Original Research Paper

Volume-7 | Issue-9 | September-2017 | ISSN - 2249-555X | IF : 4.894 | IC Value : 79.96

Anaesthesiology

ORAL CLONIDINE VERSUS ORAL GABAPENTIN AS PREMEDICATION FOR OBTUNDING HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND TRACHEAL INTUBATION

Dr. Smita Joshi — Professor, Dept of anaesthesia, Dr. D.Y. Patil Medical College, Pimpri, Pune, India

Dr. Anil Kumar — Senior resident, Dept of anaesthesia, Dr. D.Y. Patil Medical College, Pimpri, Pune, India - CORRESPONDING AUTHOR

Dr. Harshi Shah — Resident doctor, Dept of anaesthesia, Dr. D.Y. Patil Medical College, Pimpri, Pune, India

ABSTRACT

OBJECTIVES: To evaluate and compare the effect of oral clonidine and oral gabapentin for obtunding hemodynamic response (HR, SBP, DBP, MAP, RPP) to laryngoscopy and intubation in normotensive patients having physical status of Grade-I and Grade-II according to American Society of Anesthesiologists (ASA), scheduled for elective surgery under general anesthesia.
To observe the side effects in the above two drugs if any.

INTRODUCTION: Manipulation of the respiratory tract such as in laryngoscopy and tracheal intubation are associated with hemodynamic and cardiovascular responses consisting of increase in circulating catecholamines, with subsequent increase in heart rate and blood pressure. There is increase in myocardial oxygen demand and dysrhythmias may occur as well. Both Clonidine, an α2 adrenergic agonist and gabapentin which is a GABAB receptors agonist causes obtunding of hemodynamic response during laryngoscopy and tracheal intubation.

METHOD: A prospective randomized study was done in 60 patients undergoing elective surgeries under standard general anaesthesia was selected randomly and were divided into two groups. Group C - Received 300 µg of clonidine and Group G - Received 900 mg of gabapentin, orally 90 minutes prior to surgery. Parameters such as heart rate (HR), systolic blood pressure (SBP),diastolic blood pressure (DBP),mean arterial pressure (MAP), saturation (Spo2) and rate pressure product (RPP) was recorded, before premedication, before induction and during intubation at different time intervals (T0, T1, T3, T5 T10 and T15 minutes). Side effects pertaining to clonidine and gabapentine were recorded post operatively as well.

RESULT: In clonidine group the hemodynamic parameters returned below baseline after 5 minutes of laryngoscopy where as in gabapentine group the hemodynamic parameters remained above baseline throughout surgery after laryngoscopy.

CONCLUSION: Oral clonidine 300mcg given 90 minutes prior to surgery was superior to oral gabapentine 900mg in attenuation of hemodynamic response to laryngoscopy and intubation. There was no significant hypotension and bradycardia in both the groups.

KEYWORDS : .

INTRODUCTION

Induction of anesthesia and tracheal intubation may cause profound alteration of the hemodynamic state of patient, consequent to both the effects of anesthetic drugs administered preoperatively and the adrenergic state of the patient.[1] Though these undesirable changes are transitory in nature and well tolerated in healthy individuals, it may result in potentially deleterious effects in patients with co-morbid conditions like hypertension, raised intracranial pressure or coronary artery disease.

- The cardiovascular response is also directly related to the force and duration of laryngoscopy.[2] Many drugs and techniques have been used for the attenuation of response to laryngoscopy and intubation, such as [3] –
- Deeper plane of anaesthesia with intravenous or inhalation agents.
- Use of Opoids prior to induction e.g. Fentanyl, Sufentanyl or Alfentanyl.
- Use of intravenous lidocaine.
- Lidocaine sprays or gargles 3 minutes prior to intubation.
- Use of ACE inhibitors e.g. Captopril, Enalapril 45 minutes prior to intubation.
- Various antihypertensive and vasodilators e.g. IV Hydralazine, Ca+2 channel blockers like Nifedipine, beta blockers like Esmolol.
- Alpha -2 agonists like Clonidine.
- Use of Gabapentin.

