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RESEARCH ARTICLE

COMPARATIVE STUDY OF INTRAVENOUS 2% LIGNOCAINE VERSUS METOPROLOL TO ATTENUATE PRESSOR RESPONSE TO LARYNGOSCOPY

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ABSTRACT

Introduction: Laryngoscopy and endotracheal intubation are associated with reflex sympathetic stimulation known as pressor response. Transient haemodynamic instability, an inevitable outcome of laryngoscopy can have serious effects especially in patients with heart disease, hypertension which can cause major complications. We compared the attenuating effect of time – tested lignocaine versus metoprolol on the haemodynamic response to laryngoscopy and intubation in normotensive patients undergoing general anaesthesia for spine surgeries. **Method:** After the approval of the institutional ethical committee, written informed consent was obtained from each patient. 60 patients who satisfied the inclusion criteria were divided into two groups Group L (n= 30) received Inj. Lignocaine 1.5 mg/ kg IV before induction and Group M (n= 30) received Inj. Metoprolol 0.1 mg/ kg intravenous before induction HR, SBP, DBP, MAP were recorded at baseline sedation, post induction, at laryngoscopy and post intubation and 0.5, 1, 2, 5 and 10 minutes post intubation. **Statistical Analysis:** Data was analysed using Paired Students 't' test for intra group (within the group) variation, Unpaired student's 't' test for inter group (between the 2 groups) variation. Analysis of variance (ANOVA) for comparison between different baseline variables (age, weight, HR, SBP, DBP, MAP and RPP). Value of $P < 0.05$ was considered significant. **Results:** In lignocaine group, there was a significant increase in heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product in response to laryngoscopy and intubation. Values continued to remain high even after 5 minutes of post intubation as compared to metoprolol group. **Conclusion:** Intravenous metoprolol 0.1 mg/ kg given 5 minutes prior to laryngoscopy and intubation successfully attenuated the pressor response to laryngoscopy and intubation. In addition, it was found to be safer and more effective than intravenous lignocaine 2%.

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INTRODUCTION

Laryngoscopy and endotracheal intubation, which are a basic and integral part of general anaesthesia (GA), are associated with a sympathetic reflex provoked by stimulation of epipharynx and laryngopharynx, manifested by tachycardia and hypertension (Kanchi *et al*., 2011). This pressor response probably has no consequence in healthy individuals but has a potential to cause major complications such as myocardial ischaemia, ventricular arrythmia, left ventricular failure and cerebral haemorrhage (Kanchi *et al*., 2011; Vyankatesh *et al*., 2012). This response is harmful and needs to be attenuated.

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Different techniques have been shown to modify the pressor response effect of oral clonidine was compared with intravenous lignocaine on haemodynamic effects of laryngoscopy and intubation (Vyankatesh *et al*., 2012). However, we are comparing the attenuating effect of intravenous metoprolol with IV lignocaine and specifically in spine surgery cases to find safe, rapid, effective alternative to various pharmacological techniques to blunt cardiovascular response to laryngoscopy and intubation.

MATERIALS AND METHODS

A prospective, comparative randomised double blind study was conducted with sixty adult patients after obtaining Institutional Ethical Committee approval. These patients who were posted for elective spine surgeries were randomly allocated into two groups of 30 each after obtaining a written

informed consent from the patients using computes generated randomisation. Patients were randomly allocated to one of the two groups:

Group L or Group M

Group L: Received Inj. Lignocaine (preservative free) 1.5 mg/kg IV 5 minutes before induction. (n= 30)

Group M: Received Inj. Metoprolol 0.1 mg/kg IV 5 minutes before induction. (n= 30)

