A COMPARATIVE STUDY OF ORAL PREGABALIN AND CLONIDINE FOR ATTENUATION OF HEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND TRACHEAL INTUBATION

ABSTRACT

Background and objectives:

The airway instrumentation by direct laryngoscopy and tracheal manipulation are powerful noxious stimuli causing adverse hemodynamic responses. The present study is to evaluate and compare oral clonidine and pregabalin premedication on the hemodynamic responses following laryngoscopy and tracheal intubation and assess any side effects associated.

Materials and Methods:

Prospective randomized study after obtaining institutional ethical committee approval was conducted in R.L.Jalappa hospital and research center, Kolar. 60 patients of ASA Grade I, II aged between 18 to 60 years, of either sex, posted for elective surgeries under general anaesthesia were divided into 2 groups of 30 after obtaining informed written consent. Group C received 200µg clonidine and group P 150mg pregabalin. Analysis done using Chi-Square test and Student's t-test.

Results:

Group P was better in attenuating increase in BP whereas tachycardia response was better attenuated in group C and Group P causes more sedation, which were statistically significant.

Discussion:

α_2 adrenoreceptor agonist clonidine has beneficial effects on hemodynamics following laryngoscopy and endotracheal intubation. Pregabalin, structurally related to gamma-aminobutyric acid (GABA) is emerging as an effective drug as it leads to sedation, analgesia and hemodynamic stability perioperatively.

Conclusion

Both pregabalin and clonidine attenuate the hemodynamic response to laryngoscopy and tracheal intubation. Pregabalin better attenuates pressor response and clonidine better attenuates tachycardia response.

INTRODUCTION

Direct laryngoscopy and tracheal intubation are noxious stimuli that can provoke undesirable responses in the cardiovascular, respiratory and other physiologic systems.[1] The magnitude of the response is greater with increasing force and time of laryngoscopy.[2]

The pressor response of laryngoscopy and endotracheal intubation does not present a problem for most patients. However, in patients with cardiovascular or cerebral disease these transient responses can result in morbidity and mortality from the tachycardia and hypertension resulting from this stress. An array of anaesthetic techniques and drugs are available to control the hemodynamic response to laryngoscopy and intubation like administration of topical anaesthesia, reducing the duration of laryngoscopy and intubation to less than 15 seconds,[3] increasing the depth of anaesthesia,[1] and administration of drugs like topical and intravenous lidocaine,[4] vasodilators,[6,5] opiods,[8,7] beta blockers,[8,9] calcium channel blockers[10,11] and α_2 adrenergic agonists[12,13] prior to laryngoscopy. No single agent has been established as apt for this purpose.

Clonidine is a α_2 adrenergic agonist which was originally introduced as an antihypertensive. There are few studies showing clonidine to be useful in attenuating pressor response to laryngoscopy and intubation. Pregabalin a gabapentinoid is emerging as an effective and safe drug as it leads to sedation, analgesia and haemodynamic stability perioperatively. A single, oral dose of 150 mg of pregabalin premedication seems to be effective in attenuating the haemodynamic response to tracheal intubation after the first attempt, an effect which may be useful in patients suffering from coronary insufficiency.[14]

AIMS AND OBJECTIVES

1. To assess the efficacy and compare oral pregabalin and oral clonidine premedication for the attenuation of hemodynamic responses like Heart rate, Blood pressure and Rate pressure product (product of systolic blood pressure and heart rate) following laryngoscopy and tracheal intubation.
2. To assess any side effects like hypotension, bradycardia, and sedation associated with the drugs.

MATERIALS AND METHODS

SOURCE OF DATA

60 patients posted for elective surgeries under general anaesthesia at R.L.Jalappa hospital and research Centre, Tamaka Kolar during the period of January 2013 – January 2014.

INCLUSION CRITERIA

60 patients of ASA Grade 1 and 2 in the age group of 18 years to 60 years, of either sex, posted for elective surgeries under general anaesthesia were selected for the study.

EXCLUSION CRITERIA

1) Patients physically dependent on narcotics.
2) Patients with history of drug allergy to clonidine or pregabalin.
3) History of cerebrovascular, neurologic, respiratory or Ischemic heart disease.
4) Renal and hepatic dysfunction.
5) Head injury cases.
6) Patients with hypertension, pheochromocytoma and diabetes mellitus.
7) Patients on beta blockers, anti-depressants, anti-anxiety, anti convulsant or anti-psychotics.