Clonidine, an imidazoline derivative is a α2 adrenergic agonist, which stimulates α2 adrenergic receptors in the brainstem, particularly in the nucleus tractus solitarius of the medulla oblongata resulting in reduction of sympathetic outflow from central nervous system. By its central sympatholytic action, it tends to attenuate the hemodynamic response to any surgical nociceptive stimulus and to improve overall perianesthetic cardiovascular stability. Oral clonidine premedication also offers additional advantage of reduction of postoperative pain, nausea-vomiting, and shivering.[4,5]

Gabapentin causes selective activation of heterodimeric GABAB receptors. It acts by decreasing the synthesis of neurotran¬smitter glutamate and by binding to α-2δ subunit of voltage dependent calcium channel. Gabapentin has been found to be effective in reducing the noxious stimuli to laryngoscopy and intuba¬tion, thereby attenuating the hemodynamic response. [6]

METHODOLOGY

Institutional Ethics Committee approval was taken prior to commencement of the study. This prospective randomized study was conducted at Dr. D.Y. Patil Medical College, Pune. Total 60 patients undergoing elective surgeries under standard general anaesthesia was selected randomly and were divided into two groups. Group C - Received 300 µg of clonidine and Group G - Received 900 mg of gabapentin, orally 90 minutes prior to surgery. Parameters such as heart rate (HR), systolic blood pressure (SBP),diastolic blood pressure (DBP),mean arterial pressure (MAP), saturation (Spo2) and rate pressure product (RPP) was recorded, before premedication, before induction and during intubation at (T0, T1, T3, T5 T10 and T15 minutes). Side effects pertaining to clonidine and gabapentine were recorded post operatively as well.

An informed and written consent was taken for every case selected for the study. All the necessary and relevant laboratory and other investigations was carried out.

INCLUSION CRITERIA:

- ASA grades I or II.
- Ages between 20 and 50 years of either sex.
- Patient undergoing elective surgery under general anaesthesia with endotracheal intubation.
- Hemodynamically stable patients with all routine investigations within normal limits.

EXCLUSION CRITERIA:

- Patient refusal
- Patients with ASA physical status III or more.
- Patients with anticipated difficult intubation.
- Patients posted for emergency surgery.

- Patients on any opioid or any sedative medication in the week prior to the surgery.
- Patients who are known allergic to any of the test drugs.

ANAESTHESIA TECHNIQUE:

In the operating room, ECG, peripheral oxygen saturation and non-invasive blood pressure monitors were attached to the patient and the patient's heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP),mean arterial pressure (MAP), saturation (Spo2) and rate pressure product (RPP) was recorded again. Ringer lactate infusion was started through 20G i.v cannula. All patients were premeditated with inj. ondansetron 4mg and inj. glycopyrrolate 0.2mg i.v before induction of anaesthesia. After 3 minutes of preoxygenation, anaesthesia was induced with inj. propofol 2mg/kg followed by inj. succinylcholine 2mg/kg to facilitate tracheal intubation. Obtundation of hemodynamic responses during laryngoscopy and intubation was observed and recorded. All the patients were maintained with 33% oxygen, 66% nitrous oxide, 0.5-1% isoflurane and intermittent bolus of inj. vecuronium. Intra operative analgesia was provided with inj. fortwin 0.3mg/kg.

At the end of the surgery neuromuscular blockade was reversed with inj. neostigmine 2.5mg and inj. glycopyrrolate 0.2mg before extubation. Following parameters i.e. heart rate (HR), systolic blood pressure (SBP),diastolic blood pressure (DBP),mean arterial pressure (MAP), saturation (Spo2) and rate pressure product (RPP) was recorded, before premedication, before induction and during intubation at (T0, T1, T3, T5 T10 and T15 minutes). ECG was continuously monitored. Side effects pertaining to clonidine and gabapentine were recorded post operatively as well.

