Attenuation of Pressor Response to Laryngoscopy and Tracheal Intubation - Comparison of Intravenous Esmolol with Intravenous Clonidine

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ABSTRACT

BACKGROUND

Sudden changes in haemodynamic parameters is a major concern during laryngoscopy and intubation which can cause deleterious effects in patients with heart disease, intracranial aneurysm, and hypertension. We wanted to compare the efficacy of premedication with intravenous clonidine and esmolol to blunt the haemodynamic response to laryngoscopy and tracheal intubation.

METHODS

After approval from the ethics committee, 60 consenting adult patients of either gender undergoing surgeries at Amrita Institute of Medical Sciences, Kochi, Kerala, were studied from December 2009 to October 2011. The study was planned as a randomized, single blinded pilot study. These patients were divided into two groups : Group A and Group B by closed envelope technique. Group A - patients received intravenous clonidine 2 micrograms / Kg body weight as a bolus 10 minutes prior to induction. Group B - patients received injection esmolol 2 mg / Kg body weight IV bolus 2 minutes before laryngoscopy and tracheal intubation.

RESULTS

Both drugs effectively attenuated systolic, diastolic and mean arterial pressure responses to laryngoscopy and intubation. Esmolol was more effective than clonidine in suppressing heart rate response to laryngoscopy and intubation. Systolic blood pressure control immediately following intubation among the groups was better with esmolol. Maintenance of diastolic blood pressure and mean arterial pressure following intubation among the groups was also better with esmolol.

CONCLUSIONS

Esmolol can be recommended as a better agent for attenuation of pressor response to laryngoscopy and intubation in comparison with clonidine.

KEYWORDS

Esmolol, Haemodynamics, Intubation, Clonidine, Laryngoscopy

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BACKGROUND

Laryngoscopy and tracheal intubation are two vital procedures during general anaesthesia which causes reflex sympathetic stimulation and results in elevated circulatory responses. Even though the increase in blood pressure and heart rate due to laryngoscopy and intubation is short lived, they can cause dangerous effects like myocardial ischaemia, infarction and heart failure in known coronary artery disease patients. It can also cause rise in intracranial pressure and even can result in intracranial haemorrhage.[1-4]

Even though tracheal intubation induces rise in nor - adrenaline, adrenaline and dopamine levels, the raise in nor - adrenaline levels is persistently associated with rise of blood pressure and heart rate.[2,3,5-7] Many strategies have been tried to minimize the hemodynamic adverse responses associated with intubation. But so far no single drug or technique has been proven to suppress the pressor response to laryngoscopy and intubation completely.[8-16]

Esmolol comes under the group of ultra - short acting β - 1 adrenergic blocking drugs. It has predominant action on β - receptors and has no significant membrane stabilizing activity. It has rapid onset and a short duration of action.[17-18] Clonidine is an - 2 adrenoreceptor agonist with central sympatholytic effect. Clonidine has proven efficacy in blunting hemodynamic stress responses to tracheal intubation. Clonidine also controls blood pressure by increasing cardiac baroreceptor reflex sensitivity.[19]

The purpose of the study is to compare the efficacy of premedication with intravenous clonidine or esmolol in attenuating the hemodynamic response following Tracheal intubation. To the best of our knowledge there is no direct comparison between the effects of intravenous esmolol and intravenous clonidine. So we decided to compare the effects of these two drugs in the present study.

METHODS

This is a randomized, single blinded pilot study conducted from December 2009 to October 2011 in Amrita Institute of Medical Sciences, Kochi, Kerala, among 60 consenting adult patients of either gender undergoing surgeries.

Inclusion Criteria

- Patients belonging to American Society of Anesthesiologists (ASA) physical status I & II undergoing surgeries under general anaesthesia.
- Age group 20 to 60 years.

Exclusion Criteria

- Patient refusal.
- American Society of Anesthesiologists (ASA) physical status grade III or higher.
- Hypertensive patients.
- Thyrotoxicosis.
- Pheochromocytoma.
- Patients with difficult airway.
- Patients on beta blockers or alpha blockers.
- Allergy to either of the study drugs.

After approval from the ethics committee, these patients were divided into two groups : Group A and Group B by closed envelope technique. Group A - patients received intravenous clonidine 2 micrograms / Kg body weight as a bolus 10 minutes prior to induction. Group B - patients received injection esmolol 2 mg / Kg body weight IV bolus 2 minutes before laryngoscopy and tracheal intubation.