All adult patients aged 18 to 60 years, belonging to ASA I and II undergoing elective spine surgeries were included in this study after taking written informed consent from the patients. Patients with predicted difficult intubation more than one attempt for laryngoscopy and intubation, duration of laryngoscopy more than 15 seconds, on pre-operative β – blocker therapy, systemic illness such as hypertension, coronary artery disease were excluded from the study. Patients allergic to lignocaine or other local anaesthetics of amide group were also excluded from the study. After a detailed pre-anaesthetic assessment and required investigations, all patients in both groups underwent the same plan of GA. All the patients ere kept nil by mouth for 6 hours. On the day of surgery patients received Inj. Glycopyrrolate 4 µg/kg IV 10 minutes prior to surgery. Starvation and consent confirmed. Monitoring included electrocardiogram, pulse oximetry and non-invasive BP. Patients in both the groups received Inj. Ranitidine 1 mg/kg and Inj. Ondansetron 0.08 mg/kg IV. After recording the baseline parameters patients received IV sedation in the form of Inj. Pentazocine 0.6 mg/kg IV and Inj. Midazolam 0.04 mg/kg IV.

After giving sedation, pulse, systolic blood pressure, diastolic blood pressure were recorded. Patients were given intravenously 10 ml solution of study drug 5 minutes before induction. This solution consisted of either 1.5 mg/kg lignocaine or 0.1 mg/kg of metoprolol diluted with NS to 10 ml. Drug preparation were made before hand by medical personnel not involved in the study (observer) and identities were kept unknown to the investigator using it, thus making the study double blind. The assignment code was not made known to the investigator until the completion of the study. The heart rate, blood pressure and SPO_2 was continuously monitored. Meanwhile patients were pre-oxygenated with 100% O_2 for 5 minutes and then all patients were induced with thiopentone sodium. In a dose of 5 mg/kg neuromuscular blockade was achieved by injection Vecuronium bromide 0.1 mg/kg. laryngoscopy and intubation were performed by a single operator in all the cases. HR, SBP, DBP, MAP were noted at laryngoscopy and at 0.5, 1, 2, 5 and 10 minutes post intubation. Anaesthesia was maintained with oxygen, nitrous oxide and top-up doses of Inj. Vecuronium. At the end of surgery neuromuscular blockade was reversed with injection neostigmine 0.05 mg/kg IV and Inj. Glycopyrrolate 8 µg/kg IV. We calculated mean and standard deviation for each parameter in both groups. Paired and Unpaired Student's 't' test along with analysis of variance (ANOVA) and Chi square test were used to analyse the data.

RESULTS

Both the groups were comparable with respect to age and weight of the patient (Table 1).

Furthermore, there was no significant difference between the two groups with respect to baseline pulse, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product (RPP). Base line mean pulse rate in Group L was 82.07 ± 10.67 per minute and in Group M was 78.10 ± 9.78 per minute. The post induction value of mean pulse rate in Group L was 88.97 ± 10.61 and in Group M was 69.13 ± 9.38 per minute. After induction there was significant increase in pulse rate in Group L whereas Group M showed a significant fall. At laryngoscopy, mean pulse rate was 92.27 ± 10.94 per minute in Group L and 76.33 ± 10.03 per minute in Group M. the rise in mean pulse rate in Group L was highly significant with baseline and post induction values. The difference was statistically significant between the two groups. Post intubation, data was compared between the two groups at 0.5, 1, 2, 5, 10 minutes interval. The difference was statistically highly significant between the two groups and also with respect to base line values.

The mean value of SBP between Group L and M is statistically significant only at 1 minute post intubation. Baseline mean SBP in Group L was 125.07 ± 9.32 mmHg and in Group M was 128.03 ± 7.31 mmHg. The post induction value of mean SBP was 116.47 ± 10.07 mmHg for Group L and 115.07 ± 7.4 mmHg for Group M. After induction there was significant fall in mean SBP more so in Group M than Group L but the intergroup statistical difference was insignificant ($P > 0.05$). At laryngoscopy, mean SBP in Group L was 128.0 ± 9.36 mmHg and Group M was 129.9 ± 7.55 mmHg. The statistical difference between the two groups was insignificant. Post intubation SBP was compared between the two groups at 0.5, 1.0, 2.0, 5.0 and 10.0 minutes intervals. Peak values were observed only at 1.0 minute post intubation which were 141.13 ± 9.64 mmHg for Group L and 132.03 ± 7.40 mmHg for Group M. The data between the two groups was highly significant at 1 minute post intubation. Thus, difference in SBP between the two groups was statistically insignificant throughout except at 1.0 minute post intubation ($P < 0.05$).

