ANAESTHESIA, PAIN & INTENSIVE CARE
www.apicareonline.com

ORIGINAL ARTICLE

A comparison between intravenous metoprolol and labetalol in prevention of cardiovascular stress response to laryngoscopy and intubation

Nishee R Swami, MBBS, DNB[1], Vaishalee K Badhe, MBBS, DNB[1], Vaishali V. Deshpande, MD, DA[2], Vaijayanti K. Badhe, MD, DA[3], Shidhaye Ramchandra Vinayak, MD, DA[3]

[1]Assistant Professor, [3]Professor

Department of Anesthesiology and Critical Care, Pravara Institute of Medical Sciences, Loni 413736 (India)

[2]Professor / Head, Department of Anesthesiology, Seth Nandlal Dhoot Hospital, Aurangabad (India)

Correspondence: Dr. Vaishalee K. Badhe, MBBS, DNB, Assistent Professor, Department of Anesthesiology and Critical Care, Pravara Institute of Medical Sciences, Loni 413736 (India); E-mail: drvaishalee@rediffmail.com

Received: 17 May 2018
Reviewed: 25 Jun 2018
Corrected: 26 Jun 2018
Accepted: 30 Jun 2018

ABSTRACT

Introduction: A prospective, randomized, double blind, clinical study was designed to compare intravenous metoprolol 30 µg/kg versus intravenous labetalol 0.2 mg/kg single dose given 5 min prior to intubation in for prevention of cardiovascular stress response to laryngoscopy and intubation in patients undergoing spine surgeries under general anesthesia.

Methodology: Sixty ASA grade I patients of either sex , comprising age group of 25-50 years , undergoing elective spine surgeries under general anesthesia were randomly distributed in two equal groups. Inj metoprolol hydrochloride 30 µg/kg in Group M and inj labetalol 0.2 mg/kg in Group L respectively were given intravenously 5 min prior to induction. Heart rate, systolic, diastolic and MBP recorded at different time intervals before and after intubation.

Results: Significant rise noted in heart rate, systolic, diastolic and MBP immediately after intubation in both groups though less in Group L that remained up to 2 min; returned to baseline between 2 to 5 min and became significantly lower than baseline at 5 min and onwards.

Conclusion: Labetalol is superior to metoprolol in attenuating the cardiovascular stress response to laryngoscopy and intubation.

Key words: Labetalol, Metoprolol, Presser response, Laryngoscopy, Tracheal intubation

Citation: Swami NR, Badhe VK, Deshpande VV, Badhe VK, Shidhaye RV. A comparison between intravenous metoprolol and labetalol in prevention of cardiovascular stress response to laryngoscopy and intubation. Anaesth Pain & Intensive Care 2018;22(2):180-186

INTRODUCTION

The frequent occurrence of cardiovascular responses to laryngoscopy and tracheal intubation has attracted the attention of anesthesiologists for several years. Marked circulatory effects of laryngoscopy and tracheal intubation like reflex tachycardia (rise up to 20%) and hypertension (rise up to 40-50%) is encountered during intubation[1]. A number of responses to intubation occur, including hypertension, tachycardia, arrhythmia, raised intracranial and intraocular pressure. The cardiovascular responses may have serious consequences including myocardial ischemia, dysrrthymias, pulmonary edema, sudden left ventricular failure, cerebrovascular hemorrhage and at times even cardiac arrest.[2] These changes are tolerated quite well by healthy patients, because of their transient nature and there are no grave sequelae. However patients suffering from coronary artery disease, hypertension, valvular heart disease, stroke, penetrating eye lesion, intracranial lesions are not able to withstand them. In principle this response

