Original Research Article

Indian Journal of Anesthesia and Analgesia
2019; 6(6) (Part - I): 2041-2048
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6619.28

A Comparative Study of Oral Clonidine Vs Oral Pregabalin as Pre-Medication to Attenuate Pressor Response to Direct Laryngoscopy and Endotracheal Intubation

R Srinivasa[1], Archana Endigeri[2]

[1]Assistant Professor, Department of Anesthesiology, Subbaiah Institute of Medical Science and Research Centre, Shivamogga, Karnataka 577222, India. [2]Assistant Professor, Department of Anesthesiology, S.N. Medical College, Bagalkot, Karnataka 587103, India.

Abstract

Introduction: Laryngoscopy and endotracheal intubation are routine procedures of modern balanced general anesthesia technique. Endotracheal intubation has become an integral part of the anesthetic management and critical care of the patient and has been practiced following its description by Rowbotham and Magill in 1921. *Materials and Methods:* Present clinical study was conducted in Department of Anesthesiology, Subbaiah Institute of Medical Science and Research Centre, Purle, Shivamogga. After approval from the hospital ethics committee, study was conducted during the period between *October 2016* and *September 2018*. It was a prospective study. A total of 60 patients undergoing elective surgery were selected. Patients in each group received respective drugs as per timing and dose mentioned earlier. On arrival in the operating room, patient's basal parameters-Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MBP), Rate Pressure Product (RPP) and Electrocardiography are monitored using, pulse oximetry, Non-invasive Blood Pressure (NIBP), and ECG monitor. Intravenous access using 18 G cannula was established and an I.V. infusion of ringer lactate was started. All patients were pre-oxygenated with 100% oxygen for *3 minutes* before induction with a tight fitting face mask. *Results:* All the patients received Tab. Alprazolam for night sedation, day before. One hour before the expected time of induction, Group P received tab. Pregabalin *150 mg* orally with sips of water and Group C received *0.3 mg* orally with sips of water. Base line parameters, after pre-medication, after induction and subsequently at *1 minute, 3 minutes, 5 minutes*, and *10 minutes* post-intubation were recorded. Data was tabulated and analyzed using Microsoft Office version 2010. The demographic profile (age wise, gender wise and weight wise distribution) was comparable in all the groups. Laryngoscopy and endotracheal intubation resulted in increased heart rate and blood pressure (SBP, DBP and MAP) in all the groups with maximum values at *1 minute*. The percentage rise in hemodynamic parameters was as given below Heart Rate: 10% rise above the baseline in Pregabalin Group 7.8% fall from the baseline in Clonidine Group Systolic blood pressure: 9.65% rise above the baseline in Pregabalin Group 4.67% rise from the baseline in Clonidine Group, Diastolic blood pressure: 11.91% rise above the baseline in Pregabalin Group 7.91% rise from the baseline in Clonidine Group, Mean arterial pressure: 11.16% rise above the baseline in Pregabalin Group, 7.72% rise from the baseline in Clonidine group. *Conclusion:* Both oral Clonidine *0.3 mg* and Oral Pregabalin *150 mg* effectively attenuates the hemodynamic response to laryngoscopy and endotracheal intubation. Clonidine was found to be more effective than Pregabalin in lowering of blood pressure and heart rate changes associated with laryngoscopy and endotracheal intubation. Pregabalin gives better post-operative analgesia, more sedation and less bradycardia as compared to Clonidine.

Keywords: Laryngoscopy; Clonidine; Pregabalin; Alprazolam.

How to cite this article:

R Srinivasa, Archana Endigeri. A Comparative Study of Oral Clonidine Vs Oral Pregabalin as Pre-medication to Attenuate Pressor Response to Direct Laryngoscopy and Endotracheal Intubation. Indian J Anesth Analg. 2019;6(6 Part -I):2041-2048.

Corresponding Author: Archana Endigeri, Assistant Professor, Department of Anesthesiology, S.N. Medical College, Bagalkot, Karnataka 587103, India.