The baseline mean DBP in Group L was 80.0 ± 5.33 mmHg and Group M was 81.93 ± 5.46 mmHg. Post induction in diastolic BP in Group L was 72.93 ± 6.11 mmHg and Group M was 74.93 ±5.84 mmHg. After induction, there was a significant fall in DBP more so in Group M than in Group L, but intergroup statistical difference was insignificant. At laryngoscopy, the DBP in Group L was 79.0 ± 6.02 mmHg and Group M was 80.03 ± 5.60 mmHg. The statistical difference between the two groups was insignificant. Post intubation, peak value for mean DBP were observed at 1 minute interval in both the groups. Mean value for Group L was 93.87 ± 5.90 mmHg and for Group M was 85.0 ± 5.57 mmHg. Thus, the difference in DBP between the two groups was statistically was insignificant till laryngoscopy and statistically significant difference ($P < 0.05$) was observed from 0.5 minute post intubation onwards. The baseline mean MAP in group L was 95.04 ± 5.32 mmHg and group M was 97.30 ± 4.08 mmHg. Post induction mean MAP in group L was 87.44 ± 5.60 mmHg and in group M was 88.31 ± 4.43 mmHg. After induction, there was significant fall in MAP more so group M than in group L, but intergroup statistical difference was insignificant. At laryngoscopy, the statistical difference between the two groups was not significant. Post intubation, peak values were observed at 1 minute interval in both groups, mean MAP was 109.62 ± 5.31 mmHg (group L) and 100.68 ± 4.14 mmHg (group M).

Table 1. Group wise distribution of various variables in the subjects

Variables		Group		ANOVA applied		
		Lignocaine	Metoprolol	F	P	Significance
AGE	Mean	41.0	38.07	0.0719	0.360	NS
	SD	11.89	12.72			
WEIGHT	Mean	55.97	52.80	0.889	0.246	NS
	SD	10.60	10.33			
BL-P	Mean	82.07	78.10	0.641	0.139	NS
	SD	10.67	9.78			
BL-SBP	Mean	125.07	128.03	0.196	0.175	NS
	SD	9.32	7.31			
BL-DBP	Mean	80.0	81.93	0.727	0.198	NS
	SD	5.83	5.46			
BL-MAP	Mean	95.04	97.3	0.159	0.070	NS
	SD	5.32	4.08			
BL-RPP	Mean	10259.3	9998.97	0.596	0.484	NS
	SD	1501.74	1359.62			

Note: NS: Difference is not significant (P > 0.05)
S: Difference is significant (P < 0.05)
Abbreviations used in the following sections:
BL = Baseline
AS = After Sedation
PL = Post induction
AL = At laryngoscopy
ANOVA = Analysis of Variance

