



Comparison of Gabapentin and Labetalol in Attenuating the Stress Response to Laryngoscopy and Intubation

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ABSTRACT

Background: Laryngoscopy and tracheal intubation increase blood pressure (BP) and heart rate (HR). The aim of this study was to evaluate the effect of gabapentin and labetalol given before operation on the hemodynamic response to laryngoscopy and intubation.

Methodology: 90 ASA I and II patients undergoing elective surgery were randomly allocated to three groups of 30 each. Group A patients received 800mg of Gabapentine orally 60 minutes before induction of anaesthesia, Group B patients received 100 mg oral Labetalol 60 minutes prior to induction of anaesthesia and Group C patients were not given any treatment and served as the control group for the study. Anaesthesia was induced with inj. propofol and inj. rocuronium. Heart rate, systolic BP, diastolic BP and mean arterial pressure were recorded as baseline, after induction, at tracheal intubation (0 min.); and then at 1, 3, 5, 10 min following tracheal intubation.

Results: mean heart rate, mean systolic blood pressure, mean diastolic blood pressure and mean arterial blood pressure remained significantly lower in group A as compared to group B and group C.

Conclusions: Gabapentin, under present study design, attenuates the pressor response associated with laryngoscopy and intubation.

Keywords: Intubation; Laryngoscopy; Gabapentin, Labetalol.

Introduction

In 1940 Brace first established haemodynamic variation with laryngoscopy, irrespective of type of laryngoscopy blade used. Direct laryngoscopy and intubation causes afferent vagal stimulation and efferent vagal sympatho-adrenal response, this causes increase in blood pressure (BP), heart rate (HR) and cardiac arrhythmias in some patients, these changes constitute pressor response which is

transient, variable and unpredictable. Usually these changes are well tolerated by healthy individuals. However these changes may be fatal in patients with hypertension, coronary artery disease, intracranial hypertension and aneurysm (Pyrns-roberts, Green LT 1971).¹

Keeping in view the frequency with which pressor response is observed during direct laryngoscopy and intubation various drugs and techniques have

been utilized to blunt this response with variable degree of success.

Beta blockers have been recommended by various authors. Prys-Roberts et al (1973) used practolol and found it significantly attenuate hemodynamic response associated with laryngoscopy and endotracheal intubation.² A number of beta blockers have been used since then Labetalol (Scott et al ; 1978), Metoprolol (Coleman; 1980) Esmolol (Miller and Martineau; 1989, Helfman et al; 1991) were reported to be effective.^{3,4,5} Chung K S et al 1992 demonstrated that intermediate dose of Labetalol blunts heart rate response to laryngoscopy and intubation in healthy patients but has minimal effect on blood pressure.⁶ Recently studies have generated interest in use of Gabapentine for attenuation of pressor response to laryngoscopy and intubation. Gabapentine is a second generation anti epileptic that is effective in treatment of neuropathic pain. Turan et al (2004) reported that preoperative oral Gabapentine decrease pain scores and post operative tramadol consumption in patients pretreated with Gabapentine.⁷

Aims and Objectives

1. To compare the relative effectiveness of gabapentine and Labetalol in attenuation of pressor response to direct laryngoscopy and intubation.
2. To find out other desirable effects and complications of both drugs.

Material and Methods

After obtaining informed consent and approval from hospital ethical committee, the randomized control trial was conducted in department of anaesthesiology and intensive care, SHERI KASHMIR INSTITUTE OF MEDICAL SCIENCES (SKIMS), DEEMED UNIVERSITY. Our study was conducted on 90 patients of ASA grade I and II between age group of 18-65 years of either sex, undergoing elective surgery under general anaesthesia with endotracheal intubation. A preanaesthetic check up was done one day prior

to surgery that included detailed history, thorough clinical examination and relevant clinical investigations. Patients with anticipated difficult intubation, ASA grade III or greater, Age greater than 65 years, history of consumption of antihypertensive drugs, sedatives, hypnotics, antidepressants drugs preoperatively, pre-existing cardiovascular disease, patients with significant respiratory, hepatic, renal, haemopoietic and endocrine disorder and patients on treatment with clonidine, methyldopa, β -blockers, benzodiazepines and MAO inhibitors were excluded from the study. Patients were prepared with 8 hours preoperative fasting. Tablet Alprazolam 0.25mg was given at bed time day before surgery. Patients also received Omeprazole 40 mg at bed time, a day before surgery. After obtaining informed consent, patients were allocated to receive treatment according to a randomized plan. The patients were randomly allocated to one of the following three groups after arrival in preoperative room

Group A: Patients in this group received 800mg of Gabapentine orally 60 minutes before induction of anaesthesia.