E-mail: sathishkumard11@gmail.com

Received on 19.08.2019, **Accepted on** 23.10.2019

Introduction

Forbes and Laryngoscopy and endotracheal intubation are routine procedures of modern balanced general anesthesia technique. Endotracheal intubation has become an integral part of the anesthetic management and critical care of the patient and has been practiced following its description by Rowbotham and Magill in 1921. Dally (1970) described the circulatory response to laryngeal and tracheal stimulation following laryngoscopy and tracheal intubation as reflex sympathoadrenal stimulation.[1] Although increase in heart rate and blood pressure due to sympathoadrenal response is short lived they may have detrimental effects in high risk patients especially those with cardiovascular diseases, increased intracranial pressure or anomalies of cerebral vessels.[2] Laryngoscopy and tracheal intubation induced pressor responses have been associated with increase in catecholamine levels. Norepinephrine, epinephrine levels rise. Rise of these catecholamine's are associated with elevation of blood pressure and heart rate.[3] Some authors consider the intubation period one of the greatest risk in surgical patients with coronary artery diseases. Although the response may be transient, it is invariable, significant, often persistent, and of great concern.[4] The techniques of laryngoscopy and tracheal intubation are not confined only to the operating room, but are also employed for non anesthetic purposes.

Materials and Methods

Present clinical study was conducted in Department of Anesthesiology, Subbaiah Institute of Medical Science and Research Centre, Purle, Shivamogga. After approval from the hospital ethics committee, study was conducted during the period between *October 2016* and *September 2018*. It was a prospective study. A total of 60 patients undergoing elective surgery were selected.

Inclusion Criteria

- Patients aged between *18* and *50 years* of age of both genders;
- American Society of Anesthesiologist's Grade I and II patients;
- Patients with Mallampatti airway Grade I and II;
- Patients undergoing elective major or minor surgical procedures under general anesthesia.

Exclusion Criteria:

- Patient's refusal;
- Age less than *18 years* and more than *50 years*;
- Patients with Mallampatti airway Grade III and IV;
- Patients with comorbities like Hypertension, Ischemic Heart Diseases, Arrhythmias, Renal, Respiratory, Cerebral Diseases, Asthmatics and Epileptics;
- Anticipated difficult intubation;
- If, patient is allergic to any of drugs used in the study;
- Patients taking sedatives, hypnotics.

Pregnancy: Emergency Procedures

Laryngoscopy duration of > *20 seconds* or more than 1 attempt of laryngoscopy.

A total of 60 patients were divided into two Groups of 30 each, Group C (Clonidine), and Group P (Pregabalin).

Thorough pre anesthetic evaluation was done for all the patients. Written, valid informed consent was obtained both for conduct of study as well as for surgery and anesthesia. Patients were kept nil by mouth from midnight before surgery and Tab. Alprazolam (*0.25 mg*) was administered.

- Nil per oral status confirmed in the morning and patient's baseline Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Heart Rate were recorded.
- During this period, 60 patients were selected

They were divided into two groups:

- Group C (n = 30): Received Tab Clonidine *0.3 mg*. Group P (n = 30): Received Tab Pregabalin *150 mg*.
- Group C received tab Clonidine (*0.3 mg*) and Group P received tab Pregabalin (*150 mg*) with sips of water, *60 minutes* before the expected time of induction of anesthesia.

Preparation of the operation theatre:

The anesthesia workstation was checked. Appropriate sized endotracheal tubes, working laryngoscope with medium and large sized blades and working suction apparatus were kept ready before induction.

Anesthetic Technique

Patients in each group received respective drugs as per timing and dose mentioned earlier.

On arrival in the operating room, patient's basal parameters-Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MBP), Rate Pressure Product (RPP) and Electrocardiography are monitored using, pulse oximetry, Non-invasive Blood Pressure (NIBP), and ECG monitor. Intravenous access using 18 G cannula was established and an I.V. infusion of ringer lactate was started. All patients were pre-oxygenated with 100% oxygen for *3 minutes* before induction with a tight fitting face mask. All the patients were pre-medicated with intra-venous metoclopramide *10 mg*, Glycopyrrolate *0.2 mg*, and Fentanyl *2 mcg/kg*.

After pre-oxygenation, patients in each group was induced with thiopentone sodium *5 mg/kg* I.V. slowly till the loss of eyelash reflex. This was followed by Vecuronium bromide *0.1mg/kg* I.V.

Patient's lungs were manually ventilated with 100% oxygen before orotracheal intubation.