SAMPLING PROCEDURE

After obtaining informed written consent, patients will be randomly divided into 2 groups of 30 each. Randomization is done by computer generated table.Group "P" received- 150mg pregabalin and group "C" received - 200µg clonidine.All patients were examined a day before surgery. All were kept fasting overnight after 10:00pm and received tab. Diazepam 10mg orally and tab. Ranitidine 150 mg as premedication on the night before surgery. On the morning of surgery all patients received either oral Pregabalin or Clonidine randomly 60 to 90 mins before admission to OT. Baseline parameters like pulse rate and systolic blood pressure, diastolic blood pressure, mean blood pressure, oxygen saturation and ECG were recorded. Intravenous line was secured and all were started on intravenous fluids 5 ml/kg/hr.

The level of sedation was assessed by four point score described by Chernik et al.
Grade 0- patient wide awake.
Grade 1-patient is sleeping comfortably but responding to verbal commands.
Grade 2-deep sleep but arousable.
Grade 3-deep sleep, unarousable.

After 3 mins of pre-oxygenation with 100% oxygen, premedication was done with 5 µ/kg of IV glycopyrolate, 2.5 µg/kg IV fentanyl was given for analgesia. Patient was induced with IV thiopentone 5 mg/kg followed by IV suxamethonium 2 mg / kg for intubation. Anaesthesia was maintained with N_2O+O_2+Isoflurane. Muscle relaxation was achieved with IV vecuronium 0.1mg per kg (loading dose) and 0.02 mg per kg (maintenance dose) later.

During laryngoscopy and endotracheal intubation, heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure were recorded at 0,1,3,5 and 10 minutes.

The study required the following investigations:

Complete haemogram, bleeding time and clotting time, random blood sugar, blood urea and serum creatinine, serum electrolytes, urine analysis for sugar, albumin and microscopy, ECG and chest X-ray.

STATISTICAL ANALYSIS

Data will be analyzed using statistical tests, Chi-Square test and Student's t-test. $p<0.05$ will be considered statistically significant.

RESULTS

DEMOGRAPHIC DATA

Table 1: Age distribution of patients studied (p = 0.534)

Age in years	Group P		Group C	
	No	%	No	%
18-25	11	36.67	12	40.00
26-35	11	36.67	7	23.33
36-45	5	16.67	5	16.67
46-55	3	10.00	6	20.00
>55	0	0.0	0	0
Total	30	100.0	30	100.0
Mean ± SD	31.07±10.044		32.83±11.742	

Table 2: Gender distribution (p > 0.05)

Gender	Group P		Group C	
	No	%	No	%
Male	11	37	20	67
Female	19	63	10	33
Total	30	100.0	30	100.0

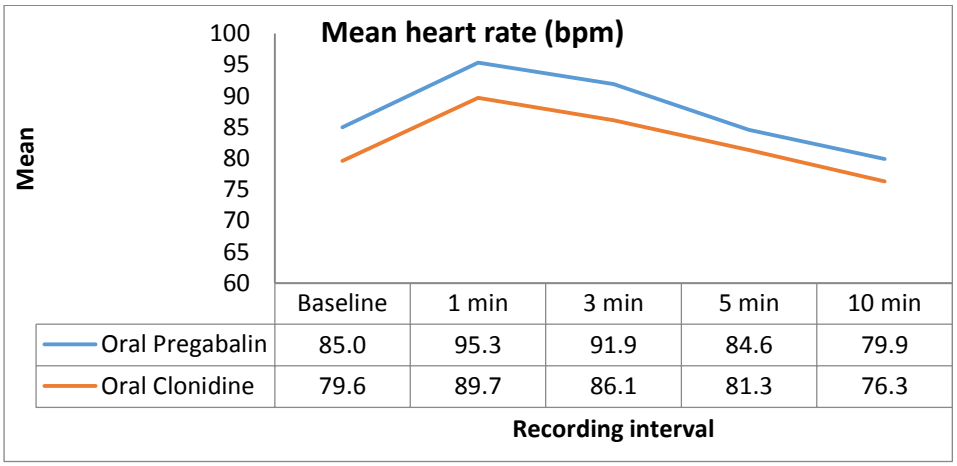
Table 3: Weight (kg) distribution of patients studied (p = 0.498)

Weight (kg)	Group P		Group C	
	No	%	No	%
41-50	2	6.66	5	16.66
51-60	22	73.33	19	63.33
61-70	6	20.00	6	20.00
>70	0	0	0	0
Total	30	100.0	30	100.0
Mean ± SD	56.93±4.185		56.17±4.511	

We conclude that the sample studied are age, gender and weight matched.

