Original Research Article

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Compare the Effect of Oral Pregabalin and Clonidine for Attenuation of Hemodynamic Responses to Laryngoscopy and Tracheal Intubation

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Abstract

Laryngoscopy and endotracheal intubation are powerful stimuli which can increase the sympathetic activity leading to tachycardia, hypertension and dysrhythmias. These hemodynamic changes are associated with the release of catecholamine (cortisol, epinephrine and nor-epinephrine). To compare the effect of oral Pregabalin and Clonidine for attenuation of hemodynamic responses to laryngoscopy and tracheal intubation

Keywords: Laryngoscopy; Pregabalin; Clonidine; Haemodynamic Response; Endotracheal Intubation.

Introduction

Laryngoscopy and endotracheal intubation are powerful stimuli which can increase the sympathetic activity leading to tachycardia, hypertension and dysrhythmias. These hemodynamic changes are associated with the release of catecholamine (cortisol, epinephrine and nor-epinephrine).

Pre-emptive analgesia with Pregabalin and Clonidine blunt the stress response to anaesthetic and surgical stimuli, also reduce the narcotic and anaesthetic doses in the peri-operative period. Accordingly, this study was designed to compare oral pregabalin and clonidine for attenuation of hemodynamic responses to laryngoscopy and tracheal intubation.

Clonidine is an alpha-2 adrenergic agonist which was originally introduced as an antihypertensive. There are quite a number of studies have shown clonidine is useful in attenuating pressor response to laryngoscopy and intubation.

Pregabalin, a pregabalinoid is emerging as an effective and safe drug as it leads to sedation, analgesia and hemodynamic stability peri-operatively [1].

Aim of the Study

To compare the effect of oral Pregabalin and Clonidine for attenuation of hemodynamic responses to laryngoscopy and tracheal intubation.

Methods and Materials

After obtaining approval from the Institutional Ethical Committee and written informed consent from all the patients, the study was conducted in SBMCH, Operation theatre in patients scheduled for elective Surgery under general anaesthesia.

Study Design

Randomized, clinical study, Group A (Pregabalin) will receive 150mg Tab.

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Pregabalin, Group B (Clonidine) receiving 0.2 mg Tab. Clonidine.

Inclusion Criteria

Age: 18 – 60 years.

Weight: BMI < 30 Kg/m2 American Society of Anesthesiologist physical status I & II patients.

Surgery: Elective

Mallampattiscores: I & II Patients who have given valid informed consent.

Exclusion Criteria

Patients who are not satisfying inclusion criteria.

Patients posted for emergency surgery

Patients with difficult airway

Lack of written informed consent

H/O seizures and any neurological deficit

Renal or liver disease.

Recent consumption of analgesics in past 24 hours

Known allergy or sensitivity to the drugs.

Ongoing therapy with sustained release opioids.

Cases which have been converted from laparoscopic to open surgery.

Description

In our study we have taken 60 as the sample size

N=30 in Group Pregabalin

N=30 in Group Clonidine

Materials

Monitors: ECG, NIBP, SpO_2, $EtCO_2$.

Drugs: Injection Midazolam, Injection Glycopyrrolate, Inj.Fentanyl, Inj.Thiopentone Sodium, Inj. atracurium, Inj.Neostigmine, sevoflurane, emergency drugs, Normal Saline and Ringer Lactate.

Airway Devices: Mactintosh Laryngoscope, Guedel's Oral Airway, Gum elastic Bougie. Boyles anaesthesia machine.

Patients satisfying inclusion criteria were randomly allocated by closed envelope method into 2 groups: Group A (Pregabalin), Group B (Clonidine), Group about the study methods, the visual analogue scale chart and along with information sheet. All were orally premedicated with alprazolam 0.5mg at 9.00 pm, the day before surgery.

In the preoperative room, A good intravenous access was secured and baseline parameters were noted which includes heart rate (HR), systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP) and pulse-oximetry (SpO_2).

Patients in group A received Tab Pregabalin 150 mg orally, Group B patients will received Tab. Clonidine 0.2mg 90 minutes prior to induction. Vital parameters were recorded 3 minutes before induction. After premedication with Inj.Glycopyrrolate 0.2 mg IV, Inj.Midazolam 1mg IV, Inj.Fentanyl 2 mcg/ kg IV was given and preoxygenation done.

Anaesthesia was induced with Inj.Thiopentone sodium 5 mg/kg IV followed by a muscle relaxant Inj. Atracurium 0.5 mg/ kg IV. Patients were ventilated by mask for at least 3 minutes using 100% oxygen with sevoflurane 1%. Laryngoscopy was performed with a Macintosh laryngoscope and trachea was intubated with appropriate sized endotracheal tube by a trained anaesthesiologist.