Blood pressure was measured by non - invasive blood pressure monitoring, heart rate by electrocardiography (ECG Lead II) and oxygen saturation by pulse oximetry. All patients received a standardized anaesthetic protocol. After pre oxygenation with 100 % oxygen for 3 minutes, all patients received fentanyl 2 micrograms / Kg body weight and were induced with intravenous propofol 2 mg / Kg body weight. Skeletal muscle relaxation was provided with intravenous vecuronium 0.1 mg / Kg body weight to facilitate laryngoscopy and tracheal intubation. Patients were mechanically ventilated with face masks with 70 % nitrous oxide, 30 % oxygen and 1 % isoflurane. A quick and gentle laryngoscopy lasting less than 15 seconds was performed and intubation done with 7.5 size cuffed endotracheal tube for females and 8.0 size cuffed endotracheal tube for males. After intubation, bilateral air entry was confirmed and endotracheal tube was fixed.

Maintenance of anaesthesia was also under standard anaesthesia protocol with Nitrous Oxide 66 %, Oxygen 33 % and Isoflurane 1 %. Mechanical ventilation was continued with a tidal volume of 8 mL / Kg body weight and a respiratory rate of 12 to 15 per minute to maintain end tidal carbon dioxide levels between 30 to 35 mm of Hg.

If mean arterial blood pressure increased to more than 160 mm of Hg, level of anaesthesia was deepened with injection propofol 30 mg bolus and the patient was ousted from study. If MAP decreased to less than 50 mm of Hg, injection ephedrine in increments of 3 mg was given and patient was removed from the study. The following parameters were recorded: Heart rate (HR) in beats per minute, Systolic blood pressure (SBP) in mm Hg, Diastolic blood pressure (DBP) in mm Hg, The mean arterial pressure (MAP) in mm Hg.

The heart rate and blood pressures (systolic, diastolic and mean arterial pressures) were measured at the following intervals: Pre induction and 1, 3, 5, 10, 15, 30 minutes following tracheal intubation.

Statistical Analysis

Data was analysed in SPSS software. Descriptive statistical tools such as mean used to represent the continuous data and percentage used to represent the categorical data. Differences between groups were analysed using independent sample t - test. Chi square test was used to find out the association between categorical variables.

RESULTS

The group comparison demonstrated no significant difference in its distribution among two groups with regard to age, sex and ASA physical status.

Group	Mean	SD	N	t	P
Clonidine	105.1	11.2	30	3.51**	0.001
Esmolol	96.7	6.7	30		

Table 1. Comparison of HR at Pre-Induction

The average value of HR of patients at pre induction stage in Clonidine group is 105.1, where as its value in Esmolol is 96.7. The student t test ($p < 0.01$) shows that the HR is significantly high in Clonidine group at pre induction stage [Table 1]. Since the baseline value (pre induction) of heart rate significantly differs between the groups, Analysis of covariance (ANCOVA) is used to determine whether the groups differ in heart rate at different stages such as 1 minute, 3 minutes etc.

Stages	Clonidine		Esmolol		F#	P
	Unadjusted	Adjusted	Unadjusted	Adjusted		
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		
1 minute	84.5 ± 7.6	83.4 ± 1.8	80.7 ± 11.3	81.8 ± 1.8	0.38	0.540
3 minutes	85.8 ± 11.9	88.5 ± 1.5	80.8 ± 7.1	78.1 ± 1.5	22.87**	<0.001
5 minutes	74.8 ± 9	75.6 ± 1.3	79.5 ± 4	78.7 ± 1.3	2.55	0.116
10 minutes	80.3 ± 4.4	80.3 ± 1	85.5 ± 6	85.5 ± 1	11.98**	0.001
15 minutes	84.9 ± 5.6	86.5 ± 0.6	82 ± 3.7	80.4 ± 0.6	40.32**	<0.001
30 minutes	89.4 ± 4.1	90.9 ± 1.3	86.9 ± 10.1	85.3 ± 1.3	8.06**	0.006

Table 2. Comparison of HR at Different Stages

#: ANCOVA (Comparison of adjusted value of HR for the variation at pre induction stage)** : - Significant at 0.01 level

The average HR in Clonidine and Esmolol group after 1 minute and 5 minutes does not differ between the group ($p > 0.05$). At 3, 15- and 30-minute HR is significantly less in Esmolol group as compared to Clonidine ($p < 0.01$). At 10-minute HR is significantly high in Esmolol group as compared to Clonidine ($p < 0.01$) [Table 2].

