Original Research Paper

Volume-8 | Issue-9 | September-2018 | PRINT ISSN No 2249-555X

Anesthesiology

ORAL PREGABALIN PREMEDICATION FOR ATTENUATION OF HEMODYNAMIC PRESSURE RESPONSE OF AIRWAY INSTRUMENTATION DURING GENERAL ANAESTHESIA: DOSE RESPONSE STUDY

Dr Mitali Vilas Patkar — Senior Resident,Department of Anaesthesiology and Critical Care Grant Medical College, Mumbai

Dr Poornima Ashwin Sonkamble* — Associate Professor,Department of Anaesthesiology and Critical Care Grant Medical College, Mumbai *Corresponding Author

Dr Ashwin Pralhad Sonkamble — Associate Professor,Department of Anaesthesiology and Critical Care Grant Medical College, Mumbai

ABSTRACT

Introduction: Entotracheal intubation is one of the most frequently performed procedure in anaesthesia practice involving general anaesthesia. The process of laryngoscopy and intubation produces noxious stimuli and is associated with intense sympathetic activity marked by tachycardia and hypertension. Various methods and drugs have been used to attenuate this haemodynamic response which includes use of LMA, nerve blocks, inhalational agents, topical and intravenous lignocaine, calcium channel blockers, narcotics, vasodilators, Pregabalin , gabapentine etc.

New agent Pregabalin, primarily used as anticonvulsant has been found to have reduced haemodynamic respone to airway instrumentation.. so we compared the effect of 2 different doses of Pregabalin(75 mg & 150 mg) to the laryngoscopy and intubation response.

Patients and Methods: After obtaining approval of institutional ethical committee, a prospective randomized study was conducted on 90 patients divided in 3 groups of 30 each. Group A received Placebo ie multivitamin tab. Group B received 75mg of Pregabalin and Group C received 150mg of Pregabalin 1 hour prior to induction of anaesthesia. Inside the OT, pts were premedicated with Ondensetron, Midazolam, Glycopyrrolate and Fentanyl and induced with propofol. Under the effect of Vecuronium, laryngoscopy and intubation was done and anaesthesia was maintained with Oxygen, Nitrous oxide, Sevoflurane and intermittent Vecuronium on controlled ventilation to maintain normocapnia. Haemodynamic parameters were noted.

Conclusion: After statistical analysis we have found that group C (150 mg Pregabalin) showed highly significant attenuation of sympathetic responses and in group B (75 mg Pregabalin), there was transient increase in all the hemodynamic parameters which were settled down in 5-10 minutes period but this increase was still less than placebo group A.

KEYWORDS : Pregabalin, Laryngoscopy And Intubation Response

INTRODUCTION

Since the time of introduction of endotracheal intubation in the last quarter of 19th century, it has became one of the most frequently performed procedure in the practice of anaesthesia.[1, 2] The process of laryngoscopy and intubation are noxious stimuli and are associated with intense sympathetic activity marked by tachycardia & hypertension [3, 4], therefore constitute a period of extreme hemodynamic stress.

Various methods have been used to attenuate the hemodynamic response to laryngoscopy & endotracheal intubation. The non - pharmacological methods like smooth & gentle intubation with a shorter duration of laryngoscopy, insertion of LMA instead of endotracheal tube[8,2] and blocking of Glossopharyngeal nerve and Superior laryngeal nerve[9] have been used to attenuate cardiovascular response to laryngoscopy and endotracheal intubation. Pharmacological methods like Inhalational agents[10], Topical and Intravenous Lidocaine[11,12], Calcium channel blockers[13,14,15,16,17], Vasodilators,[18,19] Narcotics,[20,21,22,23] and some newer agents like Pregabalin[24,25] or Gabapentine[26] have been tried.

None of the above approaches or agents had been proved to be ideal. Hence the search for an ideal agent to attenuate the hemodynamic responses is still continuing. Newer agent, Pregabalin, primarily used as an anticonvulsant has been found to reduce hemodynamic pressure response of airway instrumentation. The present study was undertaken to evaluate the safe and clinically effective dose of oral Pregabalin for attenuating hemodynamic pressure response of airway instrumentation.

We studied and compared the effects of 2 different doses of oral Pregabalin (75 mg and 150 mg) in attenuating the hemodynamic pressure response during laryngoscopy and tracheal intubation.