The period of laryngoscopy and intubation was less than 15 seconds for all patients. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, pulse-oximetry was monitored and recorded at the time of intubation and at 1,3,5,10 minutes after intubation.

Maintenance of Anesthesia with controlled ventilation was carried out using nitrous oxide and oxygen in the ratio of 2:1, sevoflurane 1-2 vol%, and Inj. Atracurium (incremental doses to maintain muscle relaxation). Patient was observed for complications like hypotension, hypertension, arrhythmias, hypoxemia, and bronchospasm and treated as required. Hypotension is defined as fall in SBP/DBP by 30% from baseline and was treated with a bolus of intravenous fluid or Inj.Ephedrine 3mg.

Bradycardia defined as decrease in heart rate to less than 60 min and it was managed with Inj. Atropine 0.6 mg iv and Tachycardia is defined as heart rate more than 100/min. Hypertension is when systolic blood pressure is more than 30% from baseline. This response was treated by increasing the concentration of inhalational anaesthetic agent Sevoflurane and supplemental bolus of fentanyl 0.5 mcg/kg.

At the end of the surgery, residual neuromuscular blockade was reversed with Inj.Neostigmine 0.05 mg/kg and Inj.Glycopyrrolate 0.01 mg/kg intravenously. Immediate post-extubation, vital

parameters, sedation score, anxiety scores were recorded. Patient was shifted to PACU and was monitored for vital parameters. VAS score and vital parameters were assessed for 1, 2, 4, 6, 8 hours postoperatively.

Observation and Results

Among the total cases, In Group A, 6% belong to the age group lesser than 20 years, 47% belong to 21–30 years, 30% belong to 31–40 years and 17% belong to 41–50 years. In Group B, 6% belong to the age group lesser than 20 years, 57% belong to the age group 21–30 years, 13% belong to the age group 31–40 years and 27% belong to 41–50 years.

It is significant from the above table that in both the groups the majority of the age group lies between 21–30 years.

There was no statistically significant difference found in age between the two groups. (paired t test applied, p Value ≥ 0.05).

Table 1: Age

Age (in years)	Group A	%	Group B	%	p-value
21 – 30	15	50	17	57	
31 – 40	10	33	5	17	0.5411
41 – 50	5	17	8	26	
Total	30	100	30	100	

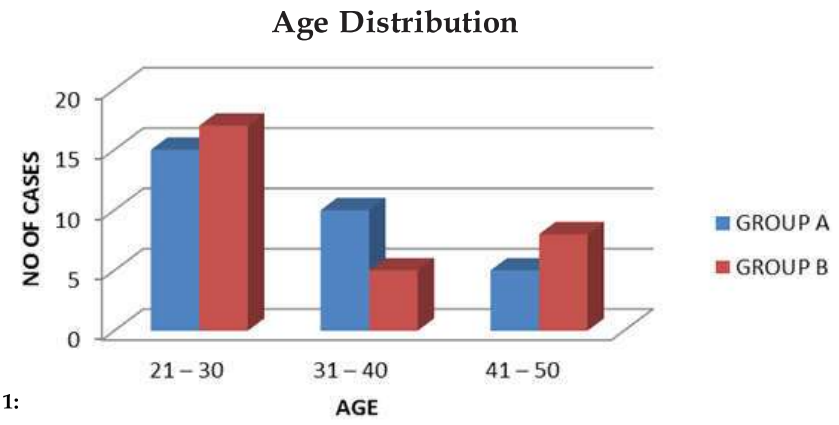

Fig. 1:

Among the total cases, in both the Groups, the gender was distributed as 63% among males and 37 % of females.

The gender distribution for both the groups shows a statistical insignificance as the p value> 0.05.