can be modified by using methods which act locally, centrally or peripherally. Cardiovascular response to laryngoscopy and intubation is a reflex phenomenon with afferent stimuli carried over glossopharyngeal and vagal pathways which activate the suprategmental and hypothalamic sympathetic centers to cause peripheral sympathoadrenal response with release of adrenaline and nor adrenaline. The elevation of blood pressure is associated with norepinephrine release whereas changes in heart rate are epinephrine related.[3] Norepinephrine levels may increase on laryngoscopy and intubation from (60-310 pg/ml) and continue to rise for 4 to 8 min, Epinephrine levels may raise 4 times from 70 to 280 pg/ml [4]. Above data indicates role of sympathoadrenergic receptor blockers (α and β blockers) in attenuating the cardiovascular stress response to intubation by attenuating the effects of catecholamines with the act of laryngoscopy and intubation. Beta blockers (e.g. etoprolol, esmolol.[5,6] labetalol[7,8] or landiolol[9]) with bradycardia, antihypertensive, antiarrythmic and anti-ischemic properties have found a role in preventing cardiovascular responses to intubation. Metoprolol is selective β_1 blocker and labetalol is selective α_1 and non-selective β blocker. Several studies on metoprolol[10-13] and labetalol[7,8,14-16] showed their effectiveness in attenuating the cardiovascular stress response to intubation. Additionally metoprolol and Labetalol found role in providing controlled hypotension to provide bloodless field as required in spine surgeries .Though researchers have compared esmolol and different other drugs with metoprolol and labetalol[10,11,14, 16] we couldn't find studies comparing metoprolol and labetalol in prevention of cardiovascular stress response to laryngoscopy and intubation. With this background we designed this prospective, randomized, double blind, comparative clinical study to assess the degree of effectiveness of IV metoprolol 30 μg/kg versus IV labetalol 0.2 mg/kg single dose given 5 min prior to intubation in prevention of cardiovascular stress response to laryngoscopy and intubation in patients undergoing spine surgeries under general anesthesia.

METHODOLOGY

After approval from the hospital ethical committee, a prospective randomized double blind clinical study was conducted on 60 ASA grade I patients (30 in each group) of either sex , comprising age group of 25-50 y, undergoing elective spine surgeries under general anesthesia. Excluding criteria were: systemic disorder like diabetes mellitus, hypertension, heart disease, having bradycardia or heart block, respiratory disease like asthma, COPD, having history of any drug allergy and patients not willing to participate. After valid informed written consent selected patients were randomly allocated to two groups.

Group M: Inj metoprolol hydrochloride 30 μg/kg intravenously 5 min prior to induction

Group L: Inj labetalol 0.2 mg/kg intravenously 5 min prior to induction

Method of Randomization: Method of randomization was blocked randomization. Randomization was carried out based on blocking. A total of 15 blocks of size 4 with treatment allocation of 1:1 for Group M and Group L were created with the help of computer software. Coded envelopes (fifteen) were used and each envelope was used for four patients leading to random assignment of one subject to one group.

Sample size calculation was based on previous studies.[14] Sample size was estimated to be 46 (23 in each group) to get the difference of 10 % in mean arterial pressure (MAP) measured at intubation in Group L and Group M using a two sample *t* test, assuming a two sided type I error of 5% ($\alpha = 0.05$) and power at 80 ($\beta = 0.20$)

All patients received tablet diazepam 10 mg orally on the night prior to surgery. After conforming nil by mouth status and written informed consent every patient was taken to operation table. Intravenous (IV) line was secured with 20G Angiocath™ cannula, ringer lactate drip was started and midazolam 0.02 mg/kg and pentazocine 0.3 mg/kg was injected IV as premedication.

