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Original Research Article

A randomized, controlled study to compare the effects of intravenous labetalol and esmolol on haemodynamic changes during laryngoscopy and intubation

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ABSTRACT

Background: Direct laryngoscopy and endotracheal intubation frequently induce cardiovascular stress response characterised by hypertension and tachycardia due to reflex sympathetic stimulation. Considering the clinical significance of these changes stress attenuation is needed to blunt these responses. β- blockers are used to reduce the unwanted hemodynamic responses. Esmolol is ultra-short acting cardio selective β blocker. Labetalol is useful in not only attenuating the response to laryngoscopy and intubation but also in preventing perioperative cardiovascular events. Present study compared the efficacy of esmolol and labetalol for attenuation of sympathomimetic response to laryngoscopy and intubation.
Methods: It was a prospective, randomized, controlled study carried out in 75 adult patients with ASA 1 and ASA 2 posted for elective surgeries. Patients were allocated randomly into Group-1 (esmolol) and Group-2 (labetalol) and Group-3 (placebo) of 25 patients each. Inj. esmolol (1mg/kg) or Inj. labetalol (0.4 mg/kg) or placebo (0.9NS) dissolved up to 5 ml in distilled water was injected intravenously 5 minutes prior to intubation. All patients premeditated with Inj. glycopyrrolate (4µg/kg). Patient were then induced with Inj. propofol (2mg/kg), Inj. scoline (2mg/kg) given followed by laryngoscopy and intubation. Haemodynamic readings were noted at T0 (baseline before injecting the drug), T1 (1 minute after injecting the drug), T2 (after intubation), T3 (2 minutes after intubation), T4 (4 minutes after intubation), T5 (6 minutes after intubation), T6 (8 minutes after injection), T7 (10 minutes after injection).
Results: Gr-1, Gr-2 and Gr-3, when compared with each other for systolic BP, diastolic BP, mean BP, and HR, showed a statistically significant difference at different intervals.
Conclusions: Both the drugs are found to be effective in attenuation of hemodynamic reflex without any side effects. Further studies are recommended to substantiate the findings in present study.

Keywords: Esmolol, Haemodynamic changes, Intubation, Laryngoscopy, Labetalol

INTRODUCTION

Despite the evidence of new airway devices in the recent years, rigid laryngoscopy and tracheal intubation still remain the gold standard in airway management. The hemodynamic changes stemming from airway instrumentation are due to sympthoadrenal discharge caused by epipharyngeal and parapharyngeal stimulations (Singh et al).[1] Direct laryngoscopy and endotracheal intubation frequently induces a cardiovascular stress response characterized by hypertension and tachycardia due to reflex sympathetic stimulation. The response is transient occurring 30 seconds after intubation and lasting for less than 10 minutes (Stoelting).[2] Although these changes may be well tolerated in healthy people, they may be hazardous in patients with hypertension, coronary artery disease, cerebrovascular disease, myocardial infarction and thyrotoxicosis (Fox et al).[3]

Different pharmacologic agents like lidocaine, vasodilator agents inhibiting sympathoadrenal response, α-and β-adrenergic blockers, and opioids can be administered prior to tracheal intubation in order to prevent hemodynamic responses. (Helfmann et al; Sharma et al; Mikawa et al; Kindler et al; Saitoh et al).[4-8] β-blockers are used to reduce the necessity of anaesthetic drugs by their sedative properties and reduce unwanted hemodynamic responses.

Esmolol is an ultrashort-acting β_1 cardio selective β blocking agent with a short half-life (9 minutes). This agent has been used to reduce the increase in heart rate and blood pressure in response to tracheal intubation (Wolman and Fiedler; Barbier et al).[9,10] Labetalol has been found to be useful in not only attenuating the response to laryngoscopy and intubation but also in preventing perioperative cardiovascular events (Kim et al; Chung et al; Inada et al; Ramanathan et al).[11-14] In the present study, an attempt has been made to compare the two drugs in order to find out the relative advantages of their use..