OBSERVATIONS AND RESULTS

There was no statistically significant (P>0.05) difference in terms of demographic characteristics of the patients ie age, sex, body weight, and ASA grade among the two groups as shown in Table 1.

Table 1: Demographic profile (Mean ± SD)

Demographic Profile	Group C	Group G	P Value	Significance
Age (years)	32.33±6.58	33.10±7.20	0.339*	P > 0.05 NOT SIGNIFICANT
Weight (Kg)	66.13±6.32	64.07±6.35	0.081*	
Sex (M : F)	18:12	16:14	0.6023**	
ASA Grading	Grade I =19 Grade II =11	Grade I =21 Grade II =9	0.5838**	

(* - paired 't' test, ** - Chi-square test)

Table 2: Preoperative vital parameters (Mean ± SD) using paired't' test

BEFORE PREMEDICATION

Vital Parameters	Group C	Group G	P Value	Significance
Pulse Rate (bpm)	79.43±8.97	76.267±6.35	0.056	NOT SIGNIFICANT
SBP	127±11	123±6.4	0.1	NOT SIGNIFICANT
DBP	75±6	73±3.9	0.1	NOT SIGNIFICANT
MAP (mm Hg)	92.144±7.19	89.62±3.73	0.059	NOT SIGNIFICANT
RPP	10091.6±1722.92	9469.47±983.5	0.065	NOT SIGNIFICANT

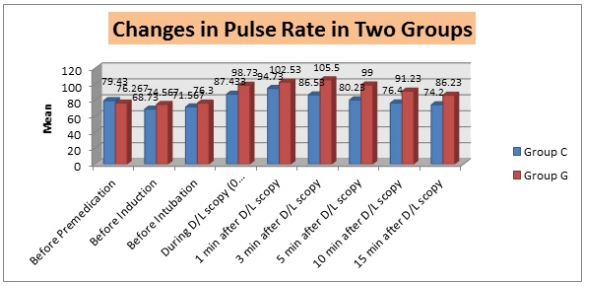
Baseline parameters (Pulse rate, SBP, DBP, MAP, RPP) in both the groups before premedication were comparable and their P value (<0.05) was not significant as shown in table 2.

Comparison of Hemodynamic Response of Patients of Group C (Clonidine) and Group G (Gabapentine) at different time interval.

Table 3: Changes in pulse rate in two groups (using paired't' test)

Pulse Rate (bpm)	Group C (Mean±SD)	Group G (Mean±SD)	P Value	Significance
Before Premedication	79.43±8.97	76.267±6.35	0.056	NS
Before Induction	68.73±7.43	74.567±5.41	0.0003	HS
Before Intubation	71.567±7.6	76.3±3.3	0.0022	HS
During D/L scopy (0 min)	87.433±12.39	98.73±9.1	0.0001	HS
1 min after D/L scopy	94.73±7.67	102.53±8.19	<0.0001	HS
3 min after D/L scopy	86.53±7.47	105.5±8.68	<0.0001	HS
5 min after D/L scopy	80.23±6.58	99±8.13	<0.0001	HS
10 min after D/L scopy	76.4±6.32	91.23±6.89	<0.0001	HS
15 min after D/L scopy	74.2±5.33	86.23±5.7	<0.0001	HS

NS- Not significant, HS- Highly significant



After 5 minutes of laryngoscopy heart rate returned below baseline ie before premedication in clonidine group but in gabapentine group heart rate remained above baseline after laryngoscopy and their P value (<0.05) was highly significant (HS) at different time of interval after laryngoscopy as shown in table 3.