Multipara monitor (Vista 120™, Drager, Germany) measuring pulse rate, ECG, noninvasive blood pressure (NIBP), capnography ($EtCO_{2)}$ and oxygen saturation ($SO_{2)}$ was applied. Heart rate and blood pressure [systolic blood pressure (SBP), diastolic blood pressure (DBP) and MAP] were measured at base line. (10 min prior to induction). Inj metoprolol 30 μg/kg and inj labetalol 0.2 mg/kg were given intravenously to respective group patients 5 min prior to induction by an anesthetist who was blinded for the study. Preoxygenation was done with 100% oxygen for 5 min. Induction of anesthesia was done with inj thiopentone 5 mg/kg. Intubation was facilitated with inj suxamethonium hydrochloride 2 mg/kg. Laryngoscopy and endotracheal intubation was done by the same anesthetist trained in the technique for 2 y. Anesthesia was maintained with nitrous oxide and oxygen (50:50%) + isoflurane (0.6%). Muscle

relaxation was achieved using inj atracurium (0.5 mg/kg) with subsequent boluses of (0.1 mg/kg) as per requirement. Mechanical ventilation was done targeting $EtCO_2$ 32-36 mmHg.

Neuromuscular block was reversed at the end of surgery with inj. neostigmine 0.05 – 0.06 mg/kg and inj. glycopyrrolate 0.008-0.01 mg/kg. Heart rate, SBP, DBP, MAP (non-invasive) were measured at 10 min and 5 min prior to induction, immediately after induction, during intubation (0 min), at 01, 02, 3, 5,10, 30 and 60 min post intubation by the anesthetists who were blinded to the drug given. No surgical stimulation was allowed in first 10 min. Cases, where intubation was difficult and that took more than 20 sec and required more than one attempt, were excluded from the study.

Intra operative oozing and clarity of surgical field was assessed by oral questionnaire to surgeon. Upon completion of surgery patients were extubated after reversal of neuromuscular block and were observed for 8 hr in the postoperative period for side effects like bradycardia, hypotension, nausea, vomiting, difficult respiration.

Appropriate treatment for side effects was planned. For severe bradycardia atropine 7 μg/kg was given. For persistent bradycardia isoprenaline infusion 2-25 μg/min was kept ready. Hypotension was treated by fluid challenge. Vasopressors like dopamine 5-15 μg/kg /min was given if required. Increase in airway resistance if any was treated with terbutaline inhalation.

Statistical analysis:

All the observations for the above mentioned parameters were collected in a master chart. Demography parameters were analyzed by Student's unpaired-t test. Categorical data was analyzed by Chi square test. For finding the statistical significance between the two groups unpaired-t test was applied to ascertain the pattern and magnitude of differences. Paired-t test was applied for intra group comparison. A p value of < 0.05 was considered as significant and p value of < 0.01 was considered as highly significant.

RESULTS

The patients in both the groups were comparable with respect to age, sex, height, weight, duration of surgery and time required for intubation. (Table 1).

Table 1: Demographic characteristics

Parameter	Group M Mean ± SD	Group L Mean ± SD	P value
Age (y)	33 ± 5.40	33.5 ± 5.32	> 0.05
Weight (Kg)	54.26 ± 3.46	54.4 ± 3.60	
Height (cm)	159.83 ± 3.16	159.63 ± 2.89	
Sex (M/F)	15/15	15/15	
Duration of surgery (min)	95.66 ± 9.25	96.16 ± 8.57	
Time required for intubation (sec)	11.76 ± 1.95	12 ± 1.87	

p-value significant at < 0.05

Table 2-A shows the hemodynamic parameters at different time intervals in both groups and Table 2-B shows the percent change in the hemodynamic parameters at different time intervals in both groups. There was no significant difference in heart rate after premedication and induction in both groups.

The maximum change in the heart rate was seen immediately after intubation in both groups. The rise in heart rate remained up to 2 min ; returned to baseline between 2 to 5 min and became significantly lower than baseline at 5 min and onwards . However the difference between the two groups at all the time intervals was not significant. No group showed arrhythmias following intubation. Fall in SBP clinically not significant to require treatment was observed in both groups as a result of induction of anesthesia. It was more in Group L. There was a significant rise in SBP in both the groups at intubation, 1 min and 2 min post intubation but the rise was less in Group L. This rise in SBP at intubation remained up to 2 min post intubation and returned to baseline between 2 to 5 min post intubation and became significantly lower than baseline thereafter. Both groups were comparable regarding systolic BP at 2 min post intubation and thereafter though initial rise at intubation was less in Group L. Similarly there was decrease in DBP and MAP at induction in both groups, more being in Group L. There was rise in DBP and MAP in both groups at intubation, 1 min and 2 min post intubation. The rise in DBP and MAP was more in Group M as compared to Group L till 2 min post intubation. At 5 min and onwards DBP and MAP were significantly less than the baseline values in both groups. DBP and MAP were lower in Group L as compared to Group M at 10, 30 and 60 min post intubation. Significant hypertension or hypotension (> 30% change from baseline) was not found in any group at intubation. One patient