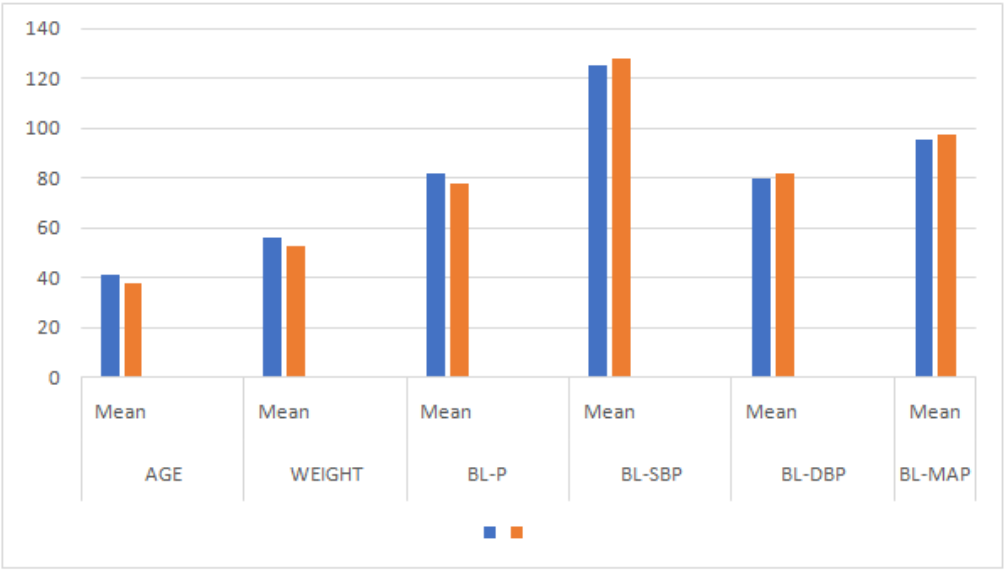


Table 2. Distribution of Pulse Rate at different time intervals between lignocaine and metoprolol groups

Pulse Per minute	Group			
	Lignocaine	Metoprolol	P value	Significance
Base line	82.07 ± 10.67	78.10± 9.78	0.139	NS
After Sedation	79.93 ± 10.40	73.90± 9.57	0.023	S
Post induction	88.97± 10.61	69.13± 9.38	2.18E – 10	S
After Laryngoscopy	92.27± 10.94	76.33± 10.03	2E – 07	S
0.5 minute	95.13± 10.40	80.00± 10.00	4E –07	S
1 minute	101.97± 10.70	82.00± 10.37	8E – 10	S
2 minutes	94.17± 11.10	79.93± 9.97	2E – 06	S
5 minutes	85.0± 10.60	74.97± 9.61	3E – 04	S
10 minutes	82.67± 10.59	72.97± 9.60	4E – 04	S

Note: NS: Difference is not significant (P > 0.05)
S: Difference is significant (P < 0.05)

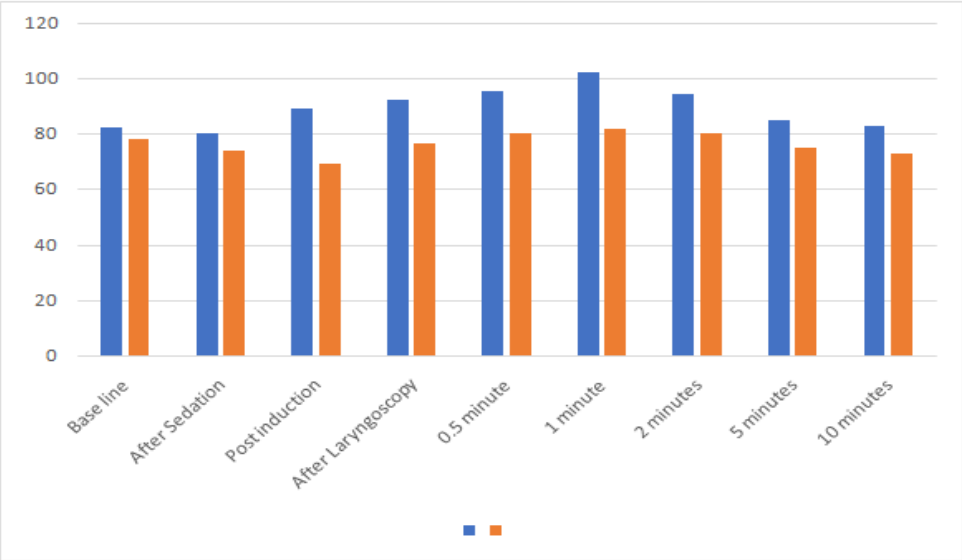


Table 3. Distribution of SBP at different time intervals

SBP mmHg	Group			
	Lignocaine	**Metoprolol**	**P value**	**Significance**
Base line	125.07 ± 9.32	128.03 ± 7.31	0.1754	NS
After Sedation	121.03 ± 9.34	124.77 ± 7.73	0.097	NS
Post induction	116.47 ± 10.07	115.07 ± 7.40	0.542	NS
After Laryngoscopy	128.0 ± 9.36	129.9 ± 7.55	0.351	NS
0.5 minute	134.03 ± 9.38	129.87 ± 7.06	0.06	NS
1 minute	141.13 ± 9.64	132.03 ± 7.40	1E – 04	S
2 minutes	131.0 ± 9.41	129.0 ± 7.37	0.355	NS
5 minutes	126.0 ± 9.39	126.03 ± 7.28	1.00	NS
10 minutes	124.03 ± 9.32	123.0 ± 7.51	0.637	NS