Table 4 Changes in systolic blood pressure in two groups (using paired 't' test)

Systolic Blood Pressure (mm Hg)	Group C (Mean±SD)	Group G (Mean±SD)	P Value	Significance
Before Premedication	126.5±11.13	122.833±6.3	0.075	NS
Before Induction	112.067±10.29	119.7±7.37	0.0011	HS
Before Intubation	110.4±12.57	121.533±9.6	0.0002	HS
During D/L scopy (0 min)	134.66±8.14	141.7±7.7	0.0003	HS
1 min after D/L scopy	132±7.85	156.53±9.61	<0.0001	HS
3 min after D/L scopy	123.1±7.74	157.67±9.88	<0.0001	HS
5 min after D/L scopy	117.03±7.4	148.53±9.45	<0.0001	HS
10 min after D/L scopy	113.87±8.52	139.83±9.3	<0.0001	HS
15 min after D/L scopy	113.27±8.81	132.13±10.44	<0.0001	HS

NS- Not significant, HS- Highly significant

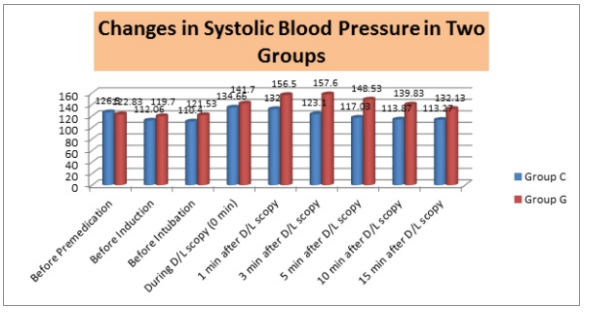
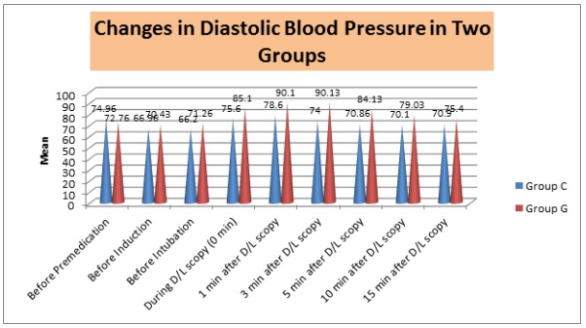


Table 4: clearly shows that systolic blood pressure returned below baseline ie before premedication after 1 minutes of laryngoscopy in clonidine group but it remained above baseline after laryngoscopy in gabapentine group.

Table 5: Changes in diastolic blood pressure in two groups (using paired't' test)

Diastolic Blood Pressure (mm Hg)	Group C (Mean±SD)	Group G (Mean±SD)	P Value	Significance
Before Premedication	74.967±6.05	72.767±3.918	0.053	NS
Before Induction	66.967±4.795	70.433±3.701	0.0005	HS
Before Intubation	66.2±7.572	71.267±2.476	0.0005	HS
During D/L scopy (0 min)	75.6±6.322	85.1±5.441	<0.0001	HS
1 min after D/L scopy	78.6±7.049	90.1±5.108	<0.0001	HS
3 min after D/L scopy	74±5.521	90.133±5.197	<0.0001	HS
5 min after D/L scopy	70.867±4.183	84.133±4.606	<0.0001	HS
10 min after D/L scopy	70.1±2.99	79.03±5.149	<0.0001	HS
15 min after D/L scopy	70.967±3.44	75.4±5.875	0.0008	HS

NS- Not significant, HS- Highly significant

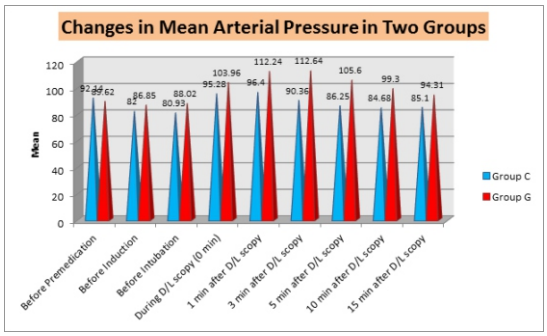


Diastolic blood pressure returned below baseline ie before premed ication after 1 minutes of laryngoscopy in clonidine group but it remained above baseline after laryngoscopy in gabapentine group as shown in table 5 and their P value (>0.05) was highly significant.