Table 2-A: Hemodynamic parameters

Time	HR (beats / min)		SBP (mmHg)		DBP (mmHg)		MBP (mmHg)	
	Group M Mean ± SD	Group L Mean ± SD	Group M Mean ± SD	Group L Mean ± SD	Group M Mean ± SD	Group L Mean ± SD	Group M Mean ± SD	Group L Mean ± SD
10 Min before induction (Base Line)	82.46 ± 13.08	83.3 ± 12.96$	114.53 ± 8.88	114.73 ± 8.49$	73.73 ± 5.29	73.7 ± 5.27$	87.4 ± 6.27	87.43 ± 6.08$
5 min before induction (After premedication)	80.93 ± 13.85*	81.76 ± 12.83*$	112.9 ± 9.50*	113.1 ± 8.39$*	72.43 ± 7.01*	72.13 ± 5.8$*	85.53 ± 7.25**	86.06 ± 5.77$**
Immediately after Induction	83.66 ± 13.332*	84.9 ± 12.43*$	105 ± 8.2***	100 ± 6$$***	67 ± 5***	64 ± 4$$***	79.43 ± 5.70***	76.16 ± 4.83$$***
During intubation (0 min)	88.6 ± 14.00***	91.46 ± 14.18 $***	132.43 ± 9.03 ***	123.93 ± 8.97$$$***	85.03 ± 5.10***	79.26 ± 5.40$$$***	100.76 ± 6.03***	94.16 ± 6.22$$$***
1 min post-intubation	86.9 ± 13.68***	89.43 ± 14.06$***	128.5 ± 9.0***	121.5 ± 8.93$$$***	82.2 ± 6.00***	77.8 ± 5.05$$$***	97.53 ± 6.54***	92.37 ± 6.05$$$***
2 min post intubation	83.9 ± 12.97***	85.43 ± 12.89$***	121.2 ± 8.83***	117.9 ± 8.87$***	77.93 ± 4.55***	75.3 ± 5.52$***	92.33 ± 5.52***	89.6 ± 6.35$***
5 min post intubation	79.53 ± 13.04***	81.9 ± 13.44$***	112.5 ± 8.78***	112.1 ± 8.17$***	72 ± 5.23***	71 ± 5.06$***	85.53 ± 6.18***	84.77 ± 5.82$***
10 min post intubation	77.36 ± 12.89***	80.13 ± 12.09$***	104.6 ± 6.25***	101.77 ± 7.62$***	63.06 ± 3.67***	61.4 ± 4.36$$***	77.6 ± 3.97***	74.9 ± 5.29$$***
30 min post intubation	72.73 ± 11.57***	75.73 ± 11.71$***	103.03 ± 5.67***	100.4 ± 6.13$***	63.3 ± 3.81***	61.2 ± 4.40***$$	76.5 ± 3.73***	74.26 ± 4.75$$***
60 min post intubation	72.46 ± 11.01***	75.4 ± 11.63$***	102.03 ± 5.15***	100.47 ± 6.01$***	63.13 ± 3.81***	61.6 ± 4.24$***	76.7 ± 3.59***	74.23 ± 4.57$$***

*p-value > 0.05 ** p-value significant at 0.05 *** p-value significant at 0.01

When intra group heart rate variation at various time inter-valsvas compared by using student paired t test with two tailed distribution