METHODS

This was a prospective, randomized controlled double blinded study comparing two adrenergic antagonists esmolol (β1 selective) and labetalol (non-selective) in decreasing the pressor response during laryngoscopy and intubation. After taking ethical committee approval 75 adult patients aged 18-55 years with ASA 1 and 2 requiring general anaesthesia for elective surgery were included in the study. Informed written consent was obtained from all the patients. Patients with cardiovascular failure, renal failure, hepatic dysfunction, pulmonary disease, BMI>35, those on β-blockers were excluded from study. The patients were randomly allocated into one of the three groups of 25 each.

- Group-1 (esmolol) = 1mg/kg diluted up to 5 ml in distilled water
- Group-2 (labetalol) = 0.4mg/kg diluted up to 5ml in distilled water
- Group-3 (control or placebo) = 0.9% normal saline diluted up to 5 ml in distilled water.

Test doses were given 5 minutes prior to intubation. Patient were kept nil orally for 8 hours prior to surgery. All the patients were premeditated with Inj. glycopyrrolate (4μg/kg). Preoxygenation with 100% oxygen for 3 minutes was done. Patient were then induced with Inj. propofol (2mg/kg). Thereafter they were administered Inj. succinylcholine (2mg/kg) followed by laryngoscopy and intubation. Haemodynamic readings were noted at T0 (baseline before injecting the drug), T1 (1 minute after injecting the drug), T2 (after intubation), T3 (2 minutes after intubation), T4 (4 minutes after intubation), T5 (6 minutes after intubation), T6 (8 minutes after intubation), T7 (10 minutes after intubation).

Statistical analysis

The statistical analysis was done using SPSS (Statistical package for social sciences) Version 15.0 statistical analysis software. The values were represented in number (%) and Mean±SD.

RESULTS

The present study was carried out with the aim to compare the hemodynamic effects of esmolol and labetalol to establish the clinical advantage of anaesthetic.

Table 1 compares the three groups for demographic characteristics. Comparison of three study groups for age, weight, and gender ratio revealed no statistical significant difference (p>0.05).

Table 1: Demographic characteristics of the patients.

Variable	Group-1	Group-2	Group-3	F	‘p’
Mean age ± SD (years)	35.00±11.03	34.40±11.65	36.16±12.77	0.143	0.867
Mean weight ± SD (kg)	56.60±6.81	55.88±8.45	57.64±5.64	0.393	0.677
Male:female	9:16	11:14	6:19	X^2=2.237 (df=2)	0.327

Table 2 shows comparison of groups for mean SBP (systolic blood pressure) at different time intervals. This table shows that Group 1 and 2 shows significant difference just after intubation to 10 minutes time interval after intubation. Group 2 and 3 also shows statistically significant difference in mean SBP from just after intubation to 10 minutes after intubation time interval.

Table 3 shows comparison of groups for mean DBP (diastolic blood pressure). Group-1 and 2 shows significant difference at all times except 4 minutes, 6 minutes, 10 minutes from just after intubation. Group1 and 3 shows significant differences at all times interval from just after intubation time but Group 2 and 3 show significant difference up to 6 minutes after intubation.

Table 2: Comparison of mean SBP between groups at different time intervals (student 't' test).

Variable	Group 1 versus Group 2		Group 1 versus Group 3		Group 2 versus Group 3	
	"t"	"p"	"t"	"p"	"t"	"p"
0 minute	0.066	0.948	1.890	0.065	1.844	0.071
1 minute after test drug	-0.065	0.948	0.686	0.496	0.798	0.0429
After intubation	-5.182	<0.001	-9.099	<0.001	-6.184	<0.001
2 minutes after intubation	-5.815	<0.001	-9.587	<0.001	-5.777	<0.001
4 minutes after intubation	-0.966	0.339	-7.589	<0.001	-8.367	<0.001
6 minutes after intubation	-2.545	0.014	-4.137	<0.001	-2.941	0.005
8 minutes after intubation	1.203	0.235	3.414	<0.001	2.639	0.011
10 minutes after intubation	-2.005	0.051	2.330	0.024	4.370	<0.001

Table 3: Comparison of mean DBP between groups at different time intervals (student's 't' test).