MATERIALS AND METHODS

After the approval of institutional ethical committee, a prospective randomized study was conducted in ninety patients of either sex, aged between 18 to 80 yrs and ASA grade I or II undergoing elective surgery under general anaesthesia. Patients who refused to be part of the study, pregnant females, posted for emergency surgeries, weighing > 80kg, with anticipated difficult intubation, with cardiac, renal, pulmonary disease, allergic to any anaesthetic medication, patients taking antihypertensive drugs, sedatives, hypnotic drugs and patients taking oral Pregabalin were excluded from the study.

All the patients were evaluated preoperatively, informed valid written consent was taken and kept NBM overnight. On the day of surgery, patients were randomly allocated in 3 groups ;

Group A: received placebo (multivitamin).
Group B: received oral Pregabalin 75 mg
Group C: received oral Pregabalin 150 mg

They received the study drug 1 hour prior to induction of anaesthesia in preoperative room after noting down the baseline parameters.

In the operating room, monitors viz. ECG, NIBP, pulse oximeter were attached and the values of heart rate(HR), systolic blood pressure(SBP), diastolic blood pressure (DBP), mean arterial blood pressure(MAP), SpO2(saturation), ECG were recorded. All the patients were premedicated with Ondansetron (4 mg), Glycopyrrolate (0.04 mg/kg), and Midazolam (0.015 mg/kg), Fentanyl (2µg/kg). After preoxygenation for 3 min with 100% Oxygen, anaesthesia was induced with Propofol (2 mg/kg), the neuromuscular blockade was achieved with Vecuronium 0.1mg/kg. Direct laryngoscopy and intubation was performed after 3 minutes. Anaesthesia was maintained with Oxygen, Nitrous Oxide, Sevoflurane and intermittemt Vecuronium(0.02mg/kg). The patients were mechanically ventilated to maintain normocapnia. After completion of surgery, residual blockade was antagonized with Neostigmine (0.05 mg /kg) and Glycopyrrolate (0.01 mg/kg) and extubation was performed when respiration was adequate.

Intra-operatively, the heart rate (HR), mean arterial blood pressure(MAP), systolic(SBP) and diastolic(DBP) arterial blood pressure, ECG, SpO2 and EtCO2 levels were monitored at following intervals:

1) Baseline- before giving study drug.
2) 30 min after study drug
3) 60 min after study drug
4) Before induction.
5) After induction.
6) During laryngoscopy.
7) 1, 2, 3, 4, 5, 10, 15 Minutes after intubation.

Intraoperatively, patients were observed for any complications like hypotension, hypertension, arrhythmias, hypoxemia, and bronchospasm and were treated as required. After extubation, patients were transferred to post anaesthesia care unit and monitored for 1 hour .

STATISTICALANALYSIS:

The statistical analysis was done by using SPSS-20. For detail analysis, Chi-square test, Student-t test, ANOVA, repeated measure ANOVA and mixed model ANOVA were used to calculate the P value and to establish correlation between study groups.

Obesrvations:

TABLE NO 1 : Demographic Data

	Group A	Group B	Group C	F value	p value
Age	36.7 ± 14.15	42.17 ± 13.39	35.10 ± 12.54	2.302	0.106
Male	16	15	13		0.733
Female	14	15	17		
Weight	62.63 ± 9.75	59.03 ± 10.23	61.80 ± 9.70	1.082	0.344
ASA I	70%	60%	66.70%		0.709
ASA II	30%	40%	33.30%		