$p-value > 0.05 $$ p-value significant at 0.05 $$$ p-value significant at 0.01

When intergroup heart rate variation at various time inter-valsalvas compared by using student unpaired t test with two tailed distribution

in Group M developed bradycardia up to 48 beats/ min during reversal of residual muscle relaxation with neostigmine and glycopyrrolate, however, blood pressure was normal. This change in heart rate was more than 30% of baseline and it responded to atropine 7 μg/kg. In Group L one patient developed transient hypotension up to 80/50 mmHg, which responded by putting off isoflurane and giving Ringer lactate 200ml. One patient in Group L developed transient hypotension in recovery room on changing to sitting position up to 84/50 mmHg which got improved by giving supine position and giving ringer lactate .No other specific treatment was required .Two patients in Group M and three patients in Group L had nausea and vomiting post operatively in recovery room. Question was asked to operating surgeon regarding oozing and clarity of operating field. Operating field was clear and bloodless in 80 % of patients in Group M as against in 83.33% patients in Group L.

DISCUSSION

The cardiovascular response to the act of tracheal intubation is a reflex phenomenon with the afferent stimuli carried over both glossopharyngeal and vagal pathways. Such stimuli activate suprategmental and hypothalamic sympathetic centers to cause a peripheral sympathoadrenal response with release of adrenaline and noradrenaline.[19] Metoprolol and labetalol do not decrease release of catecholamines but attenuate responses of elevated catecholamines following laryngoscopy and intubation. Different researchers have studied different doses of metoprolol ranging from 0.5 mg to 4 mg[10-13] and different doses of labatalol[8,14-17] ranging from 0.15 mg/kg to 2 mg/kg for prevention of cardiovascular stress response to Laryngoscopy and intubation. We used optimum doses of metoprolol 30 micrograms /kg and labetalol 0.2 mg/kg so as to get desired effect and avoid undesirable side effects, 5 min

Table 2B :Hemodynamic parameters (% change with respect to baseline)

TIME	Heart rate (beats per min)		SBP (mmHg)		DBP (mmHg)		MBP (mmHg)	
	Group M	Group L	Group M	Group L	Group M	Group L	Group M	Group L
10 Min before induction (Base Line)	82.46 ± 13.08	83.3 ± 12.96	114.53 ± 8.88	114.73 ± 8.49	73.73 ± 5.29	73.7 ± 5.27	87.4 ± 6.27	87.43 ± 6.08
5 min before induction (After premedication)	-1.86%	-1.85%	-1.434%	-1.431%	-1.77 %	-2.14%	-2.14%	-1.61%
Immediately after Induction	1.45%	1.92%	-8.33%	-12.84%	-9.13%	-13.17%	-9.12%	-12.9%
During intubation (0min)	7.44%	9.79%	15.62%	8.01%	15.32%	7.54%	15.28%	7.69%
1 min post intubation	5.38%	7.35%	12.19%	5.90%	11.48%	5.56%	11.59%	5.65%
2 min post intubation	1.74%	2.55%	5.82%	2.76%	5.69%	2.17%	5.64%	2.48%
5 min post intubation	-3.56%	-1.69%	1.78%	-11.30%	-2.35%	-3.67%	-2.14	-3.05%
10 min post intubation	-6.19%	-3.81%	- 8.6%	-11.29 %	-13.12%	-16.69%	-11.22%	-14.34%
30 min post intubation	-11.80	-9.09%	-10.05%	-12.50%	-14.15%	-16.97%	-12.48%	-15.07%
60 min post intubation	-12.13%	-9.49%	-10.22%	-12.43%	-14.38%	-17.16%	-12.25%	-15.10%