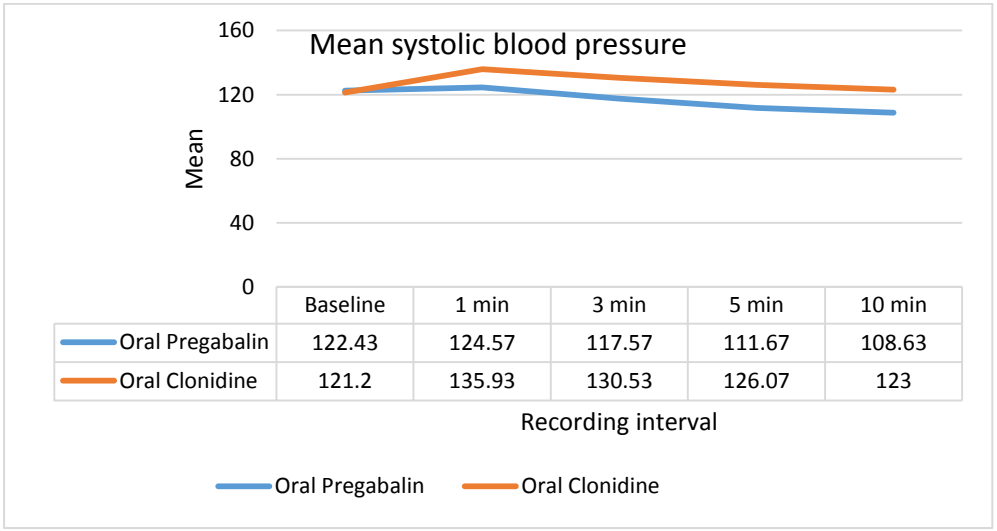
COMPARISON OF HAEMODYNAMIC PARAMETERS

Graph 1: Mean heart rate at different recording intervals

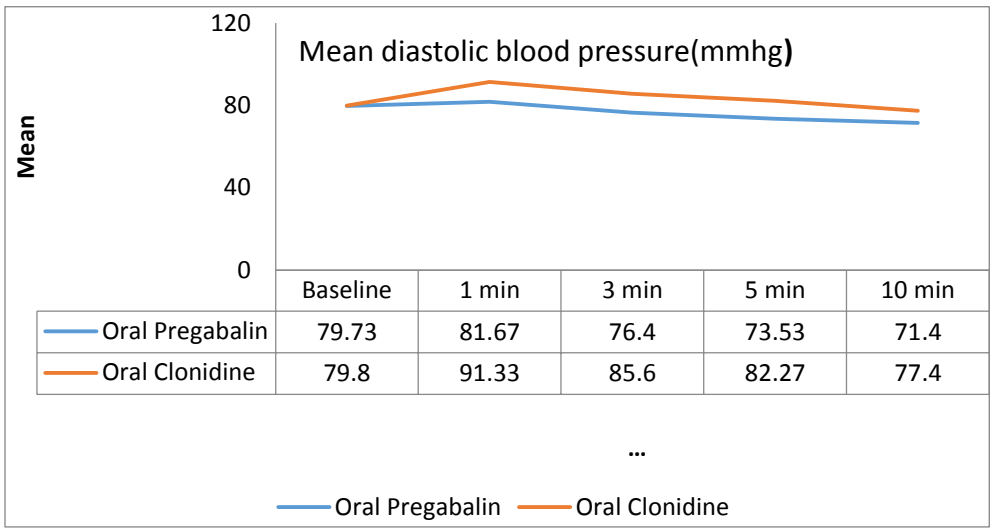


At baseline, 1 min and 3 minutes heart rate response to laryngoscopy and intubation in the clonidine group is clinically lesser than pregabalin group and statistically significant (p=0.05 at baseline = 0.044 at 1 minute and P =0.043 at 3minutes). Values were insignificant at 5(0.254) [and] 10 minutes(0.156). Clonidine better attenuates tachycardia response.