Group B: Patients in this group received 100 mg oral Labetalol 60 minutes prior to induction of anaesthesia.

Group C: Patients in this group were not given any treatment and served as the control group for the study.

In the preoperative room a crystalloid infusion was started through an intravenous cannula inserted in a peripheral vein and Injection ondansetron 0.1mg/ kg was given 10 minutes before induction. After receiving patients in operating room, monitors were attached to the patients and all parameters like heart rate, blood pressure, oxygen saturation and ECG were noted. After 3 minutes of preoxygenation, anaesthesia was induced with propofol 2.5mg/kg body weight over 30 seconds and injection rocuronium 0.6mg/kg body weight. All intubations were performed by experienced anaesthesiologist. The duration of laryngoscopy and intubation was

limited to minimum possible time being similar in all patients. Depending upon the type and duration of surgery all the patients were maintained with 33% Oxygen, 66% nitrous oxide, 1% isoflurane and Rocuronium 0.15mg/kg as intermittent boluses. Parameters like heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure were recorded before intubation and at 0, 1, 3, 5 and 10 minutes after intubation. At the end of the surgery neuromuscular blockade was reversed with injection Neostigmine 0.05mg/kg and injection Glycopyrolate 0.01mg/kg before extubation.

The data was analyzed with the help of computer software SPSS. 12. 0. MICROSOFT excel for windows and presented as mean and standard deviations. The baseline characteristics evaluated to ascertain comparability among groups were assessed by repeated measures ANOVA. Appropriate tests were used to evaluate statistical

significant difference among different groups. A p value < 0.05 was considered as statistically significant unless specified otherwise. All analysis were done as intention to treat biases.

Results

Table 1: Comparison of Age And Weight In Three Groups

Group	Age(in years)	weight(in kg)
Group A	36.63±11.17	54.62± 5.15
Group B	38.70 +6.48	57.13 ±5.02
Group C	36.03 ±7.23	55.93± 4.95
	p-value-0.774	p-value 00.445

The mean age (years) and weight (kg) in Group A was 36.63± 11 17 and 54.62 ±5 15, in Group B was 38.70 +6.48 and 57.13 ±5.02, and in Group C was 36,03 ±7.23 and 55.93± 4.95, respectively. On comparing the three groups using ANOVA, the difference among the groups was statistically insignificant (p-value>0.05).

Table 2: Comparison of the three Groups Before Induction of Anaesthetics

Variable	Group A	Group B	Group C	P-value	Remarks
Heart rate (beats/min.)	84.23±6.34	85.20±8.38	87.03±9.89	0.63	N.S
SBP(mmHg)	127.17±8.15	127.80±10.66	128.43±11.18	0.81	N.S
DBP(mmHg)	83.93±6.11	82.33±7.07	80.47±8.56	0.34	N.S
MAP(mmHg)	97.87±5.33	96.77±8.02	97.23±9.43	0.86	N.S

The above table depicts the mean Heart Rate, Systolic Blood Pressure and mean Arterial Pressure in the three groups before induction of anaesthesia. When intergroup comparison was

done using ANOVA, no statistically significant difference was found amongst the groups (p-value >0.05).

Table 3: Significance of Heart Rate Changes in the Groups before and after Laryngoscopy and Intubation

Time	Group A		Group B		Group C	
	Mean±S.D	P-value	Mean±S.D	p-value	Mean±S.D	p-value
Before induction	84.23±6.34		85.20±8.38		87.03±9.89	
Before intubation	77.63±7.43	0.001	78.40±9.19	0.005	79.53±8.57	0.002
After laryngoscopy and intubation						
0 min	90.27±7.15	0.002	103.80±9.70	0.000	104.87±11.17	0.000
1 min.	88.10±6.94	0.032	100.77±9.45	0.000	102.27±10.27	0.000
3 min	85.40±6.68	0.490	94.60±7.87	0.000	96.60±10.17	0.001
5 min	81.13±6.23	0.066	89.30±7.53	0.045	92.90±9.70	0.027
10 min	78.53±4.23	0.000	84.97±6.47	0.906	84.20±8.96	0.254
The mean difference is significant at p-value <0.05 and highly significant at p-value <0.001						

The above table shows that there was statistically significant rise in heart rate after laryngoscopy and intubation at 0 min in all the groups (p<0.05) .

Heart rate decreased to insignificant levels in group A (p-value > 0.05) at 3 min., whereas it remained significant in group C and D upto 5 min.

Table 4: Significance of Systolic Blood Pressure Changes in the three Groups before and after Laryngoscopy and Intubation.