prior to induction considering peak action of both drugs being at 5 min after administration. To avoid confounding effect on cardiovascular response to intubation by drugs used for induction, we induced all patients with inj thiopentone sodium 5 mg/kg like previous investigators[12,14,15] and inj Suxamethonium hydrochloride 2 mg/kg to facilitate intubation. Propofol was avoided as it attenuates the presser response to intubation [17]. As duration of laryngoscopy and intubation also has confounding effect all patients having prediction for difficult intubation were excluded. Laryngoscopy was done by trained anesthetist with two years of experience. Same type of laryngoscope blade, Macintosh blade size 3 was used for laryngoscopy considering the observations of Haidry MA et al.[18] that the use of different type of laryngoscope blades can attenuate the presser response to intubation. King BD et al.[1] observed the onset of the presser response within 5 to 15 sec of elevating epiglottis during laryngoscopy and returning at the end of 5 min. Bruder et al.[2] observed that the response lasted for 5 to 10 min. Hence we monitored the parameters till 10 min after intubation. Readings at 30 and 60 min were taken to observe hemodynamic status. In our study both the groups showed significant increase in heart rate after intubation which remained up to 2 min, reached to baseline between 2 and 5 min and became significantly lower than baseline at 5 min and onwards. Though the percentage change in heart rate immediately following intubation was found to be less in Group M (7.44%) than in Group L (9.79%), this intergroup difference was not statistically significant. Comparable changes in heart rate with metoprolol and Labetalol were found by previous investigators. Kumar et al.[12] found increase in heart rate by 10.26% and Pratheeba N et al.[11] found increase in heart rate by 16.59 % immediately following intubation in metoprolol pretreated group. While Shende SY et al.[10] who used higher dose of metoprolol (80 micrograms /kg) found only 3.37 % rise in heart rate. Ekta Ratnani et al.[8] found 4.9 % rise and Lakshmi BS et al.[16] found 13.94 % rise in pulse rate immediately following intubation in labetalol pretreated group similar to our findings. King BD teal 1951[1] stated a marked cardiovascular response to laryngoscopy and intubation with increase in pulse rate up to 20 % without any preventive medication. B. Sowbhagya Lakshmi et al.[16] found even upto 39 % increase in pulse rate without any preventive medication. Thus metoprolol and Labetalol both significantly attenuated the increase in the pulse rate during intubation. In metoprolol pretreated group at 1 min post intubation we found 5.38 % increase in pulse rate like Gurudatta KN et al.[13] who found 5.08 % and Shende SY et al.[10] who found 6.52 % .In labetalol pretreated group at 1 min post intubation we found 7.35 % increase in pulse rate while Ekta Ratnani et al.[8] found 2.6 % rise and Lakshmi BS et al.[16] found 14.66 % rise in pulse rate. In our study, none of the patients had tachycardia or arrhythmias during intubation. One patient in Group M developed sinus bradycardia during reversal of residual nondepolarizers with neostigmine and glycopyrrolate which responded to atropine 7 μg/kg IV. Kumar et al.[12] similarly observed sinus bradycardia in one patient in Group M during reversal of nondepolarizers. None of the patient in