Note: NS: Difference is not significant (P > 0.05)
S: Difference is significant (P < 0.05)

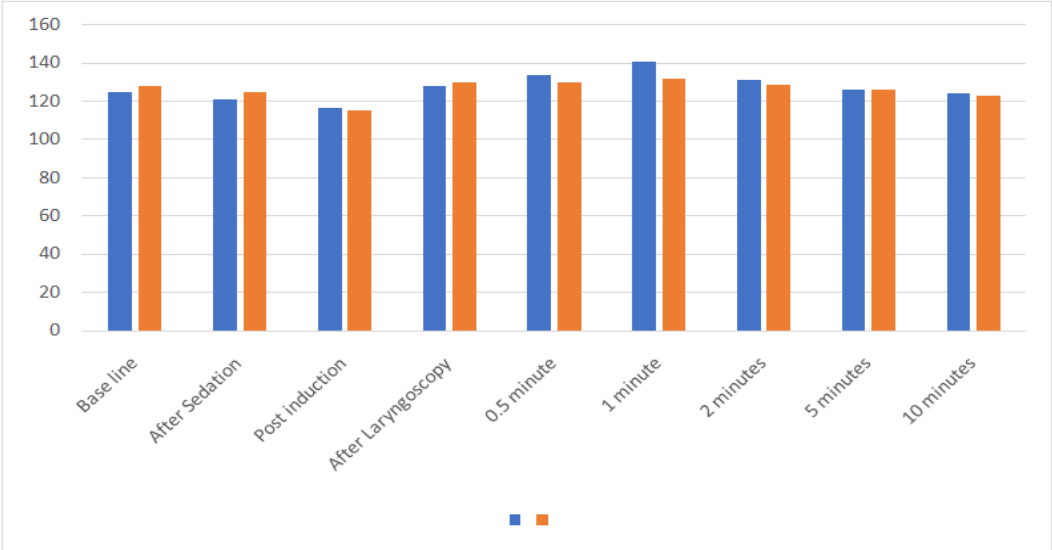


Table 4. Distribution of DBP at different time intervals

DBP mmHg	Group			
	Lignocaine	**Metoprolol**	**P value**	**Significance**
Base line	80.0± 5.83	81.93± 5.46	0.198	NS
After Sedation	77.0± 5.85	78.97± 5.57	0.181	NS
Post induction	72.93± 6.11	74.93± 5.84	0.20	NS
After Laryngoscopy	79.0± 6.02	80.03± 5.60	0.494	NS
0.5 minute	88.97± 6.03	84.0± 5.56	0.002	S
1 minute	93.87± 5.90	85.0± 5.57	1E – 07	S
2 minutes	90.9± 6.13	83.0± 5.56	2E – 06	S
5 minutes	84.0± 5.82	80.0± 5.57	0.008	S
10 minutes	80.97± 6.04	77.23± 6.54	0.025	S

Note: NS: Difference is not significant (P > 0.05)
S: Difference is significant (P < 0.05)