TABLE NO 2 : Comparison Of Heart Rate Between All Study Groups

Events	Group A	Group B	Group C	p value (Between Group A & B)	p value (Between Group A & C)	p value (Between Group B & C)
Baseline	80.63 ± 4.56	80.83 ± 4.53	80.60 ± 4.59	0.865	0.980	1.000
30 mins after study drug	80.83 ± 5.20	83.50 ± 3.74	79.43 ± 3.13	0.041	0.573	0.001
60 mins after study drug	80.73 ± 6.34	80.00 ± 4.03	80.43 ± 3.97	1.000	1.000	1.000
Before Induction	80.77 ± 4.33	79.13 ± 5.19	78.07 ± 3.70	0.476	0.063	1.000
After Induction	78.13 ± 9.25	76.47 ± 4.02	74.10 ± 4.49	0.942	0.049	0.462
During Laryngoscopy	109.70 ± 11.72	91.20 ± 6.72	85.40 ± 5.96	0.000	0.000	0.030
1 min after intubation	109.60 ± 10.60	95.87 ± 5.43	88.33 ± 5.86	0.000	0.000	0.001
2 min after intubation	109.20 ± 10.67	92.30 ± 8.63	86.37 ± 7.31	0.000	0.000	0.037
3 min after intubation	105.73 ± 10.94	84.57 ± 6.60	84.13 ± 6.54	0.000	0.000	1.000
4 min after intubation	104.20 ± 12.53	82.10 ± 7.60	81.90 ± 6.42	0.000	0.000	1.000
5 min after intubation	101.40 ± 11.29	82.37 ±5.37	80.93 ± 8.05	0.000	0.000	1.000
10 min after intubation	96.63 ± 10.79	79.27 ± 3.77	79.83 ± 8.80	0.000	0.000	1.000
15 min after intubation	92.47 ± 7.44	76.07 ± 8.85	79.93 ± 6.16	0.000	0.000	1.000

TABLE NO 3: Comparison Of Systolic Blood Pressure Between All Study Groups

Events	Group A	Group B	Group C	p value (Between Group A & B)	p value (Between Group A & C)	p value (Between Group B & C)
Baseline	120.00 ± 7.80	120.07 ± 7.69	118.73 ± 9.49	1.000	1.000	1.000
30 mins after study drug	123.23 ±7.78	120.83 ± 7.10	117.57 ± 9.41	0.772	0.026	0.373
60 mins after study drug	122.97 ± 6.38	119.97 ± 5.56	115.6 ± 8.27	0.277	0.000	0.046
Before Induction	121.10 ± 5.07	119.90 ± 5.46	113.53 ± 7.82	1.000	0.000	0.000
After Induction	114.50 ± 4.90	111.60 ± 5.92	108.50 ± 8.00	0.249	0.001	0.193
During Laryngoscopy	144.87 ± 8.86	131.23 ± 5.93	123.27 ± 7.07	0.000	0.000	0.000
1 min after intubation	142.87 ± 7.93	129.07 ± 6.47	121.40 ± 6.62	0.000	0.000	0.000
2 min after intubation	139.00 ± 8.23	128.27 ± 5.58	119.17 ± 6.66	0.000	0.000	0.000
3 min after intubation	137.07 ± 7.97	126.03 ± 5.36	116.37 ± 7.00	0.000	0.000	0.000
4 min after intubation	135.27 ± 7.70	124.67 ± 4.90	114.30 ± 6.72	0.000	0.000	0.000
5 min after intubation	133.73 ± 7.37	122.93 ± 5.39	112.93 ± 5.50	0.000	0.000	0.000
10 min after intubation	128.07 ± 6.96	115.67 ± 5.44	109.80 ± 4.80	0.000	0.000	0.001
15 min after intubation	125.53 ± 6.56	114.53 ± 5.58	107.30 ± 5.07	0.000	0.000	0.000

TABLE NO 3 : Comparison Of Diastolic Blood Pressure Between All Study Groups

Events	Group A	Group B	Group C	p value (Between Group A & B)	p value (Between Group A & C)	p value (Between Group B & C)
Baseline	79.87 ± 4.24	82.07 ± 3.49	80.7 ± 5.53	0.180	1.000	0.729
30 mins after study drug	83.37 ± 3.61	83.6 ± 3.90	80.87 ± 5.03	1.000	0.000	0.000
60 mins after study drug	85.1 ± 3.92	80.77 ± 3.61	74.87 ± 6.06	0.002	0.000	0.000
Before Induction	85.97 ± 4.99	78.27 ± 4.22	72.13 ± 4.85	0.000	0.000	0.000
After Induction	78.57 ± 4.39	73.77 ± 3.37	68.93 ± 5.64	0.000	0.000	0.000
During Laryngoscopy	93.2 ± 4.68	90.1 ± 3.33	82.7 ± 5.21	0.026	0.000	0.000
1 min after intubation	91.1 ± 3.72	87.07 ± 3.00	81.53 ±5.49	0.001	0.000	0.000
2 min after intubation	88.97 ± 4.29	87.3 ± 5.47	78.1 ± 2.66	0.409	0.000	0.000
3 min after intubation	87.33 ± 4.20	86.27 ± 5.95	75.43 ± 3.97	1.000	0.000	0.000
4 min after intubation	87.1 ± 4.45	81.87 ± 4.78	74.17 ± 3.38	0.000	0.000	0.000
5 min after intubation	86.17 ± 4.13	81.83 ± 3.69	73.7 ± 3.74	0.000	0.000	0.000
10 min after intubation	80.57 ± 3.85	78.07 ± 4.72	73.07 ± 3.14	0.049	0.000	0.000
15 min after intubation	79.23 ± 3.97	77.17 ± 5.40	73.2 ± 2.52	0.169	0.000	0.001