Group	Mean	SD	N	t	P
Clonidine	122.4	9.9	30	4.4**	<0.001
Esmolol	131.9	6.5	30		

Table 3. Comparison of SBP at Pre-Induction

The average value of SBP at pre induction stage is significantly high in esmolol group. The average SBP after adjusting for the initial difference (at pre induction), the result of ANCOVA shows that the SBP at 1, 3, 5, 15, 30 minutes was significantly high in clonidine group [Table 3].

The average value of DBP of patients at pre induction stage in Clonidine group is 76.9, where as its value in Esmolol is 86.8. The student t test ($p < 0.01$) shows that the SBP is significantly high in Esmolol group at pre induction stage [Table 4].

The result of ANCOVA shows that the esmolol group showed a significantly high DBP at 1, 3 and 10 minutes and a significantly low DBP at 5 and 30 minutes. There was no significant difference between groups at 15 minutes [Table 5].

Stages	Clonidine		Esmolol		F#	P
	Unadjusted	Adjusted	Unadjusted	Adjusted		
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		
1 minute	112.5 ± 13.3	117.0 ± 1.7	106.1 ± 9.7	101.6 ± 1.7	35.05**	<0.001
3 minutes	107.5 ± 12.1	112.5 ± 1.4	100.2 ± 10.2	95.2 ± 1.4	67.69**	<0.001
5 Minutes	106.9 ± 10.6	107.5 ± 1 .9	100.9 ± 8.5	100.3 ± 1.9	6.23*	0.015
10 minutes	103.1 ± 15.3	102.7 ± 2.2	109.4 ± 3.6	109.7 ± 2.2	4.44*	0.040
15 minutes	108.1 ± 15.5	111.1 ± 2	104.1 ± 4.4	101.0 ± 2	11.13**	0.002
30 minutes	113 ± 15.6	116.1 ± 2.7	109.9 ± 13.4	106.8 ± 2.7	5.18*	0.027

Table 4. Comparison of SBP at Different Stages

#: ANCOVA (Comparison of adjusted value of SBP for the variation at pre induction stage)

Group	Mean	SD	N	t	P
Clonidine	76.9	4.7	30	2.76**	0.008
Esmolol	86.8	19.1	30		

Table 5. Comparison of DBP at Pre Induction

Stages	Clonidine		Esmolol		F#	P
	Unadjusted	Adjusted	Unadjusted	Adjusted		
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		
1 minute	79.8 ± 6.1	78.8 ± 1.2	82 ± 7.8	83 ± 1.2	5.66*	0.021
3 minutes	71.8 ± 9.4	71.1 ± 1.6	76.1 ± 7.6	76.9 ± 1.6	6.49*	0.014
5 minutes	76.4 ± 7	75.7 ± 1	68.5 ± 2.9	69.2 ± 1	21.87**	<0.001
10 minutes	64.3 ± 4.7	62.7 ± 0.9	74.7 ± 8	76.3 ± 0.9	115.67**	<0.001
15 minutes	69.8 ± 9.5	68.1 ± 1.7	66.8 ± 10.8	68.5 ± 1.7	0.03	0.860
30 minutes	73.2 ± 12.5	71.8 ± 2.1	61.3 ± 10.9	62.7 ± 2.1	8.69**	0.005

Table 6. Comparison of DBP at Different Stages

#: ANCOVA (Comparison of adjusted value of DBP for the variation at pre induction stage) **: - Significant at 0.01 level *: - Significant at 0.05 level

Group	Mean	SD	N	t	p
Clonidine	91.9	5.0	30	4.34**	<0.001
Esmolol	101.8	11.4	30		

Table 7. Comparison of MAP at Pre-Induction

Stages	Clonidine		Esmolol		F#	P
	Unadjusted	Adjusted	Unadjusted	Adjusted		
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		
1 minute	90.7 ± 7.5	89 ± 1.4	90.2 ± 7.6	91.9 ± 1.4	1.93	0.170
3 minutes	83.6 ± 10	82.6 ± 1.7	84.1 ± 7	85.1 ± 1.7	0.98	0.326
5 minutes	86.5 ± 7.9	85.4 ± 1.2	79.4 ± 4.5	80.5 ± 1.2	7.13**	0.010
10 minutes	77.3 ± 7.8	75.2 ± 1.2	86.3 ± 6.4	88.3 ± 1.2	49.88**	<0.001
15 minutes	82.4 ± 11.1	81.8 ± 1.9	79.4 ± 7.7	80 ± 1.9	0.38	0.541
30 minutes	86.4 ± 13.2	84.6 ± 2.4	77.5 ± 11.7	79.4 ± 2.4	2.08	0.154