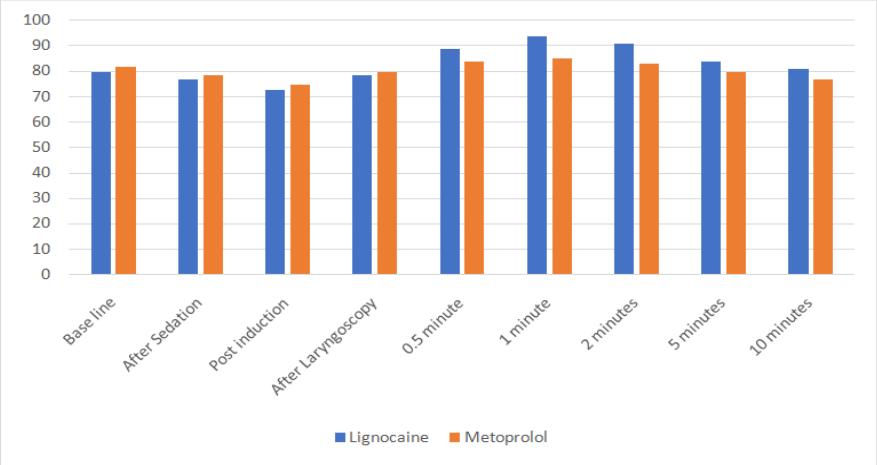
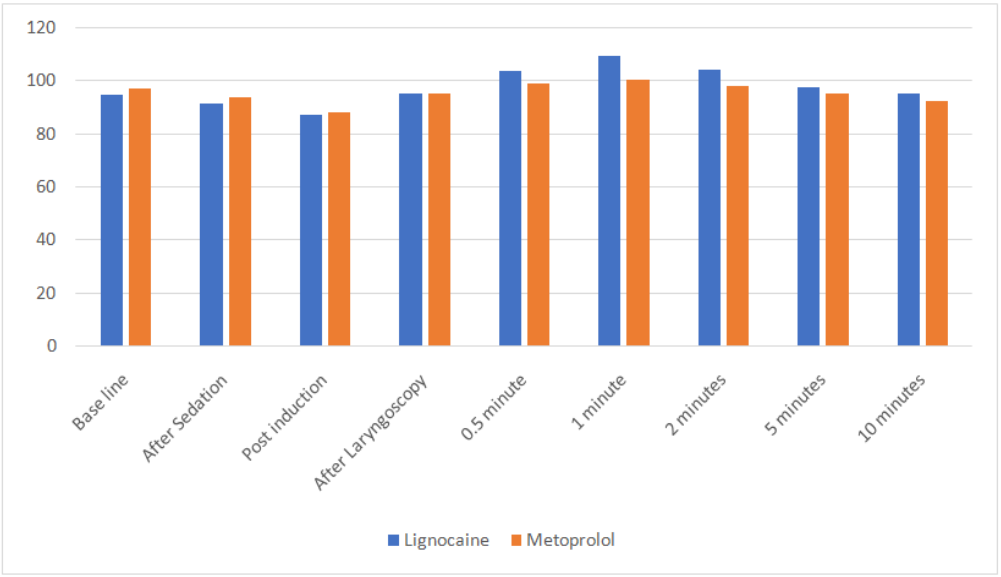


Table 5. Distribution of MAP at different time intervals

MAP mmHg	Group			
	Lignocaine	**Metoprolol**	**P value**	**Significance**
Base line	95.044± 5.32	97.30± 4.08	0.071	NS
After Sedation	91.66± 5.41	94.23± 4.30	0.045	NS
Post induction	87.44± 5.60	88.31± 4.43	0.513	NS
After Laryngoscopy	95.32± 5.33	95.32± 4.20	1.0	NS
0.5 minute	103.99± 5.37	99.29± 4.07	3.2E-04	NS
1 minute	109.62± 5.31	100.68± 4.14	1.03E-09	S
2 minutes	104.28± 5.43	98.33± 4.15	1.13E-05	NS
5 minutes	98.03± 5.27	95.34± 4.19	0.033	NS
10 minutes	95.32± 5.34	92.49± 4.72	0.034	NS

Note: NS: Difference is not significant (p>0.005)
S: Difference is significant (p<0.005)



This difference was statistically highly significant. Thus, difference in mean MAP between the two groups was statistically significant throughout post intubation period. The baseline mean RPP in Group L was 10259.30 ± 1501.74 and in Group M was 9998.87 ± 1359.62. Post induction mean RPP was 10356.80 ± 1482.8 (Group L) and 7962.63 ± 1230.35 (Group M). the difference in RPP between the groups was statistically significant. At laryngoscopy the difference between the two groups in RPP was statistically significant. Post intubation, peak value for Group L was 14385.33 ± 1746.70 and Group M was 10822.23 ± 1452.12 at 1 minute interval. This difference was statistically highly significant.