TABLE NO 4 : Comparison Of Mean Arterial Pressure Between All Study Groups

Events	Group A	Group B	Group C	p value (Between Group A & B)	p value (Between Group A & C)	p value (Between Group B & C)
Baseline	93.24 ± 2.69	94.73 ± 2.57	93.38 ± 5.10	0.351	1.000	0.459
30 mins after study drug	96.66 ± 2,86	96.01 ± 2.48	93.10 ± 4.23	1.000	0.000	0.000
60 mins after study drug	97.72 ± 2.96	93.83 ± 1.96	88.44 ± 4.38	0.000	0.000	0.000
Before Induction	97.68 ± 3.14	92.14 ± 2.05	85.93 ± 4.12	0.000	0.000	0.000
After Induction	90.54 ± 3.16	86.38 ± 2.39	82.12 ± 5.00	0.000	0.000	0.000
During Laryngoscopy	110.42 ± 2.72	103.81 ± 2.37	96.22 ± 4.29	0.000	0.000	0.000
1 min after intubation	108.36 ± 2.30	101.07 ± 2.08	94.82 ± 4.36	0.000	0.000	0.000
2 min after intubation	105.64 ± 3.65	100.96 ± 3.51	91.79 ± 2.70	0.000	0.000	0.000
3 min after intubation	103.91 ± 3.39	99.52 ± 3.87	89.08 ± 3.64	0.000	0.000	0.000
4 min after intubation	103.16 ± 3.39	96.13 ± 3.53	87.54 ± 3.50	0.000	0.000	0.000
5 min after intubation	102.02 ± 2.92	95.53 ± 3.22	86.78 ± 3.44	0.000	0.000	0.000
10 min after intubation	96.40 ± 2.56	90.60 ± 3.94	85.31 ± 2.83	0.000	0.000	0.000
15 min after intubation	94.67 ± 3.32	89.62 ± 4.38	84.57 ± 2.41	0.000	0.000	0.000

TABLE NO 5: Comparison Of Intra-operative & Post-operative Complications In All Study Groups

Complication	Study Groups		
	A	B	C
Hypotension	0	0	1
Bradycardia	0	0	0
Dizziness	0	1	1
Nausea & Vomiting	0	0	0
Headache	0	0	0
Visual disturbances	0	0	0

DISCUSSION

Laryngoscopy and tracheal intubation are considered as the most critical events during administration of general anaesthesia as they provoke transient but marked sympathoadrenal response manifesting as hypertension and tachycardia[3]. These responses are transient, variable and may not be significant in otherwise normal individuals. But in patients with cardiovascular compromise conditions like hypertension, ischemic heart disease, cerebrovascular disease and intracranial aneurysms even these transient changes in haemodynamic can result in potentially harmful effects[4]. Various agents and techniques were studied to limit the detrimental haemodynamic response to laryngoscopy and intubation. We studied Pregabalin given in two different doses.

Pregabalin is structural analogue of GABA and is primarily used in the management of partial epilepsy, relief of neuropathic pain associated with post-herpetic neuralgia, diabetic neuropathy, and post-operative pain. It also has sedative and anxiolytic effect which helps in relieving preoperative anxiety and hence may help to attenuate the pressure response to airway instrumentation.