Direct laryngoscopy performed after *3 minutes* by using appropriate sized Macintosh blade and tracheal intubation performed within *15 seconds* using appropriate cuffed endotracheal tube.

Cases where more than one attempt at laryngoscopy was made were excluded from the study.

The patients lungs was mechanically ventilated with tidal volume *6–8 ml/kg* and respiratory rate of *12 minute* to maintain end tidal $PaCO_2$ at around 30–35 *mm* of *hg*. Anesthesia was maintained with Oxygen 33%, Nitrous Oxide 66% and Isoflurane 1% on controlled ventilation. Muscle relaxant was given in intermittent doses of Vecuronium Bromide and supplemental analgesia intravenous fentanyl *1 mcg/kg* was given.

All the parameters of the study was recorded at the following stages:

- Pre-operative (baseline);
- On arrival in the operating room (pre-induction);

  Post-induction;
- Immediately after induction;

At *1 minute*, *3 minutes*, *5 minutes*, *10 minutes* after induction;

At the end of surgery reversal was given with Glycopyrrolate *10 µg/kg* I.V. and Neostigmine *0.05 mg/kg* I.V.

Extubation done when the patient was completely awake and shifted to the recovery room. SBP, DBP, MAP, HR were recorded post extubation. Any untoward effects related to the drug and Anesthesia were noted and attended to appropriately.

A fall in mean blood pressure by 30% from the baseline was treated with Ephedrine *6 mg* boluses. A fall in the heart rate less than *40 min* was treated with inj Atropine *0.6 mg*. analgesia if deemed necessary was supplemented with inj Fentanyl *1 µg/kg* I.V. Patients were followed up post-operatively at hourly basis till *8 hours* from drug administration. Any untoward effects were observed for noted and treated.

Results

Following were observations and results of the present study:

Age wise distribution was similar in both groups, shown in **Table 1**.

Table 1: Age wise distribution (n = 60)

Age in *years*	Clonidine (n = 30)	Pregabalin (n = 30)
20–29	13 (43.33%)	13 (43.33%)
30–39	11 (36.66%)	12 (40%)
40–49	06 (20%)	07 (23.33%)
Mean ± SD	31.73 ± 6.98	31.67 ± 8.03

The weight wise distribution of patients in both the groups was similar, shown in **Table 2**.

Table 2: Weight wise distribution (n = 60)

Weight in *kgs*	Clonidine (n = 30)	Pregabalin (n = 30)	p-value
45–55	16	18	0.48
56–65	14	12	
Mean ± SD	54.83 ± 5.88	54.56 ± 5.63	

Baseline (*pre-induction*): There was no statistically significant difference between the two groups (p-value = 0.16).

Post-induction: There was statistically significant difference between the two groups (p-value < 0.001)

After intubation: There was significantly rise in heart rate in pregabalin group (p-value < 0.001) till *5 minutes* after intubation (**Tables 3–6)**.

Baseline: There was no statistically significant difference between the two groups (p-value = 0.17).

Pre-induction: There was no statistically significant difference between the two groups (p-value = 0.42)

Post-induction: There was no statistically significant difference between the two groups (p-value = 0.62).

Table 3: Comparison of mean heart rate (Mean ± SD, *Beats/Min*) between Groups (*n* = 60)

Time of assessment	Clonidine (*n* = 30)		Pregabalin (*n* = 30)		*t*-value	*p*-value
	Mean	SD	Mean	SD		
Baseline	85.03 ±	7.93	87.67	5.34	1.431	0.163
Pre-induction	64.77	8.95	82.33	13.52	1.800	0.082
Post-induction	71.77	9.92	86.06	12.02	4.549	< 0.001
1 minute	78.4	9.14	96.66	14.15	5.753	< 0.001
3 minute	75.36	8.72	91.43	12.43	5.933	< 0.001
5 minute	73.16	8.97	87.33	11.27	5.767	< 0.001
10 minute	71	8.49	84.4	11.27	4.818	< 0.001