Group A had a mean weight of 57.43 kg and

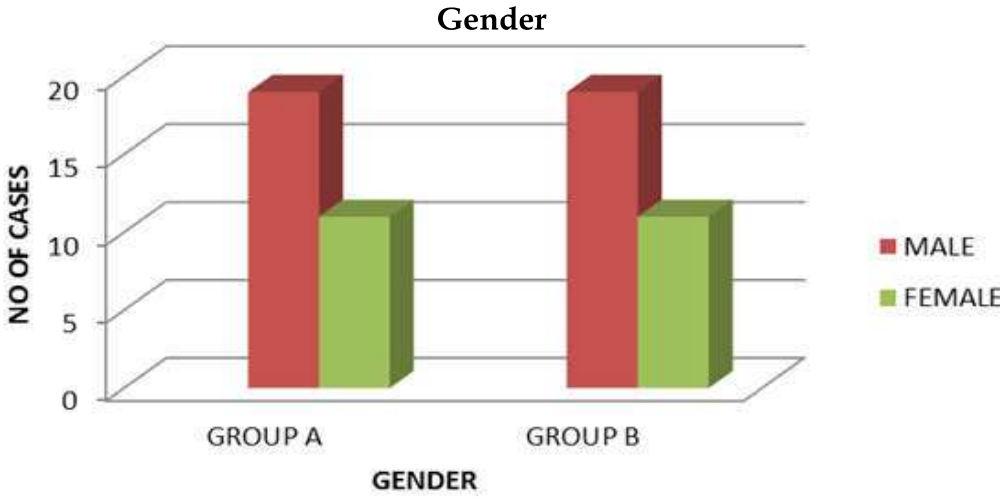

Fig. 2:

Table 2: Gender

Gender	Group A	%	Group B	%	P-Value
Male	19	63	19	63	
Female	11	37	11	37	0.7142
Total	30	100	30	100	

Table 3: Weight

Weight	Group B	Group R	P-Value
Range	44 -76	49 - 72	
Mean	57.43	59.62	0.3121
S D	4.68	5.17	
Total	**30**	**30**	

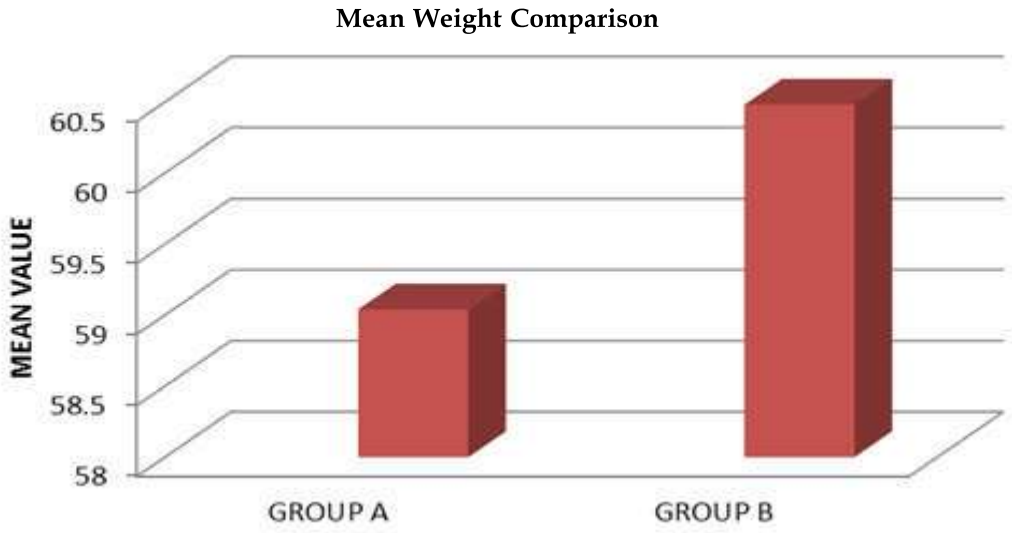

Fig. 3:

Group B had a mean weight of 59.62 kg.

Both the groups were statistically comparable and showed a statistical insignificance. ($p > 0.05$)

Among the cases, Group A has distributed as ASA I at 40% and ASA II as 60%. The same with respect to Group B is 47% and 53% respectively.

The ASA classification for both the groups shows a statistical insignificance as the p value > 0.05.

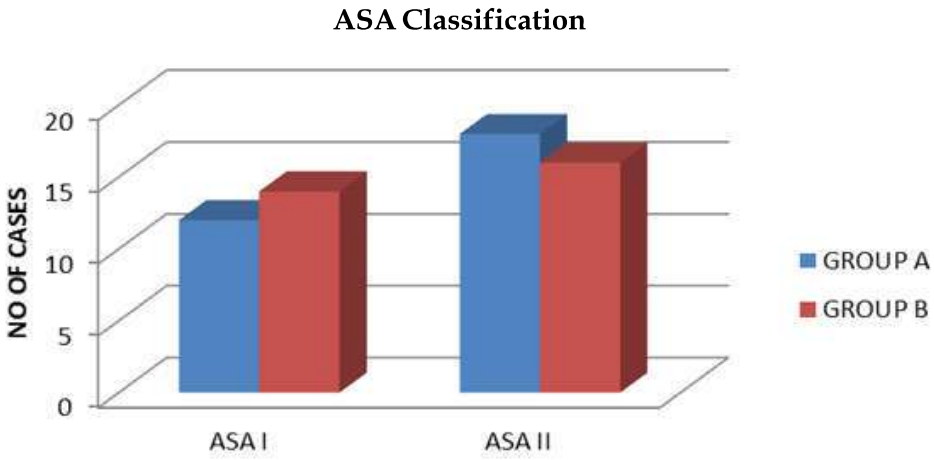

Fig. 4:

Table 4: ASA classification

ASA Classification	Group A	%	Group B	%	p-value
ASA I	12	40	14	47	
ASA II	18	60	16	53	0.7541
Total	30	100	30	100	

Table 5: Heart rate comparison

Variables	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Baseline	75.28	9.13	77.44	8.60	0.3875
3 Minutes Prior to Induction	73.64	4.20	70.40	5.91	0.0124
During Induction	74.52	4.85	69.68	4.69	0.0010
During Intubation	86.28	8.81	72.52	7.19	0.0000
1 Minute after Intubation	97.48	11.11	73.28	5.26	0.0000
3 Minutes after Intubation	96.16	11.08	72.12	4.56	0.0000
5 Minutes after Intubation	90.88	10.06	70.48	5.82	0.0000
10 Minutes after Intubation	85.64	8.04	69.80	5.18	0.0000
Postop – 0 hr	90.41	6.42	82.41	5.14	0.0000
Postop – 1hr	91.42	5.47	83.51	5.17	0.0000
Postop – 2 hrs	90.47	6.12	82.47	5.38	0.0000
Postop – 4 hrs	91.25	6.25	83.14	5.32	0.0000
Postop – 6 hrs	90.57	5.24	81.68	5.68	0.0000
Postop – 8 hrs	91.68	5.36	83.26	5.40	0.0000
Grand Mean	90.2057		80.8957		
P Value			0.0048		

Both the Groups A and B were statistically comparable with regard to the mean heart rate where it was statistically insignificant ($p > 0.05$) during the baseline.

However, it was statistically significant ($p < 0.05$) 3 minutes prior to induction, during induction, during intubation, 1 minute after intubation, 3 minutes after intubation, 5 minutes after intubation, 10 minutes after intubation & Post-Op at 0 hr, 1 hr, 2 hrs, 4 hrs, 6 hrs& 8 hrs.

Both the Groups A and B were statistically comparable with regard to the mean systolic blood pressure where it was statistically insignificant ($p > 0.05$) during the baseline.

However, it was statistically significant ($p < 0.05$) 3 minutes prior to induction, during induction, during intubation, 1 minute after intubation, 3 minutes after intubation, 5 minutes after intubation, 10 minutes after intubation & Post-Op at 0 hr, 1 hr, 2 hrs, 4 hrs, 6 hrs & 8 hrs.

Table 6: Systolic blood pressure comparison

Variables	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Baseline	123.60	10.89	124.72	10.68	0.7142
3 Minutes Prior to Induction	122.72	7.62	117.00	7.83	0.0081
During Induction	120.64	7.61	116.32	6.23	0.0399
During Intubation	125.36	8.72	117.04	7.95	0.0000
1 Minute after Intubation	125.20	5.70	116.88	6.32	0.0000
3 Minutes after Intubation	124.40	7.56	114.68	6.57	0.0000
5 Minutes after Intubation	121.28	4.94	114.56	6.57	0.0002
10 Minutes after Intubation	121.24	4.40	112.60	5.01	0.0012
Postop – 0 hr	131.12	7.25	120.92	5.57	0.0000
Postop – 1hr	119.04	2.95	113.64	6.84	0.0000
Postop – 2 hrs	118.36	4.64	113.00	7.19	0.0000
Postop – 4 hrs	119.56	4.47	114.76	6.04	0.0000
Postop – 6 hrs	122.60	4.45	116.48	6.25	0.0000
Postop – 8 hrs	123.40	4.34	117.80	4.76	0.0000
Grand Mean	122.1886		115.60		
P Value			0.0024		

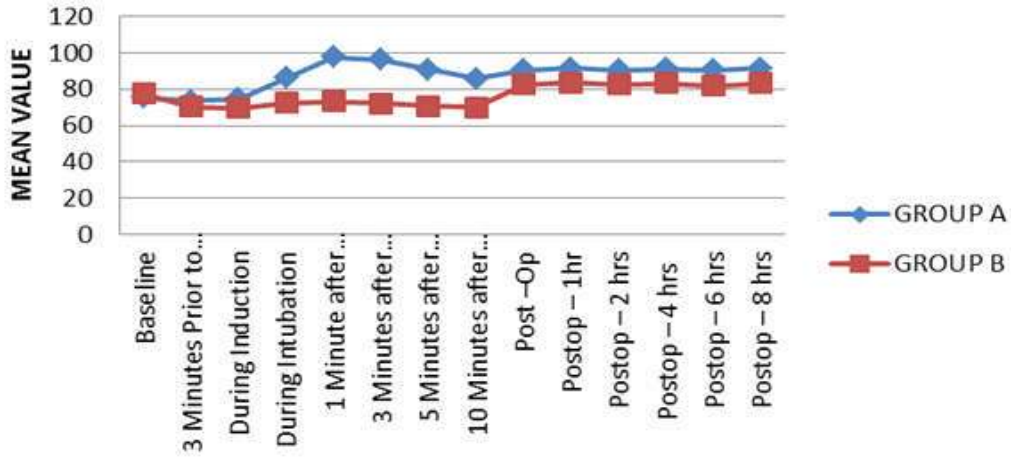

Fig. 5:

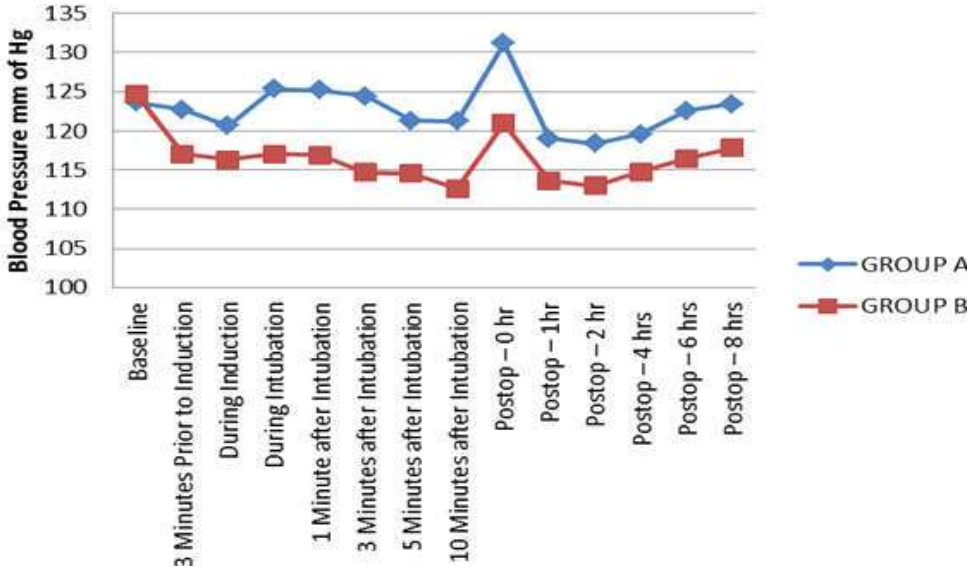

Fig. 6:

Table 7: Diastolic blood pressure comparison

Variables	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Baseline	79.20	8.07	79.12	7.76	0.9714
3 Minutes Prior to Induction	79.68	5.11	72.36	4.32	0.0112
During Induction	75.56	6.33	73.16	4.26	0.0330
During Intubation	80.40	6.89	73.00	5.14	0.0001
1 Minute after Intubation	81.80	4.48	72.68	4.42	0.0000
3 Minutes after Intubation	78.68	4.99	72.44	5.02	0.0000
5 Minutes after Intubation	77.16	4.17	72.24	4.80	0.0001
10 Minutes after Intubation	77.08	5.14	70.16	4.55	0.0014
Postop – 0 hr	83.48	6.29	73.60	5.34	0.0000
Postop – 1hr	74.16	4.62	68.48	4.98	0.0000
Postop – 2 hr	72.48	3.47	69.44	5.05	0.0000
Postop – 4 hrs	75.32	4.32	70.64	4.25	0.0000
Postop – 6 hrs	76.00	4.11	73.68	5.60	0.0000
Postop – 8 hrs	78.84	3.95	75.12	3.78	0.0000
Grand Mean	76.7657		71.5886		
P Value			0.0012		