Time	Group A		Group B		Group C	
	Mean±S.D	P-value	Mean±S.D	p-value	Mean±S.D	p-value
Before induction	127.17±8.15		127.80±10.66		128.43±11.10	
Before intubation	115.20±9.35	0.000	118.50±11.82	0.000	118.50±10.91	0.000
After laryngoscopy and intubation						
0 min	125.01±7.95	0.307	156.03±12.86	0.000	160.26±11.42	0.000
1 min.	115.67±6.32	0.000	151.20±12.08	0.000	155.67±11.90	0.000
3 min	110.53±6.49	0.000	144.47±10.75	0.000	148.40±11.06	0.000
5 min	107.30±6.35	0.000	139.90±11.58	0.000	139.00±12.44	0.000
10 min	104.90±5.58	0.000	135.10±9.99	0.004	136.93±10.64	0.001
The mean difference is significant at p-value <0.05 and highly significant at p-value <0.001						

From the above table it is observed that after laryngoscopy and intubation systolic blood pressure shot up significantly (p-value<0.001) in all the groups except in group A. In group A there

was a fall in systolic blood pressure 1 min after laryngoscopy and intubation which continued upto the 10th min.

Table 5: Significance of Diastolic Blood Pressure Changes in the three Groups before and after Laryngoscopy and Intubation.

Time	Group A		Group B		Group C	
	Mean±S.D	P-value	Mean±S.D	p-value	Mean±S.D	p-value
Before induction	83.93±6.11		82.33±7.07		80.47±8.56	
Before intubation	80.86±6.54	0.000	80.31±1.82	0.000	76.52±1.93	0.000
After laryngoscopy and intubation						
0 min	80.06±7395	0.50	96.23±2.84	0.000	98.43±1.4	0.000
1 min.	75.34±6232	0.000	94.21±3.08	0.000	94.32±3.90	0.000
3 min	74.12±1.49	0.000	93.23±4.73	0.000	94.33±5.06	0.000
5 min	73.2±4.35	0.000	92.31±4.58	0.000	93.21±2.41	0.000
10 min	72.3±3.53	0.000	90.33±1.23	0.004	92.31±1.64	0.001
The mean difference is significant at p-value <0.05 and highly significant at p-value <0.001						

From the above table it is observed that after laryngoscopy and intubation diastolic blood pressure shot up significantly (p-value<0.001) in all the groups except in group A. In group A there

was a fall in diastolic blood pressure 1 min. After laryngoscopy and intubation which continued upto the 10th min.

Table 6: Significance of Mean Arterial Blood Pressure Changes in the three Groups Before and After Laryngoscopy and Intubation.

Time	Group A		Group B		Group C	
	Mean±S.D	P-value	Mean±S.D	p-value	Mean±S.D	p-value
Before induction	97.87±5.33		96.77±8.02		97.23±9.43	
Before intubation	92.306±4.23	0.000	93.04±1.47	0.000	90.51±1.91	0.000
After laryngoscopy and intubation						
0 min	95.04±9.17	0.25	116.16±9.34	0.000	119.04±8.42	0.000
1 min.	88.78±7.32	0.000	113.21±8.08	0.000	114.77±5.43	0.000
3 min	86.26±4.33	0.000	110.31±4.18	0.000	112.35±5.89	0.000
5 min	84.57±1.67	0.000	108.17±3.90	0.000	108.47±3.55	0.000
10 min	83.17±2.53	0.000	105.25±7.23	0.004	107.18±1.34	0.001
The mean difference is significant at p-value <0.05 and highly significant at p-value <0.001						

From the above table it is observed that after laryngoscopy and intubation mean arterial blood pressure shot up significantly (p-value<0.001) in all the groups except in group A. In group A there

was a fall in systolic blood pressure 1 min. after laryngoscopy and intubation which continued upto the 10th min.

Discussion

Laryngoscopy and intubation are mandatory for most patients undergoing general anaesthesia. Direct laryngoscopy and intubation causes afferent vagal stimulation and efferent sympathico-adrenal response, this causes increase in blood pressure (BP), heart rate (HR) and cardiac arrhythmias in some patients, these changes constitute pressor response which is transient, variable and unpredictable. Usually these changes are well tolerated by healthy individuals. However these changes may be fatal in patients with hypertension, coronary artery disease, intracranial hypertension and aneurysm (Pyrson-Roberts, Green LT 1971).¹