p-value < 0.05 – significant

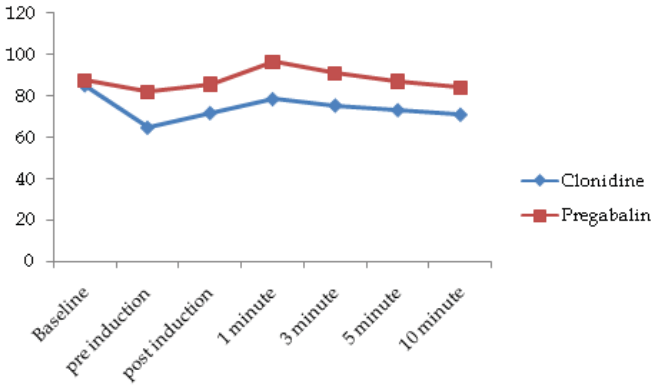

Chart 1: Comparison of mean heart rate between groups

Heart rate	Baseline	pre induction	post induction	1 minute	3 minute	5 minute	10 minute
Clonidine	85.03	64.77	71.77	78.4	75.36	73.16	71
Pregabalin	87.67	82.33	86.06	96.66	91.43	87.33	84.4

Table 4: Comparison of mean Systolic blood pressure (MEAN ± SD, *mm Hg*) between groups (*n* = 60)

Time of assessment	Clonidine(n = 30)		Pregabalin (n = 30)		*t*-value	*p*-value
	Mean	SD	Mean	SD		
Baseline	123.33	12.25	119.83	10.41	-1.380	0.178
Pre-induction	121.03	12.90	123.93	12.28	0.817	0.421
Post-induction	114.53	11.33	113.06	12.86	-0.491	0.627
1 minute	129.06	13.27	131.4	15.43	0.587	0.562
3 minute	123.3	14.07	120.8	18.84	-0.588	0.561
5 minute	119.26	14.98	115.63	19.38	-0.800	0.430
10 minute	117	14.98	113.13	18.01	-0.948	0.351

p-value < 0.05 – significant

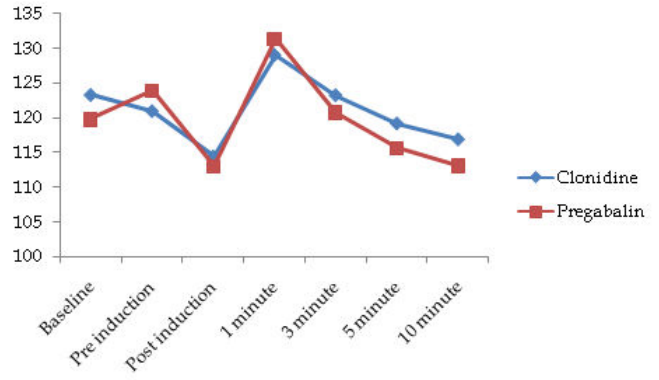

Chart 2: Comparison of mean systolic blood pressure between groups

After Intubation

At *1 minutes*, there was no significant difference between mean systolic blood pressure of two groups (*p*-value = 0.56).

At *3 minutes*, there was no significant difference between mean systolic blood pressure of two groups (*p*-value = 0.56).

At *5 minutes*, there was no significant difference between mean systolic blood pressure of two groups (*p*-value = 0.43).

At *10 minutes*, there was no significant difference between mean systolic blood pressure of two groups (*p*-value = 0.35).

Pre-induction: There was no statistically significant difference between the two groups (*p*-value = 0.13).

Post-induction: There was no statistically significant difference between the two groups (p-value = 0.62).

After Intubation:

At *1 minutes*, there was no significant difference between mean diastolic blood pressure of two groups (*p*-value = 0.69).

At *3 minutes*, there was no significant difference between mean diastolic blood pressure of two groups (*p*-value = 0.09).

At *5 minutes*, there was no significant difference between mean diastolic blood pressure of two groups (*p*-value = 0.43).

At *10 minutes*, there was no significant difference between mean diastolic blood pressure of two groups (*p*-value = 0.35).