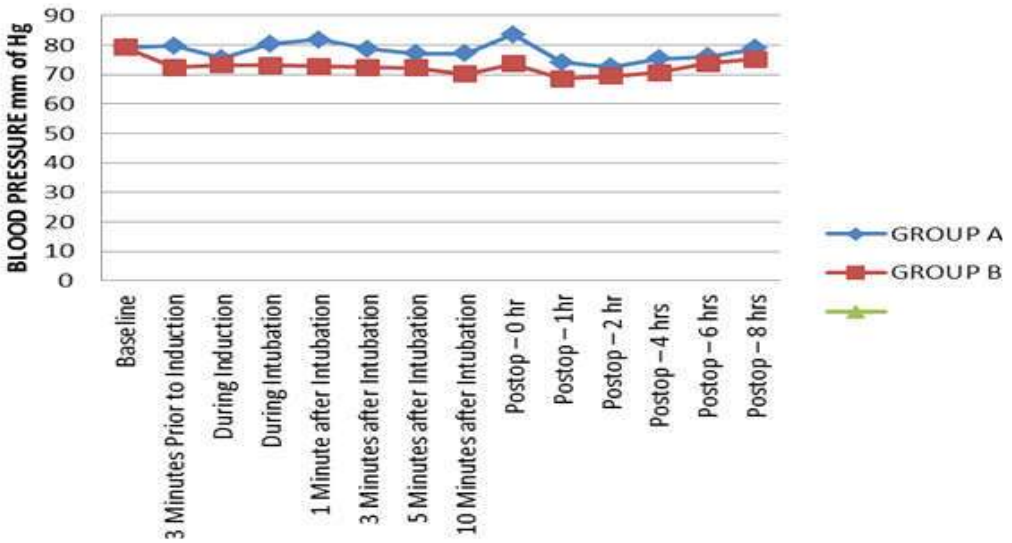

Fig. 7:

Both the Groups A and B were statistically comparable with regard to the mean diastolic blood pressure where it was statistically insignificant ($p > 0.05$) during the baseline.However, it was statistically significant ($p < 0.05$) 3 minutes prior to induction, during induction, during intubation, 1 minute after intubation, 3 minutes after intubation, 5 minutes after intubation, 10 minutes after intubation & Post-Op at 0 hr, 1 hr, 2 hrs, 4 hrs, 6 hrs & 8 hrs.

Among the cases, with respect to the VAS Score, both the groups were statistically comparable and were statistically significant during Pre-Op, at 1 hour, 2 hours, 4 hours & 8 hours.

Table 8: Visual analog score

Variables	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Pre-Op	0.40	0.50	0.72	0.46	0.0225
Post-Op 0th hour	2.08	0.57	3.80	0.65	0.0000
Post-Op 1st hour	1.96	0.54	3.56	0.58	0.0000
Post-Op 2nd hour	2.76	0.56	3.04	0.73	0.0461
Post-Op 4th hour	2.24	0.60	2.80	0.82	0.0001
Post-Op 6th hour	1.92	0.40	2.60	0.65	0.0001
Post-Op 8th hour	1.80	0.50	2.48	0.59	0.0001
Grand Mean	1.88		2.71		
P value			0.0241		

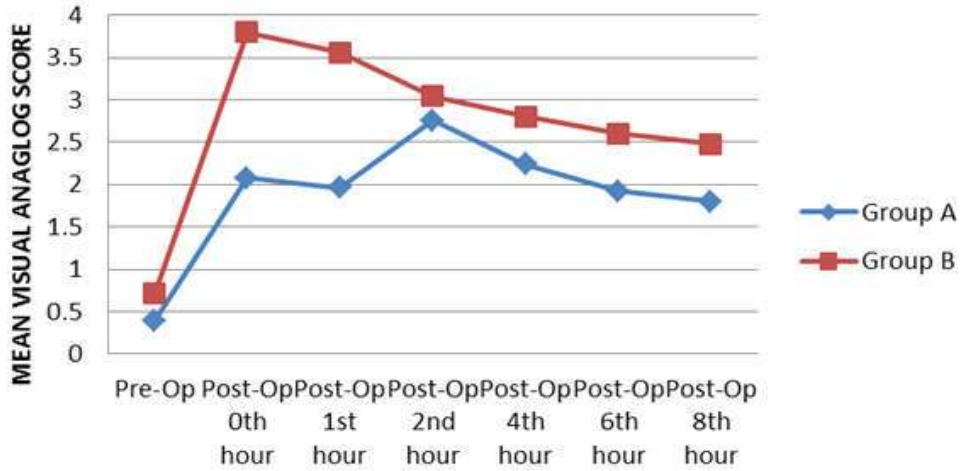

Fig. 8:

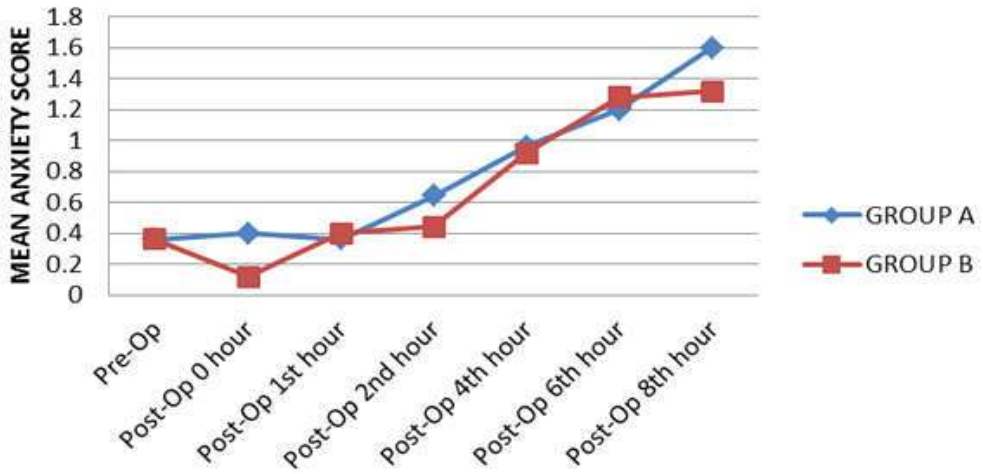

Fig. 9:

Table 9: Anxiety Score

Variables	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Pre-Op	0.36	0.49	0.36	0.49	0.0009
Post-Op 0 hour	0.40	0.50	0.12	0.33	0.0000
Post-Op 1st hour	0.36	0.49	0.40	0.50	0.0000
Post-Op 2nd hour	0.64	0.49	0.44	0.51	0.0000
Post-Op 4th hour	0.96	0.54	0.92	0.28	0.0000
Post-Op 6th hour	1.20	0.41	1.28	0.46	0.0000
Post-Op 8th hour	1.60	0.58	1.32	0.48	0.0000
Grand Mean	0.7885		0.6914		
P value			0.002		

Among the cases, with respect to the Anxiety Score, both the groups were statistically comparable and were statistically significant during Pre-Op, at 1 hour, 2 hours, 4 hours and 8 hours.

Among the cases, with respect to the Ramsay Sedation Score, both the groups were statistically comparable and were statistically significant ($p < 0.05$) at 1 hour, 2 hours, 4 hours, at 6 hours and 8 hours.

Among the cases, 67% did not have major complications, 13% had dizziness, 10% had vomit and another 10% had nausea in the Group A. In the Group B, 70% had no complications, 7% had nausea, 10% had vomit and 13% had dizziness.

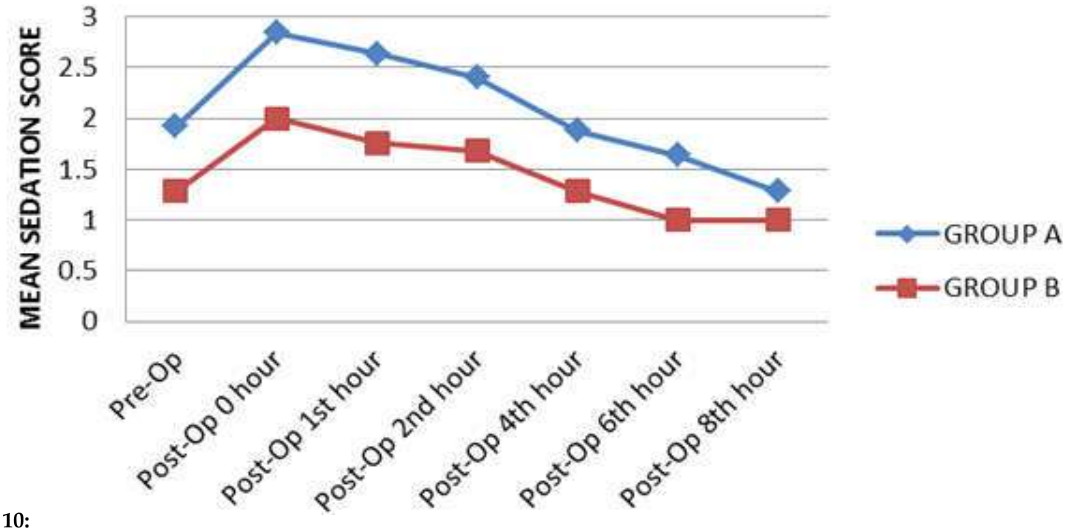

Fig. 10:

Table 10: Ramsay sedation score

Variables	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Pre-Op	1.92	0.76	1.28	0.46	0.0009
Post-Op 0 hour	2.84	0.47	2.00	0.58	0.0000
Post-Op 1st hour	2.64	0.49	1.76	0.52	0.0000
Post-Op 2nd hour	2.40	0.58	1.68	0.48	0.0001
Post-Op 4th hour	1.88	0.53	1.28	0.46	0.0000
Post-Op 6th hour	1.64	0.57	1.00	0.00	0.0012
Post-Op 8th hour	1.28	0.54	1.00	0.00	0.0162
Grand Mean	2.09		1.43		
P value			0.014		

Table 11: Complications

Complications	Group A	Percentage	Group B	Percentage
Nausea	3	10	2	07
Vomit	3	10	3	10
Dizziness	4	13	4	13
Nil	20	67	21	70
Total	30	100	30	100