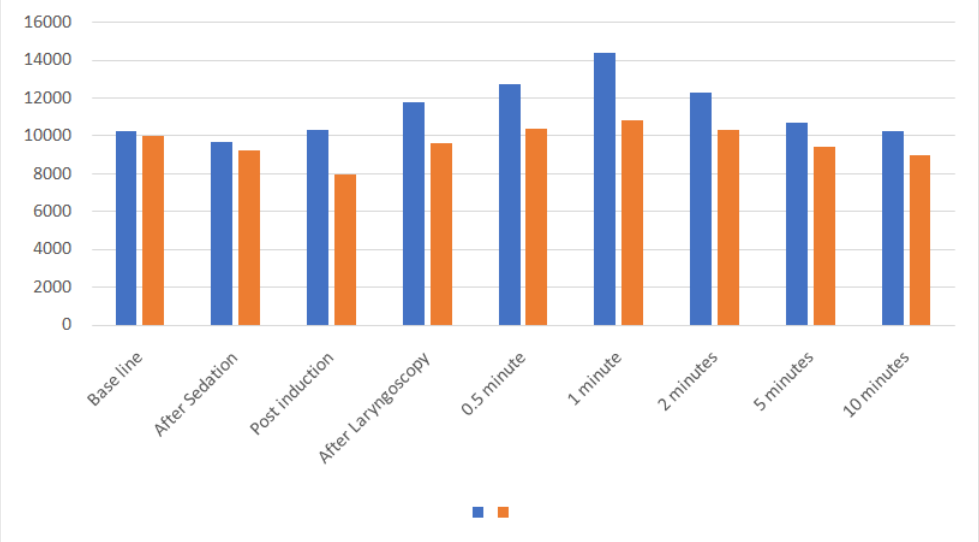
DISCUSSION

Various drugs have been used to reduce pressor response such as topical anaesthesia with lignocaine, narcotics like fentanyl, β – blockers like propranolol and esmolol, calcium channel blockers like verapamil and diltiazem. The pressor response is believed to be a reflex sympathetic response to the mechanical stimulation of pharynx and larynx and is associated with a significant increase in serum levels of epinephrine and nor – epinephrine (Montazeri *et al*., 2011). Lignocaine, a time tastetested drug for attenuation of pressor response to laryngoscopy and intubation, is used in the treatment of

Table 6. Distribution of RPP at different time intervals

RPP	Group			
	Lignocaine	**Metoprolol**	**P value**	**Significance**
Base line	10259.30± 1501.74	9998.87± 1359.62	0.484	NS
After Sedation	9671.57± 1441.10	9222.70± 1330.42	0.215	NS
Post induction	10356.80± 1482.80	7962.63± 1230.35	6.2E – 09	S
After Laryngoscopy	11803.10± 1602.30	9613.70± 1395.34	5.22E – 07	S
0.5 minute	12743.27± 1592.90	10392.3± 1399.6	1.03E – 07	S
1 minute	14385.33± 1746.70	10822.23± 1451.12	6.2E – 12	S
2 minutes	12333.10± 1643.10	10295.93± 1383.69	2.77E – 06	S
5 minutes	10703.63± 1511.50	9452.10± 1342.63	0.0012	S
10 minutes	10248.63± 1483.30	8983.03± 1342.75	0.001	S

Note: NS: Difference is not significant (p>0.005)
S: Difference is significant (p<0.005)



patients with ventricular dysrhythmias and as prophylaxis in the treatment of ventricular tachyarrhythmias especially those with myocardial infarction and mechanical irritation of cardia (Gurulingappa, 2012). AJ Coleman and E. Jordan (1980) studied IV metoprolol for attenuation of pressor response to induction of anaesthesia laryngoscopy and intubation of trachea. 42 patients were divided into 3 groups: Group 1 received placebo, Group 2 received 2 mg metoprolol IV and Group 3 received 4 mg metoprolol IV prior to induction of anaesthesia. In placebo group there was significant increase in mean heart rate and BP values whereas HR and BP was significantly reduced in Group 2 and 3 at the time of laryngoscopy and intubation as compared with Group 1.