Table 5: Comparison of mean Diastolic blood pressure (MEAN ± SD, *mm Hg*) between groups (*n* = 60)

Time of assessment	Clonidine (n = 30)		Pregabalin (n = 30)		*t*-value	*p*-value
	Mean	SD	Mean	SD		
Baseline	75.06	3.65	73.36	4.38	-1.937	0.063
Pre-induction	71.2	11.35	75.03	6.92	1.557	0.130
Post-induction	69.63	9.14	68.46	9.29	-0.497	0.623
1 minute	81	9.35	82.1	11.66	0.404	0.689
3 minute	78.43	8.91	74.33	13.35	-1.724	0.095
5 minute	73.53	10.78	71.1	14	-0.791	0.435
10 minute	72.33	9.84	69.6	12.42	-0.951	0.350

p-value < 0.05 – significant

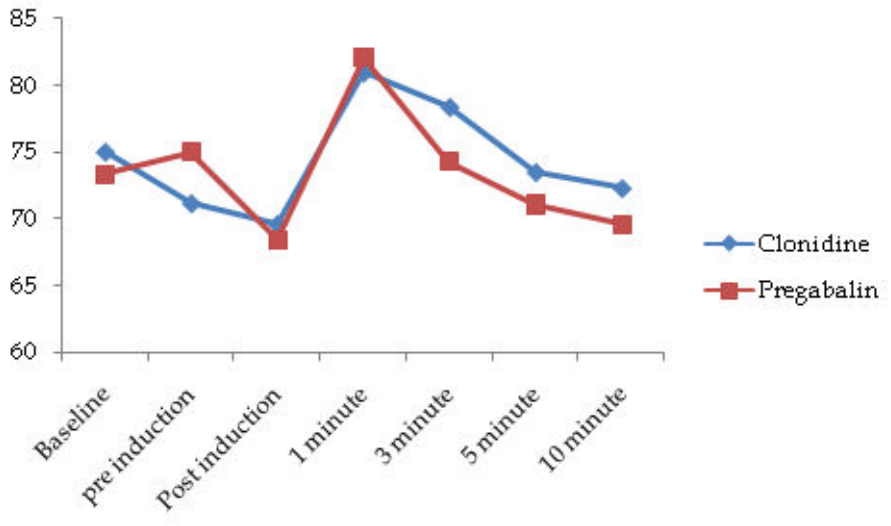

Chart 3: Comparison of mean diastolic blood pressure between groups Baseline: There was no statistically significant difference between the two groups (*p* value = 0.06).

Mean diastolic pressure	Baseline	pre induction	post induction	1 minute	3 minute	5 minute	10 minute
Clonidine	75.06	71.2	69.63	81	78.43	73.53	72.33
Pregabalin	73.36	75.03	68.46	82.1	74.33	71.1	69.6

Table 6: Comparison of mean rate pressure product (MEAN ± SD) between groups (n = 60)

Time of assessment	Clonidine (n = 30)		Pregabalin (n = 30)		t-value	p-value
	Mean	SD	Mean	SD		
Baseline	10467.13	1243.84	10498.43	1023.34	0.103	0.919
Pre-induction	7895.73	1624.96	10162.57	1717.11	1.801	0.082
Post-induction	8243.3	1511.225	9703.56	1569.23	3.367	0.002
1 minute	10171.9	1832.78	12766	2727.09	4.055	< 0.001
3 minute	9342.86	1772.41	11097.87	2568.49	3.072	0.005
5 minute	8766.23	1747.27	10116.93	2164.80	2.778	0.009
10 minute	8325.26	1519.45	9551.53	2018.89	2.625	0.014

p-value < 0.05 – significant

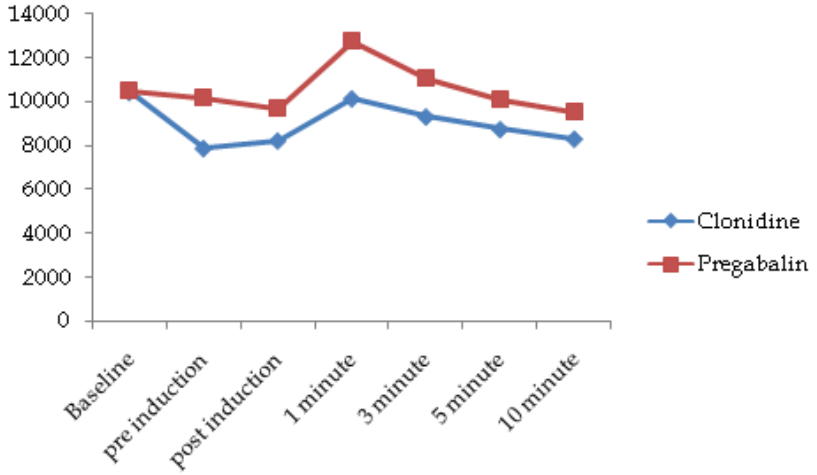

Chart 4: Comparison of mean rate pressure product between groups

Mean rate pressure	Baseline	pre induction	post induction	1 minute	3 minute	5 minute	10 minute
Clonidine	10467.13	7895.73	8243.3	10171.9	9342.86	8766.23	8325.26
Pregabalin	10498.43	10162.57	9703.56	12766	11097.87	10116.93	9551.53