Table 6: Changes in mean arterial pressure in two groups (using paired't' test)

Mean arterial Pressure (mm Hg)	Group C (Mean±SD)	Group G (Mean±SD)	P Value	Significance
Before Premedication	92.144±7.19	89.62±3.73	0.059	NS
Before Induction	82±6.202	86.855±4.286	0.0003	HS
Before Intubation	80.933±8.669	88.022±3.533	<0.0001	HS
During D/L scopy (0 min)	95.289±5.399	103.967±4.465	<0.0001	HS
1 min after D/L scopy	96.4±6.291	112.244±6.35	<0.0001	HS
3 min after D/L scopy	90.367±5.636	112.64±6.074	<0.0001	HS
5 min after D/L scopy	86.255±4.58	105.6±5.171	<0.0001	HS
10 min after D/L scopy	84.68±4.16	99.3±6.19	<0.0001	HS
15 min after D/L scopy	85.1±4.435	94.311±7.027	<0.0001	HS

NS- Not significant, HS- Highly significant



Mean arterial pressure returned below baseline ie before premedi cation after 1 minutes of laryngoscopy in clonidine group but it remained above baseline after laryngoscopy in gabapentine group as shown in table 6 and their P value (>0.05) was highly significant.

Distribution by Ramsay Sedation Score (RSS)

Table 7 shows the distribution of patients according to their RSS. It shows that (Group C) clonidine group patients were having higher sedation score as compared to gabapentine group but were arousable.

Table No. 7: Distribution by RSS

RSS	CLONIDINE		GABAPENTINE		'p' Value
	Frequency	Percentage	Frequency	Percentage	
1	0	0.0	16	53.3	<0.0001 HS
2	11	36.7	14	46.7	
3	19	63.3	0	0.0	
4	0	0	0	0.0	
5	0	0	0	0.0	

HS- Highly significant

Distribution by Dryness of Mouth

Table 8 shows the distribution of patients according to their Dryness of Mouth. It shows that the majority of patients had Dryness of Mouth (63.3%) in Clonidine group and the majority of patients in Gabapentine group did not had Dryness of Mouth (93.3%) and their P values were highly significant.

Table 8: Dryness of mouth in both the groups

Dryness of mouth	Clonidine (Group C)		Gabapentine (Group G)		'p' Value
	Frequency	Percentage	Frequency	Percentage	
Present	19	63.3	2	6.7	<0.0001 HS
Absent	11	36.7	28	93.3	

HS- Highly significant

Distribution by Hypotension

Table 9 shows the distribution of patients according to hypotension. It shows that in Clonidine group only 3 patients had hypotension but there was no hypotension in Gabapentine group and their P value was not significant.

Table 9: Frequency of hypotension in both the group.

Hypotension	Clonidine (Group C)		Gabapentine (Group G)		'p' Value
	Frequency	Percentage	Frequency	Percentage	
Present	3	10	0	0.0	0.075 (NS)
Absent	27	90	30	100	

NS- Not significant

Distribution by Bradycardia

Table 10 shows the distribution of patients according to number of episodes of bradycardia. It shows that only 2 patients had Bradycardia in Clonidine group and no patients had Bradycardia in Gabapentine group.

Table 10: Distribution by Bradycardia

Bradycardia	Clonidine		Gabapentine		P value
	Frequency	Percentage	Frequency	Percentage	
Present	2	6.7	0	0.0	0.15 NS

DISCUSSION

Tracheal intubation is a crucial skill in anaesthetic practice. It needs direct laryngoscopy to view the vocal cords for insertion of the endotracheal tube. Both laryngoscopy and passage of a tracheal tube are noxious stimuli that can incite adverse events in the respiratory, cardiovascular and other physiologic systems.[7] Endotracheal intubation has become the mainstay of modern anesthesia as it secures the airway, prevents aspiration of gastric contents, delivered predictable Fio2 and eliminates CO2 from the body.

