnesium sulphate (gr. 4).

While comparing esmolol group with control group, there is significantly less rise immediately after intubation, at 1 minute and at 3 minutes post intubation (p< 0.01). These findings resemble with that of Menkhaus et al. [5] who found that esmolol given by continuous infusion attenuated heart rate response at 1, 3 and 4 minutes after laryngoscopy and intubation. Similar findings were documented by Vacevic et al. [6] who used an infusion of esmolol in doses of 500 ug/kg/min for 2 min. as a loading dose followed by a maintenance of 100 ug/kg/min and found that the maximum heart rate after laryngoscopy and intubation in study group was significantly less than in the control group. Diltiazem Group findings are consistent with that of Mikawa et al. [7] who said that IV diltiazem (0.2 and 0.3 mgkg-1) given 1 minute before laryngoscopy failed to protect against the increase in heart rate after laryngoscopy. This was because diltiazem causes sympathoadrenal reflex stimulation by hypotension. The cardiovascular effects observed of Mg So4 in this study were particularly interesting. It might be expected that magnesium would slow the atrial rate by inhibiting the calcium mediated depolarizing current in pacemaker tissue, an effect that has been demonstrated in isolated animal hearts. However, in the intact animal the ability of magnesium to inhibit the release of acetylcholine from the vagus nerve predominates as shown in the study of Somjen GG et al. [8] and, therefore, the overall effect is the mild increase in heart rate seen in this study. These findings are in agreement with that of James MF et al. [9] who studied the effects of pretreatment with 60 ng/kg body weight magnesium sulfate intravenous on cardiovascular responses and catecholamine release associated with tracheal intubation. Magnesium pre-treatment increased heart rate by 13+_ 3.9 beats/minute, though after intubation, heart rate was unchanged in the magnesium group but increased in the control group (P < 0.05).

Present study shows an average rise in mean arterial pressure (MAP) of 31 mm Hg immediately after intubation in control group. Significant rise continued at 1 minute and 3 minutes after intubation (p < 0.01) and was insignificant at 5 minutes (p > 0.05). Esmolol group shows significant fall in MAP (p < 0.05) after giving the study drug and also there was significant rise soon after intubation and at 1 minute with near normal levels at 3 minutes and at 5 minutes post intubation. These findings are in agreement with study of Sheppard et al. [10] who found that 100 mg of esmolol decreases BP significantly at 1.5 minutes after intubation. Similar results were also reported by Miller et al. [11] who gave a bolus dose of 100 mg or 200 mg of esmolol prior to intubation and found that patients who received esmolol had significantly lower systolic blood pressure values than non-treated patients (p<0.005). Our findings of diltiazem group are similar to the result of Mikhawa et al. [12] who found that increase in

Volume : 5 | Issue : 5 | May 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

SBP and DBP was significantly less in diltiazem group (0.2 mgkg-1) 1 minute after laryngoscopy and intubation compared with control group. While similar results with magnesium sulphate were found in the study conducted by Sharma J et al. [13] who compared and evaluated the efficacy of Magnesium sulphate (MgSO4) 40 mg/kg and Esmolol 1.5 mg/kg to attenuate the cardio-vascular response to endotracheal intubation in controlled hypertensive patients. Both drugs were administered in diluted form over one minute, after induction. They found a significant rise in heart rate after endotracheal intubation in magnesium group as compared to esmolol group (p<0.05). Whereas, no significant difference in rise in systolic & diastolic blood pressure was seen in either of the group.

There were no significant complications noted in either of the groups. Bradycardia and hypotension were seen in one patient each in esmolol group and hypotension was seen in two patients in diltiazem group. Magnesium does not appear to prolong the duration of action of succinylcholine as also seen in the study of Baraka A et al. [14] but the interaction between magnesium and the non-depolarizing relaxants must be borne in mind if this technique is to be used in combination with these latter drugs.

There was no significant alteration in neonatal outcome with either of the agents. This was also confirmed in the study of Ahuja S et al. [15] who studied the effect of esmolol on hemodynamic response during endotracheal intubation in patients with pregnancy induced hypertension. Diltiazem also can be safely used in pregnant patients after the first trimester without any significant alteration in the neonatal prognosis. Crowther C et al. [16] studied that magnesium administered to the mother may have a neuroprotective effect for the newborn. Neonatal morbidity was lower and an APGAR score below 7 at one minute was significantly less frequent in infants of mothers treated by magnesium as compared to diazepam, which was similar to the readings in our study.