Baseline: There was no statistically significant difference between the two groups (p-value = 0.92).

Pre-induction: There was no statistically significant difference between the two groups (p-value = 0.08).

Post-induction: There was statistically significant difference between the two groups (p-value = 0.002).

After Intubation: There was rise in mean rate pressure product in Pregabalin group.

At *1 minutes*, there was significant difference between mean rate pressure product of two groups (p-value < 0.001). In Pregabalin group 21% rise from the baseline compared to 2.8% fall from baseline in clonidine group.

At *3 minutes*, there was significant difference between mean rate pressure product of two groups (p-value = 0.005).

At *5 minutes*, there was significant difference between mean rate pressure product of two groups (p-value = 0.009).

At *10 minutes*, there was significant difference between mean rate pressure product of two groups (p-value = 0.014).

Electrocardiogram

No ST-T changes were observed in ECG of any the patients throughout the study period.

No arrhythmias were noted in any of the patients throughout the study period.

SpO_2:

SpO_2 was maintained 98% and above in all the patients.

Discussion

Induction of general Anesthesia, direct laryngoscopy and endotracheal intubation induce marked cardiovascular changes as well as autonomic reflex activity. The response may be particularly hazardous for patients with cerebral

and cardiovascular diseases. Attenuation of these hemodynamic responses is of great importance in prevention of peri-operative morbidity and mortality. Typically blood pressure and heart rate elevations occur after about *15 seconds* of laryngoscopy and become maximal after *30–45 seconds* of laryngoscopy.[60] A rise in mean heart rate of *29.9 beats/minute* has also been noted.

Strategies to circumvent these changes have included minimizing the duration of laryngoscopy, I.V. Narcotics, I.V. and topical Lidocaine, vasodilators, Beta-blockers, Calcium channel blockers, inhaled anesthetics. Although these drugs did obtund the cardiovascular response, they failed to fulfil the desired criteria of complete attenuation.[7]

Variation of heart rate changes decrease with increasing age. Young patients show more extreme changes. Marked fluctuations in hemodynamic response are often seen in geriatric patients. In our study, we selected an optimal age range of *18* to *50 years*.[8–10]

Patients on anti-hypertensive drugs may exhibit a decrease in pressor response. We excluded the patients on anti-hypertensive medications from our study. A variable combination of drugs used for pre-medication, induction, relaxation and maintenance of anesthesia can influence the sympathetic response to laryngoscopy and intubation.[11–13]

The efficacy of clonidine in attenuating hemodynamic stress response has been studied previously in many studies and proved its effectiveness. Orally administered clonidine in pre-anesthetic period provides hemodynamic stability and attenuates the stress response to laryngoscopy and tracheal intubation. Mechanisms by which clonidine blunts the stress response of airway instrumentation are activation of central α_2-adrenoreceptors which decreases peripheral sympathetic tone and stimulation of peripheral presynaptic α_2 adrenoreceptors which leads to decreased norepinephrine release from nerve endings, hence reduced peripheral sympathetic tone.

Pregabalin is congener of gabapentine, an anti-epileptic drug, acts by inhibiting membrane voltage-gated calcium channels in central nervous system. It does not interact with GABA receptors. It has analgesic, anticonvulsant, and anxiolytic properties. It is effective in controlling neuropathic pain. Effect of pregabalin on attenuating stress response to laryngoscopy and tracheal intubation was evaluated previously in few studies. It was found to be very useful and effective pre-medicant to blunt hemodynamic stress response to tracheal intubation in all those studies.