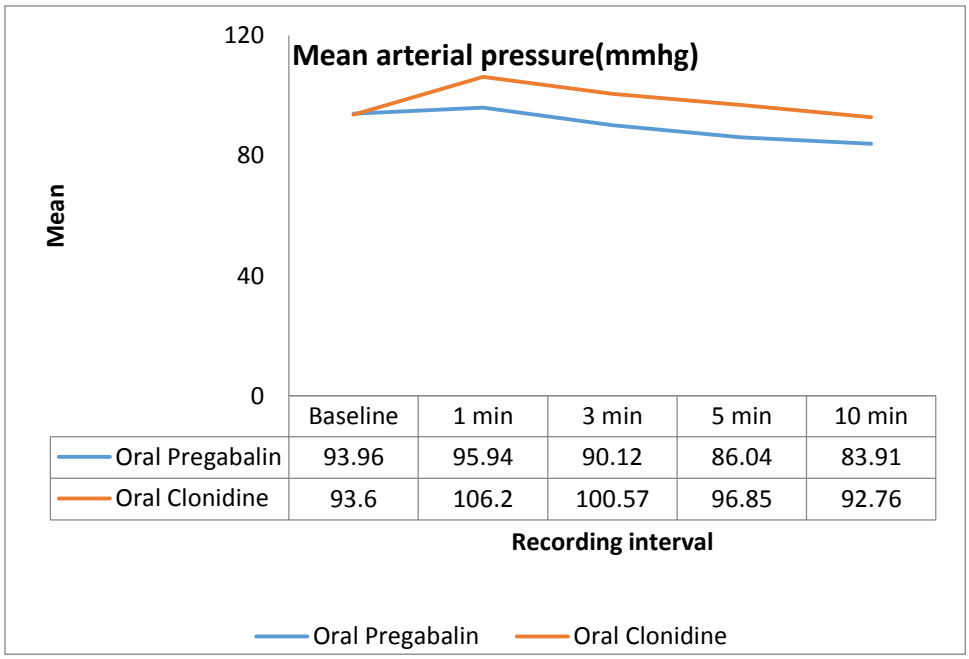
Graph 2: Mean Systolic blood pressure



Graph 2: Mean Diastolic blood pressure

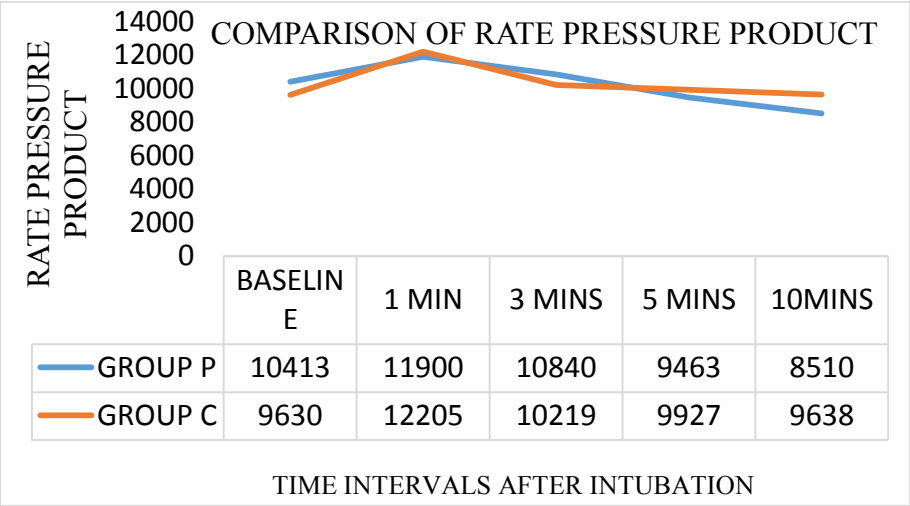


Graph 4: Mean arterial pressure at different recording intervals



The mean systolic, diastolic and mean blood pressure is clinically lesser in Pregabalin group than in the Clonidine group at all intervals. ($p<0.001$) and is statistically significant indicating Pregabalin group attenuates increase in blood pressure to laryngoscopy and intubation better compared to Clonidine group.