Table 8. Comparison of MAP at Different Stages

#: ANCOVA (Comparison of adjusted value of MAP for the variation at pre induction stage)

The average value of MAP of patients at pre induction stage in Clonidine group is 91.9, where as its value in Esmolol is 101.8. The student t test ($p < 0.01$) shows that

the MAP is significantly high in Esmolol group at pre induction stage [Table 7]. The clonidine group showed a significantly high MAP at 5 minutes and a significantly low MAP at 10 minutes. There was no significant difference between groups at other intervals [Table 8].

DISCUSSION

In the present study, the preinduction heart rate, systolic, diastolic and mean arterial pressures were significantly different between groups, probably because the patients in both groups received the drugs before induction and the effect of the drugs might have already set in. So, Analysis of Covariance (ANCOVA) was used to determine whether the groups differ in the hemodynamic parameters later at different stages as the result of drugs applied. Subsequently the heart rate, systolic, diastolic and mean arterial pressure values at different time intervals, after adjusting for the initial difference at pre induction, were derived and statistically analysed. The pre induction heart rate was significantly less in esmolol group which can be explained by the beta blocker activity of esmolol. There was no increase in HR in esmolol group following laryngoscopy and intubation up to 10 minutes. Whereas clonidine group showed an increase in HR at 3 minutes. But when the differences among groups were compared it was found that at 1 and 5 minutes after intubation there was no statistically significant difference between groups which means that the effect on heart rate by both drugs following intubation were almost similar. At 10 minutes heart rate was significantly high in esmolol group which may be because of recovery from beta blockade produced by esmolol. At 15 and 30 minutes postintubation heart rate was significantly high in clonidine group. This increase, which could not be attributed to stress response to intubation, might be due to surgical stimulation or a compensatory response in heart rate to maintain blood pressure.

So esmolol effectively suppressed heart rate response to laryngoscopy and intubation which is in agreement with previous studies by Ebert et al[20] and Bansal S et al.[21] When the systolic blood pressures were compared it was seen that there was no increase in SBP in both groups following intubation. But the clonidine group later showed a significantly high SBP at 1, 3, 5, 15 and 30 minutes compared to esmolol group which may be because the antihypertensive effects of clonidine had not taken action fully. Only at 10 minutes esmolol group showed a significantly higher SBP which again could be attributed to its short duration of action. So the SBP control immediately following intubation among the groups was better with esmolol, though both effectively suppressed an increase in SBP following intubation. When the diastolic blood pressures were compared it was seen that there was no increase in DBP in both groups following intubation. At the same time when DBP was compared among groups, it was found that the DBP was significantly high in esmolol group except at 30 minutes. Preventing an increase in DBP following intubation, but maintaining it without a significant fall, as seen in the esmolol group, could be advantageous in patients with coronary artery disease. So the maintenance of DBP following intubation among the groups was better with esmolol, though both effectively suppressed an increase in DBP following intubation. The changes in mean arterial pressures when compared, it was seen that there was no increase in MAP following intubation from the pre induction values in both groups. At the same time when it was compared among groups, it was found that the MAP was significantly high in esmolol group at 1, 3 and 10 minutes when compared to clonidine group. MAP was significantly high in clonidine group at 15 and 30 minutes. So the maintenance of MAP following intubation, up to 10 minutes, among the groups was better with esmolol, though both effectively suppressed an increase in MAP following intubation.

Strengths and Limitations

There have been no studies where the effects of intravenous esmolol and intravenous clonidine were directly compared. As the onset of action of esmolol and clonidine were different, we had to give them at different timings before induction and hence double blinding became difficult. The baseline HR, SBP, DBP and MAP before administration of study drugs were not documented and analyzed in this study. This could be the reason why the pre induction haemodynamic values were found to be significantly different in both groups. Hence, the subsequent values had to be adjusted for the initial difference at pre induction and then the data was statistically analysed using Analysis of Covariance (ANCOVA).

CONCLUSIONS

Intravenous administration of both clonidine and esmolol before induction of anaesthesia effectively attenuated pressor response to laryngoscopy and intubation. But with regard to better control of heart rate response and better maintenance of blood pressures after intubation, esmolol can be recommended as a better agent.

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