The cardiovascular responses to noxious airway manipulation are

initiated by proprioceptors responding to tissue irritation in the supraglottic region & trachea. These proprioceptors located in close proximity to the airway mucosa, consist of mechanoreceptors with small diameter myelinated fibers. The glossopharyngeal & vagal afferent nerves transmit these impulses to the brain stem which in turn causes widespread autonomic activation through both the sympathetic & parasympathetic nervous systems. In adults, the more common response to airway manipulation is hypertension & tachycardia, mediated by the cardioaccelerator nerves & sympathetic chain ganglia. This response includes widespread release of norepinephrine from adrenergic nerve terminals & secretion of epinephrine from the adrenal medulla. Some of the hypertensive response also results from activation of the renin-angiotensin system, with the release of renin from the renal juxtaglomerular apparatus, which is innervated by β-adrenergic terminals.[8]

Preoperative anxiety is an important problem because it produces undesirable effects on anaesthesia & perioperative outcome. It not only changes doses of drugs which are needed for induction, maintenance of anesthesia but also it affects psychological condition of patients. Stress and anxiety activate hypothalamous-hypophysis-adrenal axis and increase glucocorticoid level. Stress releases hormones such as cortisol, catecholamines and cytokinin. These hormones increase negative nitrogen balance and catabolism and ultimately delay wound repair and weaken immune system postoperatively.[9]

Premedication forms an integral part of anaesthetic management and some form of premedication is universally administered before any anaesthesia. The ideal premedication should be effective and pleasant to be taken orally, have analgesic and non emetic properties, should not impair cardiovascular stability or depress respiration, and should effectively alleviate apprehension of the patient.

Oral clonidine doses up to 4-5 μg/kg have been investigated frequently, primarily for their anesthetic-sparing effects in the intraoperative period and for their opioid-sparing effects in the postoperative period.[10]

Gabapentin, 1-(aminomethyl) cyclohexane acetic acid, is a structural analogue of the neurotransmitter γ–aminobutyric acid. The mechanism of gabapentin in controlling this haemodynamic response remains unknown. Since, gabapentin inhibits membrane voltage gated calcium channels (VGCCs), it is possible that it may have a similar action to calcium channel blockers. There is, as yet, no data, on the possible role of gabapentin in the attenuation of other aspects of the stress response to surgery.[11] Some studies demonstrated that the descending noradrenergic system, spinal α2 adrenergic receptors and an intact spino-bulbo-spinal circuit are crucial elements influencing the analgesic effects of gabapentin in addition to α 2A interaction of VGCCs.[12,13]

The efficacy of clonidine in attenuation of cardiovascular response is similar to our study and has been verified by many other studies.

N Ratan Singh et al [14] in 2012 did " A study on clonidine as a premedicant and its effects on perioperative hemodynamic in normotensive patients" and found that Clonidine 2 μg/kg and 3 μg/kg i.v significantly controlled the perioperative hemodynamic response especially, during laryngoscopy and intubation. We have used oral clonidine 300 μg and our findings were similar to this study.

Raval DL et al [15] in 2002 studied "Oral clonidine pre medication for attenuation of haemodynamic response to laryngoscopy and intubation" and observed reductions in SBP and DBP following premedication with oral clonidine 0.2 mg by 7.63%. In post intubation period, SBP and DBP remained below baseline value producing significant attenuation of rise in SBP due to laryngoscopy and intubation. In our study all the hemodynamic parameters returned below baseline after 5 minutes following laryngoscopy and intubation. These findings were comparable with the above mentioned study.

Bafna et al [16] in 2011 did "A comparison of different doses of gabapentin to attenuate the haemodynamic response to laryngoscopy and tracheal intubation in normotensive patients" and used 1000 mg.