Variable	Group 1 versus Group 2		Group 1 versus Group 3		Group 2 versus Group 3	
	"t"	"p"	"t"	"p"	"t"	"p"
0 minute	-1.769	0.083	-0.517	0.608	1.232	0.224
1 minute after drug	-1.066	0.292	0.368	0.714	1.573	0.122
After intubation	-4.374	<0.001	-14.481	<0.001	-6.122	<0.001
2 minutes after drug	-3.676	0.001	-13.735	<0.001	-5.612	<0.001
4 minutes after drug	1.540	0.130	-5.299	<0.001	-6.414	<0.001
6 minutes after drug	1.507	0.138	-3.171	0.003	-4.860	<0.001
8 minutes after drug	2.579	0.013	3.890	<0.001	0.060	0.953
10 minutes after drug	0.489	2.885	2.885	0.006	2.005	0,051

Table 4 shows comparison of groups for MAP (mean artery pressure) at different time intervals. For mean B.P. Group1 and 2 shows significant difference at just after intubation and 2 minutes and 8 minutes after intubation. Group 1 and 3 and Group 2 and 3 show significant difference at all times after intubation except at 8 minutes after intubation for Group 2 and 3.

Table 4: Comparison of mean MAP between groups at different time intervals (student's 't' test) between groups.

Variable	Group 1 versus Group 2		Group 1 versus Group 3		Group 2 versus Group 3	
	"t"	"p"	"t"	"p"	"t"	"p"
0 minute	-1,030	0.308	0.664	0.510	1.650	0.106
1 minute after test drug	-0.833	0.409	0.581	0.564	1.416	0.163
After intubation	-5.854	<0.001	-12.118	<0.001	-7.529	<0.001
2 minutes after intubation	-5.491	<0.001	-12.776	<0.001	-6.729	<0.001
4 minutes after intubation	0.402	0.689	-7.045	<0.001	-8.291	<0.001
6 minutes after intubation	-0.220	0.827	-4.756	<0.001	-5.821	<0.001
8 minutes after intubation	2.583	0.013	4.230	<0.001	1.135	0.262
10 minutes after intubation	-0.380	0.705	3.296	<0.002	3.374	<0.001

Table 5 shows comparison of groups for mean HR (heart rate) at different time intervals. There was no statistically significant difference in heart rate between Group 1 and 2 at different time intervals. A statistically significant difference was observed in heart rate values between group 1 and 3 at all the time intervals after intubation except at 8 minutes after intubation time interval. Group 2 and 3 shows statistically significant difference at all intervals from 1 minutes after test drug dose time interval except at 8 minutes after intubation time interval.

Table 5: Between group comparison of mean heart rate at different time intervals (student's 't' test).

Variable	Group 1 versus Group 2		Group 1 versus Group 3		Group 2 versus Group 3	
	"t"	"p"	"t"	"p"	"t"	"p"
0 minute	0.099	0.921	-0.639	0.526	-0.693	0.492
1 minute after test drug	0.871	0.388	-1.592	0.118	-2.138	0.038
After intubation	-0.697	0.489	-7.052	<0.001	-10.719	<0.001
2 minutes after intubation	-1.036	0.305	-8.830	<0.001	-13.498	<0.001
4 minutes after intubation	1.502	0.140	-6.275	<0.001	-8.710	<0.001
6 minutes after intubation	1.174	0.246	-2.715	0.009	-3.563	<0.001
8 minutes after intubation	0.777	0.441	-0.369	0.714	-1.470	0.148
10 minutes after intubation	0.629	0.532	5.812	<0.001	5.684	<0.001