Only few studies are available in literature regarding the comparison of efficacy of both these drugs in attenuating stress response to laryngoscopy and tracheal intubation. Gupta K *et al.*, evalauted and compared these drugs and found that both the drugs provide hemodynamic stability during laryngoscopy without prolongation of recovery time and side effects. The results of our study support the observations of Gupta K *et al.* According to them clonidine was found superior to pregabalin for attenuation of the hemodynamic stress responses to laryngoscopy and tracheal intubation but with increased incidence of intra- and post-operative bradycardia. No post-operative side effects were observed in pre-medicated patients.

Pre-medication with benzodiazepines has no effect on sympathetic response to laryngoscopy and intubation. Glycopyrrolate pre-medication can be moderately increase the heart rate. I.V. Metoclopramide is used as pre-medication as anti-emetic for the prevention of post-operative nausea and vomiting.[14,15]

Conclusion

Both oral Clonidine *0.3 mg* and Oral Pregabalin *150 mg* effectively attenuates the hemodynamic response to laryngoscopy and endotracheal intubation. Clonidine was found to be more effective than Pregabalin in lowering of blood pressure and heart rate changes associated with laryngoscopy and endotracheal intubation. Pregabalin gives better post-operative analgesia, more sedation and less bradycardia as compared to Clonidine.

References

1. Millar Forbes A, Dally FG. Acute hypertension during induction of Anesthesia and endotracheal intubation in normotensive man. Br J Anesth. 1970;42:618–623.
2. Bachofen M. Suppression of blood pressure increases during intubation: Lidocaine or fentanyl. Anesthesist. 1988 Mar;37(3):156-61.
3. Vincent J Collins. Principles of anesthesiology, general and regional anesthesia, 3rd edition. Vol. I and II, Philadelphia: Lea and Febiger; 1993.
4. KoSh, Kim DC, Han YJ, *et al*. Small doses of fentanyl: Optimal time of injection for blunting the circulatory responses to tracheal intubation. Anesth Analg. 1998;86(3):658–61.

5. Rastogi B, Gupta K, Gupta PK, *et al*. Oral pregabalin pre-medication for attenuation of hemodynamic pressor response of airway instrumentation during general anesthesia: A dose response study. Indian J Anesth. 2012;56(1):49.
6. Marchal JM, Gómez-Luque A, Martos-Crespo F, *et al*. Clonidine decreases intra-operative bleeding in middle ear microsurgery. Acta Anesthesiol Scand. 2001;45(5):627–33.
7. Roy S, Gupta RA, Mondal T, *et al*. Attenuation of cardiovascular responses to laryngoscopy and tracheal intubation with oral clonidine. Indian J Anesth. 1993;41:62–66.
8. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with or without tracheal intubation. Br J Anesth. 1987;59:295–99.
9. Wright PMC, Carabine UA, McClune S, *et al*. Pre-anesthetic medication with clonidine. Br J Anesth. 1990;65:628–632.
10. Roizen MF, Lichtol LJ. Pre-operative assessment and pre-medication for adults. In: Thomas EJ Healy, Cohen PJ (Eds). Wylie and Churchill Davidson's A practice of anesthesia, 6th edition. Great Britain: Amold; 1995. 613–14.
11. Derbyshire DR, Smith G. Sympathoadrenal responses to anesthesia and surgery. Br J Anesthesia. 1984:56:725–737.
12. Zalunardo MD P, Zollinger MD Andreas, Donat R Spahn, *et al.* Effects of intravenous and oral Clonidine on hemodynamic and plasma-catecholamine response due to endotracheal intubation. Journal of Clinical Anesthesia. 1997;9(2):143–47.
13. Stuhmeier KD, Mainzer B, Cierpka J, *et al*. Small oral dose of Clonidine reduces the incidence of intra-operative myocardial ischemia in patients having vascular surgery. Anesthesiology. 1996;85:706–712.
14. Matot MD Idit, Sichel MD JY, Yofe MD Valeri, *et al*. The Effect of Clonidine Pre-medication on Hemodynamic Responses to Microlaryngoscopy and Rigid Bronchoscopy. Anesthesia and Analgesia. 2000;91(4):828–833.
15. Yotsui T. Clonidine pre-medication prevents sympathetic hyperactivity but does not prevent hypothalamo-pituitary-adrenocortical responses in undergoing laparoscopic cholecystectomy. J Anesth. 2001:15(2):78–82.