CONCLUSION

Esmolol due to its rapid onset and short duration of action is a suitable drug for the attenuation of the haemodynamic response to laryngoscopy and intubation.

TABLES

Table 1. Comparison of baseline variables among study groups

Variables	Controls	Esmolol	Diltiazem	MgSo4	p-value
Age (years)	24.64 ± 3.99	24.56 ± 4.72	24.41 ± 4.74	24.65 ± 3.94	NS
Weight (Kg)	56.83 ± 6.85	56.09 ± 7.07	57.61 ± 6.98	57.83 ± 6.45	NS
Height (cm)	161.88 ± 10.04	162.27 ± 10.31	164.94 ± 8.88	160.09 ± 8.29	NS

Table 2. Comparison of pulse rate among study groups

Group	Basal	After drug administration	Post Intubation			
			0 Min	1 Min	3 Min	5 Min
Control (Group I)	94.46±	96.33 ± 11.12	110.64±	113.42±	108.08±	98.60±
	11.49	p - NS	12.4	13.81	14.47	17.58
			p < 0.01	p < 0.01	p < 0.01	p - NS
Esmolol (Group II)	91.94±	80.68± 6.10	96.52±	95.24±	93.72±	91.80±
	10.4	p < 0.01	7	5.77	5.79	6.23
			p - NS	p - NS	p –NS	p - NS
Diltiazem (Group III)	90.12±	94.00 ± 11.33	104.96±	108.88±	100.73±	96.92±
	12.63	p - NS	6.11	6.28	14.43	16.21
			p <0.01	p <0.01	p <0.01	p - NS
MgSO4 (Group IV)	92.19±	107.00 ± 10.98	106.40±	105.04±	103.20±	103.00±
	10.72	p <0.01	8.98	6.89	9.2	9.8
			p < 0.01	p < 0.01	p < 0.01	p <0.01

Table 3. Comparison of mean arterial pressure among study groups

Group	Basal	After drug administration	Post Intubation			
			0 Min	1 Min	3 Min	5 Min
Control (Group I)	109.39	107.8	140.2	128.7	118.6	112.8
	±8.50	±8.5	±7.8	±9.7	±9.8	±7.6
		p - NS	p < 0.01	p < 0.01	p < 0.01	p - NS
Esmolol (Group II)	108.39	101.5	123.6	121.3	112.3	110.7
	±7.66	±7.4	±9.8	± 11.2	±10.9	±8.8
		p < 0.05	p < 0.01	p < 0.01	p - NS	p - NS
Diltiazem (Group III)	108.17	97.5	122.8	120.9	112.7	110.7
	±8.11	±8.8	±8.9	±9.8	±8.7	±11.2
		p < 0.01	p < 0.01	p < 0.01	p - NS	p - NS
MgSO4 (Group IV)	110.66	108.6	107.5	109.3	107.6	108.4
	±7.32	±8.7	±7.8	±6.9	±8.3	±7.8
		p - NS	p - NS	p - NS	p - NS	p - NS

Table 4. Comparison of complication rate among study groups

Complications	Group I (Control)	Group II (Esmolol)	Group III (Diltiazem)	Group IV (MgSO4)
Hypotension	-	1	2	-
Bradycardia (60/ min)	-	-	1	-
Arrhythmias	-	-	-	-
Bronchospasm	-	-	-	-
Prolongation of NM Blockade	-	-	-	-
Pain on infection site	-	-	-	-
Others	-	-	-	-

Table 5. Comparison of APGAR score among study groups

APGAR	Group I (Control)	Group II (Esmolol)	Group III (Diltiazem)	Group IV (MgSO4)
1 Minute	7.71±0.91	8.03±0.97	7.90±0.69	8.17±0.56
5 Minute	8.77±0.61	8.97±0.59	8.95±0.50	8.88±0.42
10 Minute	9.60±0.33	9.49±0.40	9.60±0.26	9.52±0.32

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