

A Comparative Evaluation of Premedication with Oral Gabapentin and Pregabalin in Attenuation of Pressor Response to Endotracheal Intubation under General Anaesthesia

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Conflict of interest: Nil

Abstract

Background: In this study we wanted to compare the effects of oral Pregabalin and Gabapentin in attenuating the hemodynamic response to laryngoscopy and intubation in relation to heart rate, blood pressure-systolic and diastolic and mean arterial pressure.

Materials and Methods: Sixty patients belonging to ASA grade 1 and 2 were randomly divided into two groups of thirty each. Oral Gabapentin 600mg and oral Pregabalin 150 mg was given 1 hr prior to surgery. Both groups were premedicated with Glycopyrolate 0.005 mg/kg and Fentanyl 1.5µg/kg was given. They were induced with Thiopentone sodium 5 mg/kg and intubation was aided with Vecuronium 0.1 mg/kg. The hemodynamic parameters recorded were heart rate, systolic and diastolic blood pressure and the mean arterial pressure every minute upto 5 minutes and at 10 minutes, 15 minutes, 30 minutes and 45 minutes time interval in each group. Statistical analysis was done using Chi-square (χ^2) test of significance and Student "t" test and P value obtained.

Results: Both groups showed attenuation of stress response. Pregabalin and Gabapentin affected heart rate to same extent upto 5 minutes ($p>0.05$). In Gabapentin group, there was increase in SBP, DBP and MBP upto 3 minutes, after that it was maintained below the baseline. In Pregabalin group there was no rise in systolic and diastolic blood pressure and mean arterial blood pressure compared to the baseline from the 1st minute of intubation which is statistically significant ($p<0.001$).

Conclusion: Both Pregabalin and Gabapentin attenuate the stress response to laryngoscopy and intubation. When both these drugs were compared. Pregabalin attenuated the stress response to laryngoscopy and intubation better than Gabapentin and afforded a good hemodynamic stability.

Keywords: Anaesthesia; hemodynamic; Gabapentin; Pregabalin, laryngoscopy; intubation.

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Introduction

Recently, gamma-amino butyric acid (GABA) analogs Pregabalin and Gabapentin have gained prominence in various clinical studies, in not only alleviating peri-operative pain but also effective in attenuating pressor response to intubation and in producing perioperative sedation and anxiolysis. [1]

Gabapentin and Pregabalin *in vitro* increases the activity of partially-purified glutamic acid decarboxylase (GAD), suggesting that Gabapentin treatment might increase the synthesis of GABA from glutamate in brain tissues.

In this study we were comparing the efficacy of oral Gabapentin and Pregabalin premedication in attenuating the pressor response to endotracheal intubation under general anaesthesia.

Objectives

1. To compare the effects of oral Pregabalin and Gabapentin in attenuating the hemodynamic response to laryngoscopy and intubation in relation to heart rate, blood pressure-systolic and diastolic and mean arterial pressure.
2. To ascertain the effectiveness of oral Gabapentin 600 mg over Pregabalin 150 mg or vice versa in attenuating hemodynamic response to laryngoscopy and endotracheal intubation.

Materials and Methods

This was a randomized comparative study carried out in the Department of Anaesthesiology and Critical care, Kempegowda Institute of Medical Sciences, Bangalore from January 2021 to December 2021. Sixty patients aged between 18-60 years of physical status ASA grade 1 and grade 2 undergoing elective surgeries under general anesthesia were included in the study after ethical clearance from the college ethical committee. Each patient was visited preoperatively. The procedure was

explained and written informed consent was obtained. All the routine investigations required for preoperative evaluation and proposed surgery was done. Patients were allowed for absolute fasting period of at least 8 hours. Patients of both the groups were not permitted with any other sedative drugs before surgery.

Inclusion Criteria

1. Patients belonging to ASA grade 1 and 2
2. Age group from 18-60 years of both sexes.
3. Weighing between 50-80 kgs
4. Mallampati Class I and II
5. Patients posted for various elective surgical procedures under general anesthesia in which orotracheal intubation was required.