Memis et al 17 in 2006 studied the effect of gabapentin 400mg versus 800mg on mean arterial pressure and heart rate at induction of anaesthesia and tracheal intubation and compared it with a placebo. Their study showed that patients receiving placebo and 400 mg gabapentin showed a significant increase in blood pressure and heart rate associated with tracheal intubation compared to baseline levels and from patients receiving 800 mg of gabapentin. There was a significant decrease in heart rate and mean arterial pressure in the group receiving 800 mg gabapentin 1, 3, 5 and 10 min after intubation compared to the placebo group and 400 mg gabapentin group.

Marashi et al [18] in 2009 conducted a double blind, placebo-controlled, randomized study for elective orthopaedic surgery and concluded with contrasting results. The author used 900 mg gabapentin and 200 μg clonidine, 2 h before surgery and concluded that both gabapentin and clonidine have effective role in blunting the hyperdynamic responses following laryngoscopy and intubation more so with gabapentin. In our study, blunting the hemodynamic reflex response following laryngoscopy and intubation, clonidine has better response than gabapentin.

Both clonidine and gabapentin have certain adverse effects inherent to their structure. Most common side-effects with clonidine are dry mouth and sedation documented in almost 50% of patients and less common are hypotension and bradycardia.[19] The overall various side effects such as dryness of mouth in Clonidine group was 63.0% (19 patients out 30) which was highly significant (P<0.0001) where as in Gabapentin group only 6.7% (2 patients out of 30) complained of dryness of mouth as shown in table 13. High incidence of dryness of mouth (63%) was reported with clonidine in our study, which is associated with the effect of drug on pre-synaptic alpha-adrenoceptors in the brainstem as well as on parasympathetic nerves, which supplies the salivary gands. 20 No patients in gabapentine group had bradycardia or hypotension but in clonidine group the overall incidence of bradycardia was 6.7% and 10% patients had hypotension as shown in table 9 and table 10.

Episode of bradycardia was treated by injection Atropine 0.6mg. Overall the incidence of side effects is significantly less in gabapentine group. 63.3% of the patients in clonidine group had RSS of 3 (Responsive to commands) and 36.7% of the patients had RSS of 2 (Co-operative, oriented, calm).whereas in gabapentine group 53.3% of patients had RSS of 1 (Anxious and agitated or restless, or both) and 46.7 % had RSS of 2 (Co-operative, oriented, calm). No patients in both the groups were deeply sedated.

There are few limitations of this study. Patients with ASA physical status I and II were enrolled in the study, so the results cannot be generalized to the patients with higher ASA status. The study was conducted in a single centre. A multi-centered larger study may be more informative. Another limitation of our study was that we did not measure the stress mediators, i.e. endogenous plasma catecholamines or cortisol values perioperatively.

CONCLUSION

1. Oral clonidine 300mcg given 90 minutes prior to surgery was superior to oral gabapentine 900mg in attenuation of hemody namic response to laryngoscopy and intubation.
2. There was no significant hypotension and bradycardia in clonidine group as compared to gabapentine group.
3. Ramsay sedation score was more in clonidine group as compared to gabapentine group but the patients were not deeply sedated and were arousable.
4. Incidence of dryness of mouth was more in clonidine group which is a known side effect of clonidine but it was not distressing.