Group L developed bradycardia. No other episodes of arrhythmias with few exceptions of transitory sinus tachycardia were observed in our study .Readings at 30 and 60 min post intubation in Group M (-11.80% and -12.13%) and labetalol (-9.09% and -9.49%) group showed heart rate being significantly lower than baseline indicating controlled hemodynamic status. SBP decreased significantly than baseline immediately after induction in both groups (-8.33% vs. -12.84%). Decrease in SBP was significantly more in Group L than Group M during induction ($p = 0.0227$).However during intubation there was an increase of 15.62% and 8.01% in SBP in Group M and Group L respectively .Thus the rise in Group M was more than that of the Group L, which was statistically significant . King BD et al.[1]stated a marked rise in blood pressure up to 40-50% without any preventive medication. Lakshmi BS et al.[16] also found up to 32.71 % increase in pulse rate without any preventive medication. Thus both metoprolol and labetalol significantly attenuated the increase in SBP during intubation. But labetalol is significantly more effective in attenuating the presser response to intubation than metoprolol. The readings at 01, 02, 05, 10 min post intubation in both groups showed that the significant increase in SBP than baseline at intubation remained up to 2 min reached to baseline in 2-5 min and became significantly lower than baseline at 5 and 10 min onwards. Comparable results were obtained in metoprolol study by other researchers.[8,10,11,13,16] Readings at 30 and 60 min post intubation were significantly lower than baseline in Group M (-10.05% and -10.22%) and Group L (-12.50% and -12.43%) indicating controlled hemodynamic status. DBP and MAP showed similar behavior like SBP. Metoprolol and labetalol significantly attenuated the increase in DBP and MAP during intubation. But labetalol is significantly more effective in attenuating the presser response to intubation than metoprolol. Comparable results were obtained by other investigators in the study of metoprolol[10,11,13] and labetalol.[8,16] Rate pressure product was also calculated at intubation and 1 min post intubation in metoprolol and labetalol and it was 11746.4 ± 2128.15 vs. 11345.1 ± 2047.19 and 11176 ± 2006 vs. 10877 ± 1995.4 respectively. Rate pressure product in Group L was lower than Group M at intubation, 1 min post intubation and onwards. An intra-op study of anesthetized patients by Barash PG[20] found development of ischemic electrocardiographic changes in patients with rate pressure product greater than 12000. In both groups of our study, rate pressure product at intubation and 1 min post intubation remained below 12000.

CONCLUSION

We conclude that both metoprolol 30 μg/kg and labetalol 0.2 mg/kg given 5 min prior to induction of anesthesia significantly attenuate the cardiovascular stress response to intubation (heart rate and blood pressure). Though metoprolol is more effective in attenuating heart rate response to intubation than labetalol statistically there is no significant difference.

Labetalol is superior to metoprolol in attenuating the blood pressure (systolic, diastolic and mean arterial blood pressure) response to intubation.

Both metoprolol and labetalol are effective in maintaining controlled hypotension and minimizing the blood loss and improving the surgical view. Side effects of both drugs are few; bradycardia being observed with metoprolol and hypotension with labetalol which are easily treatable.

Conflict of interest: None declared by the authors

Authors' contribution: The authors declare that all individuals named as authors qualify for authorship in that each has: made substantial contributions to conception and design or data acquisition or data analysis and interpretation; drafted the article or revised it critically for important intellectual content; and approved the final version to be published, and as such, all persons listed as authors have participated sufficiently in the work to take public responsibility for the content of the manuscript.