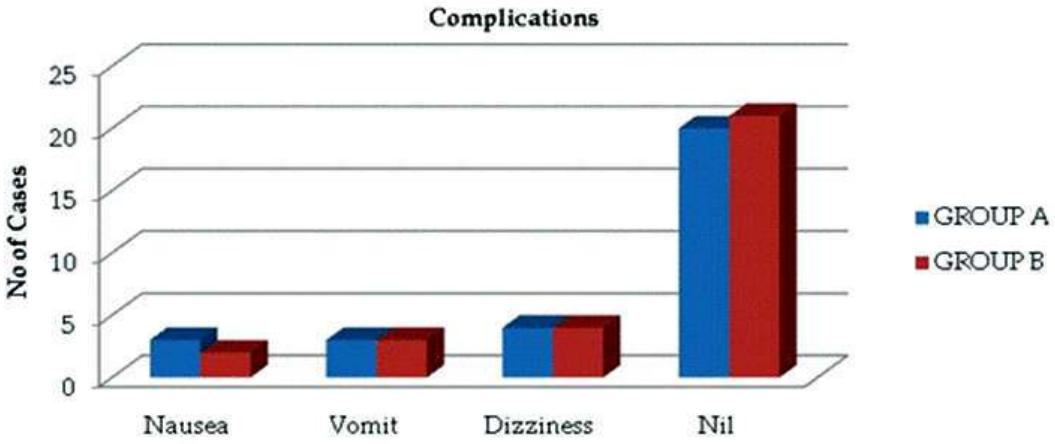

Fig. 11:

Discussion

Innumerable anaesthetic techniques have been proposed to attenuate the stress response to laryngoscopy and tracheal intubation, with variable grades of success in acute post-operative pain relief. The achievement of postoperative analgesia and smooth induction with negligible reflex haemodynamic response in the course of laryngoscopy and endotracheal intubation is an important anaesthetic goal. This study was done to assess the laryngoscopy and intubation responses of two drugs namely, Pregabalin 150mg and Clonidine 0.2mg.

The drugs were orally administered 90 minutes prior to induction, as the peak action of both the drugs are known to be 1-2 hours after oral administration. Variation of heart rate changes decreases with increasing age. Young patients show more extreme changes. Marked fluctuations in hemodynamic response are often seen in geriatric patients. To avoid these above mentioned age related variability, we selected an age range of 18-60 years in our study.

Observations in our Study

- Heart rate changes were lower in patients with oral Clonidine as compared to Pregabalin
- Systolic blood pressure, Diastolic blood pressure and the Mean arterial pressure changes were lower in patients with oral Clonidine compared to the Pregabalin
- VAS scoring were much lower in patients with oral pregabalin compared to Clonidine
- Ramsay sedation scores were higher in patients with oral pregabalin

Summary

This is a prospective randomised, clinical study to evaluate the pre-emptive analgesic effects of oral Pregabalin 150mg and oral Clonidine 0.2mg on intubation response and post-operative analgesic requirements. By giving pregabalin and Clonidine orally 90 minutes preoperatively, it reaches peak concentration in plasma at the onset of surgical stimulus thereby inhibiting central and peripheral neuronal sensitization to pain.

By inhibiting the initiation of noxious input it reduces intubation response and post-operative pain intensity and analgesic prerequisites. Sixty patients satisfying the inclusion criteria were randomly divided into two groups of thirty each. Group A received Pregabalin, group B received Clonidine, tablet 90 minutes prior to induction. Intra-operatively patients were monitored for heart rate, blood pressure, mean arterial pressure during intubation and post-operatively monitored for sedation, anxiety level, visual analogue score score and the data derived was evaluated. Observations of the study were

- Heart rate changes were lower in patients with oral Clonidine as compared to pregabalin
- Systolic blood pressure, Diastolic blood pressure and the Mean arterial pressure changes were lower in patients with oral Clonidine compared to the pregabalin
- VAS scoring were much lower in patients with oral pregabalin compared to clonidine
- Ramsay sedation scores were higher in patients with oral pregabalin

From the above observation of results we conclude that clonidine attenuates laryngoscopy and intubation response better than pregabalin .

Conclusion

Thus from our study and from all our findings, both Pregabalin and Clonidine drugs were found to be effective as good pre-emptive analgesics in attenuating hemodynamic stress response to laryngoscopy and intubation, with added benefit of providing post-operative pain relief also. Clonidine was found to be better than Pregabalin in attenuating hemodynamic stress response to laryngoscopy and intubation. Pregabalin was found to be better than Clonidine in providing post-operative pain relief.

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