Graph 5: Mean rate pressure product at different interval.



The difference rate pressure product at baseline 1 minute, 3 minute and 5 minute intervals are insignificant. At 10th minute rate pressure product of pregabalin is significantly less compared to clonidine. (p = 0.54 at I min, 0.17 at 3 min, 0.385 at 5 min and 0.014 at 10 min).

COMPARISON OF SEDATION SCORE

Table 4: preoperative sedation scores

Sedation score	**Group C**		**Group P**	
	No.	**%**	**No.**	**%**
Score 1	15	50.0	2	6.66
Score 2	13	43.3	9	30.0
Score 3	2	6.7	19	63.34
Total	30	100.0	30	100.0
Mean ± SD	1.57±0.62		2.57±0.64	

Mean sedation score is significantly less in Group C with P = 0.000

DISCUSSION

The present study assessed the effect of oral premedication with pregabalin or clonidine for haemodynamic stability following laryngoscopy and intubation. Haemodynamic responses following laryngoscopy and intubation were diminished with pregabalin and clonidine. Results of our study were in agreement with other studies done on pregabalin and clonidine.

The haemodynamic responses following laryngoscopy and intubation were first described by Reid and Brace.[15] Many techniques have been tried in an effort to offset these adverse hemodynamic responses to laryngoscopy and intubation like increasing the depth of anaesthesia, using aerosol or topical anaesthetics and using glossopharyngeal and superior laryngeal nerve blocks.

Many pharmacological methods were evaluated to attenuate these adverse responses with controversial results. In our study we have compared clonidine a α2 adrenergic receptor agonist an established drug in diminution of hemodynamic responses[16, 17] to laryngoscopy and tracheal intubation with pregabalin which is a GABA analogue and belongs to the class of anticonvulsants and is now being increasingly used for neuropathic pain in control of perioperative stress responses including that of laryngoscopy and intubation.

Pregabalin attenuates haemodynamic response to laryngoscopy and endotracheal intubation in a dose response manner. Attenuation is more with 150mg compared to 75mg.[14] In our study we used pregabalin in a dose of 150 mg 60 to 90 minutes prior to surgery. Pregabalin was found to effectively attenuate the rise in blood pressure following laryngoscopy and intubation. This correlates with the studies done by Gupta k and colleagues.[18] But in our study as we have compared pregabalin with Clonidine (at a dose of 200μg). pregabalin was found to attenuate rise in blood pressure better compared to clonidine. Clonidine was better in attenuation of heart rate response. Increase in the rate pressure product is less in pregabalin group signifying lesser load on the myocardium compared to clonidine. Sedation was more with pregabalin which correlates with studies done bu Gupta K, et al .[19]

Our reason for studying patients up to 59 years of age was that elderly patients often are on drugs such as antidepressants, hypnotics and antihypertensives and they often exhibit increased sensitivity to drugs they. Separate studies are required to study the effect of pregabalin in older age group patients.

We did not have a placebo group so we could not assess the hemodynamic attenuating effects of clonidine and pregabalin in comparison to placebo.

There are few limitations to our 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 physical 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 like endogenous plasma catecholamines or cortisol values perioperatively.

CONCLUSION

Based on our present comparative study the following conclusions were drawn:

- Oral pregabalin and oral clonidine both help in attenuating hemodynamic responses to laryngoscopy and intubation at doses of 150mg and 200 micrograms respectively.
- Oral pregabalin (150mg) attenuates the increase in systolic blood pressure, diastolic blood pressure and mean arterial pressure associated with laryngoscopy and intubation better than oral clonidine (200micrograms).
- The increase in heart rate response to laryngoscopy and tracheal intubation is better eliminated by oral clonidine.
- Increase in the rate pressure product is less in pregabalin group signifying lesser load on the myocardium compared to clonidine.
- Sedation is more in patients taking oral Pregabalin.
- Hence from our study we can conclude that pregabalin is better compared to clonidine to attenuate the pressor response associated with laryngoscopy and tracheal intubation, but the tachycardia response is not completely attenuated. There were no perioperative side effects in both the groups.

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