Present study was undertaken to study the effects of labetalol 100mg and gabapentine 800mg on attenuation of pressor response to laryngoscopy and endotracheal intubation. 90 patients ASA Grade I-II of either sex, between 20-60 years of age undergoing elective surgery were divided in three groups of 30 patients each. Patients in group A received 800mg gabapentine, group B patients received labetalol 100mg and group C acted as control. Pretreatment was given orally one hour before induction of anaesthesia. After 3 minutes of preoxygenation, anaesthesia was induced with propofol 2.5mg/kg body weight over 30 seconds and injection rocuronium 0.6mg/kg body weight. All intubations were performed by an experienced anaesthesiologist. All the patients were maintained with 33% Oxygen, 66% nitrous oxide, 0.5% halothane and Rocuronium 0.15mg/kg as intermittent boluses. Parameters like heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure were recorded before intubation and at 0, 1, 3, 5 and 10 minutes after intubation. At the end of the surgery neuromuscular blockade was reversed with injection Neostigmine 0.05mg/kg and injection Glycopyrolate 0.01mg/kg before extubation. The evaluation of these parameters has been made separately for each group. These have been further assessed for comparative analysis identifying the

drug efficacy by way of visualising the effect in attenuating the pressor response parameters.

Demographic data like age, ASA status and weight of the patients in the all three groups was statistically comparable. There was statistically nonsignificant difference in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure among the three groups before intubation.

In group A there was a significant (p-value < 0.05) increase in heart rate from preinduction value at 0 min and 1 min after laryngoscopy. There after a decline in heart rate was observed which was statistically insignificant (p-value >0.05) up to 5 min. At 10 min there was a significant (p-value < 0.05) decrease in heart rate from preinduction value. In group B and group C there was a significant (p-value < 0.05) increase in heart rate from preinduction value at 0 min to 5 min after laryngoscopy. There after a decline in heart rate was observed which was statistically insignificant (p-value >0.05) at 10 min. Mean heart rate in group A remained significantly lower as compared to group B and group C, however mean heart rate between group B and group C remained statistically non significant. Systolic blood pressure, diastolic blood pressure and mean arterial pressure amongst the three groups before induction and intubation was statistically non significant. Systolic blood pressure, diastolic blood pressure and mean arterial pressure showed a non significant change at 0 min after laryngoscopy in group A followed by a significant decrease upto 10 min of laryngoscopy. In group B and C there was a significant increase in Systolic blood pressure, diastolic blood pressure and mean arterial pressure at all time intervals from baseline value. Overall Systolic blood pressure, diastolic blood pressure and mean arterial pressure remained significantly lower in group A as compared to group B and group C, however mean Systolic blood pressure, mean diastolic blood pressure and mean arterial pressure between group B and group C remained statistically non significant. Our observation are in accordance

with of Memis et al (2006) who reported complete attenuation of reflex increase in heart rate and MAP after laryngoscopy and intubation with 800mg Gabapentine when given one hour before surgery.⁸ However in another study done by Fassoulaki et al (2006) they reported that Gabapentine attenuated increase in blood pressure but not the tachycardia response to laryngoscopy and intubation.⁹ The mechanism by which Gabapentine attenuates the pressor response to laryngoscopy and intubation is unknown. Although the molecular targets of gabapentine remain unknown, the inhibition of calcium flux in muscle cells with a consequent inhibition of smooth muscle contraction might explain the effectiveness of Gabapentine in attenuation of the pressor response to laryngoscopy. Our study results are also similar to Kong VKF and Irwin MG 2007 who concluded preoperative Gabapentine is efficacious for not only post operative analgesia, post operative nausea and vomiting but also for attenuation of pressor response.¹⁰

Kim, Chung and Lee 94 concluded in their study that intravenous Labetalol 0.25mg/kg is ineffective in controlling DBP and MAP.¹¹ Results in group B (Labetalol) were not in accordance to Amar D et al 1991 in which labetalol was given 90mts before induction of anaesthesia as against to our study where it was given 60 min before induction.¹² Results were also not in accordance to the study of Chung KS et al 1992 where intermediate dose of labetalol was given 90 min before induction of anaesthesia.¹³ Ramanathan J 1988 observed attenuation of pressor response at intermediate dose of iv labetalol during caesarian, but oral labetalol used in our study did not show significant attenuation of pressor response.¹⁴

Conclusion

Thus we concluded that pretreatment with both Gabapentine 800mg and labetalol 100mg is effective in attenuation of pressor response to laryngoscopy and intubation. However, the rise in

blood pressure is better attenuated by Gabapentine. However further studies will be required to study the synergistic effect of labetalol and gabapentine in different dosage regimens in attenuation of pressor response to direct laryngoscopy and intubation.

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