DISCUSSION

Stimulus of the laryngeal and tracheal tissues may also cause increase in both sympathetic and sympathoadrenal reflex activity (Kovac; Prys-Roberts et al).[15,16] Different pharmacologic agents like lidocaine, vasodilator agents inhibiting sympathoadrenal response, α and β adrenergic blockers, and opioids can be administered prior to tracheal intubation in order to prevent haemodynamic responses (Helfman et al; Mikawa et al).[4,17] In present study at baseline all the groups were matched for haemodynamic parameters and did not show a significant intergroup difference. However, immediately after injection of test drug (1 minute after test drug) both the test groups showed a significant decrease in SBP (systolic blood pressure) and heart rate.

However, the group differences in haemodynamic controls were observed to be significantly differentiated from after intubation interval when all the parameters except heart rate (i.e. SBP, DBP and MAP) were observed to be behaving differently in different groups. For heart rate, Group 1 and Group 2 had values near throughout the study, though at most of time intervals Group 2 had lower mean values as compared to Group 1. Both the groups showed significantly lower mean values for all the parameters when compared to control group from after intubation interval till 8 minutes after intubation intervals except for mean SBP in Group 2 which was comparable to Group 3 at 4 and 6 minutes after intubation intervals. From 8 minutes after intubation interval onwards increase in mean haemodynamic parameters were observed in both the test groups whereas in control group the decrease continued. At 10 minutes after intubation interval, in all the three groups the mean haemodynamic parameters tended to return to baseline values.

Esmolol is an ultrashort acting β_1 cardio selective, β blocking agent with a short half-life (9 minutes) and its onset of action is very prompt. This is an ideal drug to keep the haemodynamic reflex during intubation under control.

On the other hand, labetalol has an onset of action 5 minutes, and has also emerged as a possible drug of choice for haemodynamic reflex attenuation during intubation. The generally described benefit of labetalol is that apart from attenuating the response to laryngoscopy and intubation, it also prevents perioperative cardiovascular events (Kim et al.; Chung et al; Inada et al; Ramnathan et al).[11-14] In present study, we observed that except for heart rate, for all the haemodynamic parameters, esmolol showed a quicker response by bringing about a significantly higher change as compared to labetalol and placebo groups.

If study focus on MAP only then we find that Labetalol can keep the reflex response near to baseline up to after intubation interval there after a steady but slow change in MAP was observed. Singh et al, in a study concluded that labetalol (0.25mg/kg) is better than esmolol (0.5mg/kg) in attenuating the haemodynamic response to laryngoscopy and intubation.[18]

In present study, we used esmolol (1.0mg/kg) against labetalol (0.4mg/kg) and attained almost similar response. The use of esmolol at 1 mg/kg (higher than used by Singh et al) and labetalol at 0.4 mg/kg (lower than used by Singh et al) helped us to keep the side effects such as bradycardia under control following the use of labetalol while achieving similar response as obtained by esmolol. O'Connor et al, have reported esmolol to be safer than labetalol in cases of acute dissection of aorta.[19]

However, Muzzi et al, reported equal efficacy of both the drugs in control of hypertension after intracranial surgery.[20] The findings in the present study are in accordance with the findings of Yun et al, who observed that 1mg/kg of esmolol given 2 minutes before intubation or 0.2mg/kg of labetalol given 4 minutes before intubation reduce increase of blood pressure and heart rate caused by adrenergic response following endotracheal intubation, significantly.[21]

CONCLUSION

On the basis of the findings of the study, both the drugs were found to be effective in attenuation of haemodynamic reflex without any side effects. Dose modification of the drugs from the previous studies was helpful in increasing the efficacy of Esmolol while decreasing the side effects of Labetalol. Further studies are recommended to substantiate the findings in the present study.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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