They also found higher doses (4 mg) had no added effect. J. Magnusson; O. Werner (1983) *et al* in 1983 studied metoprolol and stress responses to microlaryngoscopy and found that metoprolol decreased HR and BP both before and during anaesthesia. Similar study was conducted again by J. Magnusson and O. Werner in 1986. They studied haemodynamic effect of pre-treatment with metoprolol in hypertensive patients undergoing surgery. It was found that metoprolol significantly reduced HR and BP during anaesthesia. It also improved haemodynamic stability in hypertensive patients. The findings of the present study corelates well with the findings of Coleman and Jordan (Coleman, 1980) study and two other studies conducted by J. Magnusson and O. Werner (Robert, 1979; Derbyshire *et al*., 2002) as regards, better control of mean HR and BP in response to laryngoscopy and intubation in patients pre-treated with IV metoprolol prior to induction.

Stanley Tam in 1987 studied optimal time of injection of IV lignocaine before intubation and conducted that IV lignocaine 1.5 mg/kg attenuated pressor response when given 3 minutes before intubation and offered no protection against post intubation haemodynamic changes when given at 1, 2 or 5 minutes before intubation. R. K. Stoelting (1979) studied and conducted that short duration of direct laryngoscopy ideally less than 15 seconds is extremely important in minimising the magnitude and duration of haemodynamic responses to laryngoscopy and intubation. In this study, both the groups were comparable as far as age, sex and weight of these patients were concerned. Also intergroup baseline pulse rate, SBP, DBP, MAP and RPP were also comparable. Further after induction, there was statistically significant difference in pulse rate and rate pressure product values between the two groups. At laryngoscopy, there was rise in mean pulse rate, MAP and RPR (from baseline) in Group L and fall in Group M. SBP showed rise in both the groups from respective baseline values, but percentage of rise was more in Group L as compared to Group M. Post-intubation we monitored the cardiovascular changes in both the groups at 0.5, 1, 2, 5 and 10 minutes. At 1 minute post-intubation, there was a rise from baseline values in all parameters. But the percentage rise from respective baseline values was significantly less in Group M. Thus, results obtained are similar to earlier study conducted by Stanley Tam (Stanley Tam, 1987). At 5 minutes post-intubation, the cardiovascular parameters were still higher than baseline values in Group L and were significantly lower than baseline in Group M, suggesting superior attenuation of pressor response by metoprolol as compared to lignocaine. At 10 minutes post-intubation, mean values of pulse rate, DBP and

MAP showed a rise from baseline values in Group L i. e these values had still not touched baseline values even 10 minutes post-intubation whereas in Group M, these parameters were lower than baseline. The results obtained in our study were comparable to studies conducted by J. Magnusson and O. Werner (Magnusson, 1983; Magnusson, 1986) with respect to haemodynamic effect of pre-treatment with metoprolol in patients undergoing surgery. Thus, pre-treatment with cardio selective β-blocker improved haemodynamic stability during anaesthesia and also decreased anaesthesia requirement for maintenance. Thus, IV metoprolol is safe, convenient effective and economical method of attenuation of pressor response. In this study we did not observe any major side effects such as bradycardia or significant hypotension.

Conclusion

We concluded that attenuating effect of IV metoprolol 0.1 mg/kg 10 minutes prior to laryngoscopy and intubation is far more superior to lignocaine both in controlling the HR and BP. In addition, intravenous metoprolol was found to be safe effective and economical method for attenuation pressor response to laryngoscopy and intubation.

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