REFERENCES

1. King BD, Harris LC Jr, Griefenstein FE, ElderJDJr, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during anesthesia. Anesthesiology. 1951;12(5)56-66. [PubMed]
2. Bruder N,Ortega D,Granthil C. Consequences and prevention method of hemodynamic changes during laryngoscopy and intratracheal intubation. Ann Fr Anesth Reanim 1992; 11(1):57-71. [PubMed]
3. Takki S. Tammisto T, Nikki P, Jattella A. Effect of Laryngoscopy and Intubation on plasma catecholamine levels during intravenous induction of anesthesia. Br J Anaesth.1972; 44(12):1323-3328. [PubMed] [Free full text]
4. Corck RC, Weiss JL, Homerroff SR, Bentley J. Fentanyl preloading for rapid sequence of anesthesia. Anaesth. Analg. 1984;63(1):60-64. [PubMed]
5. Miller Dr, Martineau RJ, Wynands JE, Hill J. Bolus administration of Esmolol for controlling hemodynamic response to tracheal intubation: The Canadian Multi Center Trial. Can J Anaesth. 1991;38(7):849-58.[PubMed]
6. Singh H, Vichitvejpaisal P,Guines AY, White PF. Comparative effects of Lidocaine ,Esmolol and Nitroglycerin in modifying the hemodynamic response to laryngoscopy and intubation. J Clin Anesth. 1995;7(1):5-8. [PubMed]
7. Ramanathan J, Sibai BM, Mabie WC, Chauhan D, Ruiz AG. The use of Labetalol for attenuation of the hypertensive response to endotracheal intubation in preeclampsia. Am J Obstet Gynecol. 1988;159(3):650-4. [PubMed]
8. Ratnani E, Sanjeev OP, Singh A, Tripathi M, Chourasia.HK. Comparative Study of Intravenous Esmolol, Labetalol and Lignocaine in Low Doses for Attenuation of Sympathomimetic Responses to Laryngoscopy and Endotracheal Intubation. Anesth Essays Res.2017;11(3):745–750. doi: 10.4103/aer.AER_9_17[PubMed] [Free full text]
9. YamazakiA, Kinoshita H, ShimogaiM,Fujii K, Nakahata K,Iraami H, et al. Landiolol attenuates tachycardia in response to endotracheal intubation without affecting blood pressure. Can J Anaesth.2005;52(3):254-4.[PubMed]
10. Shende SY, Gorgile RN, Sanyogita V, Naik, Marathe R. Comparison of Effect of IV Esmolol and I.V. Metoprolol For Attenuation of Pressor Response to Laryngoscopy And Intubation During Elective General Surgical Procedures Under General Anaesthesia. IOSR J Dent Med Sci. 2017;16 (1):1-6.[Free full text]
11. Pratheeba N, Remadevi R, Bhat R, Kumar SB.Attenuation of hemodynamic response to laryngoscopy and endotracheal intubation - comparison of fentanyl, esmolol and metoprolol in normotensive individuals. Ind J Clin Anaesth. 2017;4(1):88-93. [Free full text]
12. Kumar, Tikle. Attenuation of circulatory responses to Laryngoscopy and tracheal intubation with Metoprolol. Ind J Anaesth. 1995;43:385.
13. Gurudatta KN, Kumara AB. Attenuation of Cardiovascular Responses to Laryngoscopy and Intubation by Intravenous Metoprolol. Journal of Evolution of Medical and Dental Sciences. 2014;3(20):5390-5398. [Free full text]
14. Singh SP, Quadir A,Malhotra P. Comparison of esmolol and labetalol, in low doses, for attenuation of sympathomimetic response to laryngoscopy and intubation. Saudi J Anaesth 2010;4(3):163–168. doi: 10.4103/1658-354X.71573. [PubMed] [Free full text]
15. Kumar R , Gandhi R, Mallick I, Wadhwa R, Adlakha N, Bose M. Attenuation of hemodynamic response to laryngoscopy and endotracheal intubation with two different doses of labetalol in hypertensive patients. Egypt J Anaesth. 2016;32:339–344. [PubMed] [Free full text]
16. Lakshmi BS, Sree SM, Prasad PK, Rao V. To Evaluate effect of IV Esmolol (1 mg/kg) Compared to I. V. Labetalol (0.5 mg/kg) in Attenuating Pressor response during Laryngoscopy & Intubation in General Anesthesia. Journal of Evolution of Medical and Dental Sciences. 2014;3(35):9371-9378.[PubMed] [Free full text]
17. Harris CE, Murray AM, Anderson JM, Grounds RM, Morgan M. Effects of thiopentone, etomidate and propofol on the haemodynamic response to tracheal intubation. Anaesthesia. 1988;43 Suppl:32-6.[PubMed]
18. Haidry MA, Khan FA. Comparison of hemodynamic response to tracheal intubation with Macintosh and McCoy laryngoscopes. J Anaesthesiol Clin Pharmacol. 2013;29(2):196-9. doi: 10.4103/0970-9185.111710. [PubMed] [Free full text]
19. Burstein CL, Woloshin G, Newman W. Electrographic studies during endotracheal intubation: effect during anaesthesia and intravenous Procaine. Anaesthesiology.1950;11:299-14.
20. Barash PG, Kopriva CJ. The rate-pressure product in clinical anesthesia: boon or bane? AnesthAnalg. 1980;59(4):229-31. [PubMed]

★★★★★