In our study, the demographic data was comparable in all the 3 groups. The HR, SBP, DBP and MAP decreases after 30 mins of administration of the study drug in group B & C this decrease is continued till 60 mins of drug administration but with no significant difference in group B & C. There is further fall after administering inj Propofol for induction of general anaesthesia. After laryngoscopy and intubation there was rise in all the 4 parameters in all the 3 groups. But this rise was highest in Group A and it remains consistently high till the end of the observed intervals i.e. till 15 mins.

It was found that there was significant difference ($p < 0.05$) in mean HR when compared between Group A and Group B & C, but the difference between the mean HR of Group B & C were comparable ($p > 0.05$). The rise in HR returns to baseline in after 4 mins of laryngoscopy and intubation in Group B & C. This result were consistent with the study of Eren G[27] and Sunder AS[28]. Rastogi Bhawana[25] found that there is no statistically significant attenuation of HR in group receiving 150mg of Pregabalin, but the HR remained stabilized in comparison to the control, group receiving placebo. The study done by Rajesh Meena in 2016[24] evaluated the safe and clinically effective dose of oral Pregabalin for attenuation of pressure response. They observed that more attenuation of HR was seen in the group receiving 300mg of Pregabalin as compared to those receiving placebo and 150mg of Pregabalin without any side effects.

SBP, DBP and MAP decreased in the study group B & C after administration of the study drug. There is further fall after induction of anaesthesia with propofol. After laryngoscopy and intubation Group A patients had highest rise in all 3 parameters. This rise in SBP in the study group was insignificant and returned to baseline after 5 mins in group B and 2 mins in group C. DBP returned to baseline in 3 mins in group B and 1 min in group C. Similarly, rise in MAP was there more in group A as compared to group B & C. This rise was much less in group C and it touched to base line after 5 and min respectively. Similar results were obtained by Sundar AS[28], Rastogi Bhawana[25] and Rajesh Meena in 2016[24]

After analysis we have found that group C (150 mg Pregabalin) showed highly significant attenuation of sympathetic responses and all the hemodynamic parameters after intubation remain below the baseline after 2-3 minutes. In group B (75 mg Pregabalin), there was transient increase in all the hemodynamic parameters which were settled down in 5-10 minutes period but this increase was still less than placebo group A.

CONCLUSION

On the basis of the observations and results of this study, following conclusions were drawn:

1. Oral Pregabalin 75 mg and 150 mg given 1 hr prior to induction are effective in controlling the heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure after laryngoscopy and intubation as compared to control group.
2. However 150 mg Pregabalin given 1 hr before induction stands better due to its more effective control of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure after laryngoscopy and intubation with least side effects as compared to placebo group as well the patients who received 75 mg Pregabalin.

REFERENCES

1. Rowbathom ES, Magill I. Anaesthetics in the plastic surgery of Face and Jaws. Proceeding of the Royal Society of Medicine 1921; 14: 17-27.
2. Magill I. Endotracheal Anaesthesia. Journal of the Royal Society of Medicine 1928; 22: 83-88.
3. Reid LC, Brace DE. Irritation of respiratory tract and its reflex effect on heart. Surgery Gynaecology Obstetrics 1940;70:157.
4. King BD, Harris LC, Griefenstein FE, Elder JD Jr, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anaesthesia. Anaesthesiology 1951;12:556-566.
5. Rose DK, Cohen MM. The airway : Problems and predictions in 18,500 patients. Can J Anaesth 1994;41:372-383.
6. Derbyshire DR, Chmielewski A, Fell D, Vaters M, Achola K, Smith G.Plasma catecholamine response to tracheal intubation. Br J Anaesth 1983;55:855-859.
7. Fox EJ, Sklar GS, Hill CH, Villanue Var, King BD. Complications related to the pressor response to endotracheal intubation. Anaesthesiology 1977;47:524-525.
8. Karl S. Insertion of LMA in place of endotracheal intubation to attenuate the cardiovascular response. IJA 1999;43:30-35.
9. Kumar A. Blocking Glossopharyngeal and Superior laryngeal nerves to attenuate the cardiovascular response to laryngoscopy and endotracheal intubation.IJA 1993;41:20-25
10. Zbinden AM, Peterson-Felix S, Thomson DA. Anaesthetic depth defined using multiple noxious stimuli during Isoflurane/Oxygen Anaesthesia:II. HaemodynamicResponses. Anesthesiology 1994;80:253-260.
11. Stoelting RK. Circulatory changes during direct laryngoscopy and tracheal intubation: Influence of duration of laryngoscopy with or without prior lignocaine. Anaesthesiology.1977:47:381-383.
12. Stoelting RK. Blood pressure and heart rate changes during short duration laryngoscopy for tracheal intubation: Influence of viscous or intravenous lignocaine. Anaesth Analg 1978;57:197-199.
13. Puri GD, Batra YK.Effects of Nifedipine on cardiovascular response to laryngoscopy and intubation .Br J Anaesth 1988;60:579-581.
14. Nishikawa T, Naiki A. Attenuation of the pressor response to laryngoscopy and tracheal intubation with IV verapamil. Act Anaesthesiologica Scandinavica 1989;33:232-235.
15. Mikawa K, Ikegaki J, Maekawa N,Goto R, Kaetsu H, Obara H. The effect of diltiazem