REFERENCES

1. Iannuzzi E, Iannuzzi M, Cirillo V, Viola G, Parisi R, Cerulli A, et al. Periintubation cardiovascular response during low dose remifentanil or sufentanil administration in association with propofol TCI. A double blind comparison.Minerva Anestesiol 2004; 70(3): 109-15.
2. King BD, Harris LC, Griefenstein FE, Elder JD, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. Br J Anaesth 1951; 12: 556-66.
3. Gandhi S, Goya V, Radhakrishnan K, Balakrishnan M : Comparison of Dexmedetomidine with Fentanyl in Attenuation of Pressor Response during Laryngoscopy and Intubation. IOSR Journal Of Pharmacy 2014; 4(2): 28-38.
4. Kalra NK, Verma A, Agarwal A, and Pandey HD: Comparative study of intravenously administered clonidine and magnesium sulfate on hemodynamic responses during laparoscopic cholecystectomy. J Anaesthesiol Clin Pharmacol 2011; 27(3): 344–348.
5. Bhandari D, Tidke S, Sharma V, Dongre H , Garg D, Dhande P: Hemodynamic changes associated with laparoscopic cholecystectomy: Effect of oral clonidine premedication. IOSR Journal of Pharmacy 2012; 2(4): 72-77.
6. Raouf A, Gohary M, Salah El-din Ashmawi H, El-Kerdawy HM, Essa HH: Efficacy of Preoperative Oral Gabapentin in Attenuation of Neuro-Endocrine Response to Laryngoscopy and Endotracheal Intu¬bation. Journal of Medical Sciences. 2009; 9:

24–9.
7. Henderson J. Airway management in the adult. In: Miller RD, editor. Miller's Anaesthesia, 7 th ed. Churchill Livingstone: Philadelphia; 2010.
8. Paul F White, Alejandro R F. Ambulatory anaesthesia. In : Miller's Anaesthesia 6th ed. Elsevier Ltd.2005; Chapter 68:p5759-5863.
9. Ashgan R A et al. efficacy of pre-operative gabapentin in attenuation of neuroendocrine response to laryngoscopy & endotracheal intubation. J Med Sci,2009;9:24-29.
10. Brest AN. Hemodynamic and cardiac effects of clonidine. J Cardiovasc Pharmacol 1980;2:S39-46.
11. Kong VK, Irwin MG. Gabapentin: A multimodal perioperative drug? Br J Anaesth 2007;99:775-86.
12. Suzuki R, Rahman W, Rygh LJ, Webber M, Hunt SP, Dickenson AH. Spinal, supraspinal serotonergic circuits regulating neuropathic pain and its treatment with gabapentin. Pain 2005;117:292-303.
13. Tanabe M, Takasu K, Kasuya N, Shimizu S, Honda M, Ono H. Role of descending noradrenergic system and spinal alpha2 adrenergic receptors in the effects of gabapentin on thermal and mechanical nociception after partial nerve injury in the mouse. Br J Pharmacol 2005;144:703-14.
14. Singh NR, Rajkumar G, Singh SS, Jamatia P, Singh TH, Singh T. A study on clonidine as a premedicant and its effects on perioperative hemodynamic in normotensive patients. J Med Soc 2012;26:180-3.
15. Raval DL, Mehta MK. Oral clonidine for attenuation of pressor response. Indian J Anaesth 2002;46:124-9.
16. Bafna U, Goyal VK, Garg A. A comparison of different doses of gabapentin to attenuate the haemodynamic response to laryngoscopy and tracheal intubation in normotensive patients. J Anaesth Clin Pharmacol 2011;27:43-46.
17. Memis D, Turan A, Karamanlioglu B, Seker S, Ture M. Gabapentin reduces cardiovascular responses to laryngoscopy and tracheal intubation. Eur J Anaesthesiol 2006; 23:686-90.
18. Marashi SM, Ghafari MH, Saliminia A. Attenuation of hemodynamic responses following laryngoscopy and tracheal intubation – Comparative assessment of clonidine and gabapentin premedication. Middle East J Anaesthesiol. 2009;20:233–7.
19. Westfall TC, Westfall DP. Adrenergic agonist and antagonist. In: Bruton LL, Lazo JS, Parker JS, editors. Goodman and Gilman's the Pharmacological Basis of Therapeutics. 11th ed. USA: McGraw-Hill; 2006. p. 255-6.
20. Faheim SM, Hassanin M, Hafez AA. Gabapentin versus clonidine oral premedication for attenuation of pressor response to laryngoscopy and endotracheal intubation. Tanta Med Sci J 2008;3:12-20.