on the cardiovascular response to tracheal intubation. Anaesthesia 1990;45:289-293.
16. Omote K, Kirita A, Namiki A, Iwasaki H. Effects of nicardipine on the circulatory responses to tracheal intubation in normotensive and hypertensive patients. Anaesthesia 1992;47:24-27.
17. Miwaka K, Nishina K, Maekawa N, Obara H. Comparison of Nicardipine, diltiazem and Verapamil for Group Aling the cardiovascular responses to tracheal intubation. Br J Anaesth 1996;76:221-226.
18. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with Sodium Nitroprusside. Anaesth Analg 1979;58:116-119.
19. Fossoulaki A, Kaniasis P. Intranasal administration of Nitoglycerine attenuates the pressor response to laryngoscopy and intubation of the trachea. Br J Anaesth 1983;55:49-52.
20. Dahlgren N, Messeter K. Treatment of stress response to laryngoscopy and intubation with fentanyl. Anaesthesia 1981;36:1022-1026.
21. Hall AP, Thompson JP, Leslie NA, Fox AJ, Kumar N, Rowbotham DJ. Comparison of different doses of remifentanil on cardiovascular response to laryngoscopy and tracheal intubation. Br J Anaest2000; 84: 100-102.
22. Safavi M, Honardmand A. Attenuation of cardiovascular responses to laryngoscopy and tracheal intubation: Intravenous Sufentanil and Pethidine. M. E. J. Anesth 2008;19:1349-1359.
23. Del Rio Vellosillo M, Gallego GJ, Soliveres RJ, Abengochea CA, Barber AM. Bolus administration of Fentanyl Vs continuous infusion of Remifentanil for Group A of haemodynamic responses to laryngoscopy and orotracheal intubation: A randomized double-blind trial. Revista Espanola de Anestesiologia Reanimacuon 2009;56:287-291.
24. Meena R, Meena K, Prakash S. Study of Attenuation of Cardiovascular Response during Laryngoscopy and Intubation Using Two Different Doses of Pregabalin as Premedication in Controlled Hypertensive Patients-A RCT. J Anesth Clin Res. 2016;7(607):2.
25. Rastogi B, Gupta K, Gupta PK, Agarwal S, Jain M, Chauhan H. Oral pregabalin premedication for attenuation of haemodynamic pressor response of airway instrumentation during general anaesthesia: A dose response study. Indian journal of anaesthesia. 2012 Jan;56(1):49.
26. Fassoulaki A, Melemeni A, Paraskeva A, Petropoulos G. Gabapentin attenuates the pressor response to direct laryngoscopy and tracheal intubation. BJA: British Journal of Anaesthesia. 2006 Apr 4;96(6):769-73.
27. Eren G, Kozanhan B, Hergunsel O, Bilgin U, Demir G, et al. (2008) Pregabalin blunts cardiovascular response to laryngoscopy and tracheal intubation. J Anesthesiol Reanimation 7: 82-87.
28. Sundar AS, Kodali R, Sulaiman S, Ravullapalli H, Karthekeyan R, Vakamudi M. The effects of preemptive pregabalin on attenuation of stress response to endotracheal intubation and opioid-sparing effect in patients undergoing off-pump coronary artery bypass grafting. Annals of cardiac anaesthesia. 2012 Jan 1;15(1):18.