Exclusion Criteria

1. History of allergy to either Gabapentin or Pregabalin.
2. Predicted difficulty in intubation
3. Duration of laryngoscopy exceeding 20secs
4. More than one attempts for intubation
5. Pregnancy, lactating women
6. Patients with coronary artery diseases, ischemic heart diseases, heart blocks.
7. Patients with history uncontrolled hypertension, renal dysfunction, hepatic dysfunction.
8. Patients on antihypertensives, any other sedatives, hypnotics or analgesics for chronic pain.

Study Groups

60 Patients were randomly allocated into two groups of 30 each on basis of a sealed envelope technique to receive one of the following drugs.

Group G (n=30): receiving Gabapentin, 600mg orally

Group P (n=30): receiving Pregabalin, 150mg orally

Statistical Analysis

The following methods of statistical analysis have been used in this study. Data was entered in Microsoft excel and analyzed using the Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc. Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements were presented on Mean \pm SD. Student t test (two tailed, independent) and Chi-square/ Fisher Exact test has been used to find the significance of study parameters. In all the above test “p” value of less than 0.05 was accepted as indicating statistical significance.

Results

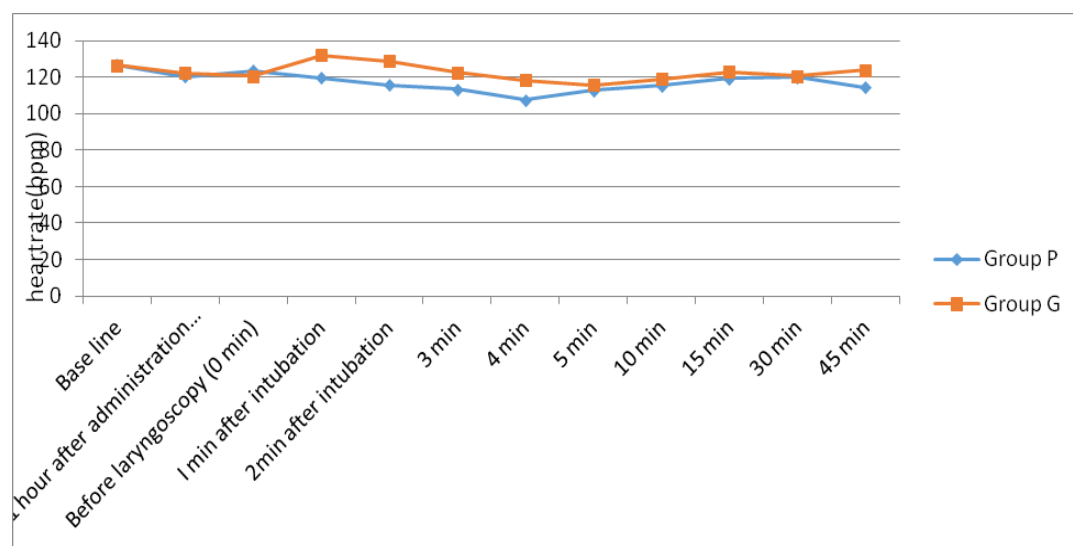


Figure 1: Comparison of Heart rate (bpm) distribution in two groups of patients studied

In our study, the mean HR of patients in the Pregabalin group was 87.13 ± 14.09 and the mean HR of patients in Gabapentin group was 86.67 ± 13.04 . Hence the mean Heart Rate of the patients in both the groups were comparable at baseline ($p=0.895$).

We observed that, the heart rate increased in Gabapentin group at 1 minute i.e., 93.33 ± 13.53 . After 1 minute, there was

In our study, the mean age of patients in Gabapentin group was 40.97 and that of patients in Pregabalin group was 34.83 years. The distribution of age of the patients in the two groups was significant ($p=0.022$).

In our study, the number of males and females in Gabapentin group and Pregabalin group were equal. There was no significant difference in sex distribution among patients of both groups ($p=1$).

In our study, the mean weight of the patients in Gabapentin group was 63.73 and in Pregabalin group was 68.63. There was no significant difference in the mean weight of patients between two groups ($p=0.024$).

fall in the HR compared to the baseline in Pregabalin group. We observed that, in both the group, there was decrease in the HR as compared to 1 minute and HR was consistently lower compared to baseline from 1 min to 5 min. ($p < 0.001$ at 1 min, $p < 0.001$ at 2 min, $p = 0.002$ at 3 min and $p < 0.001$ at 4 min and $p = 0.014$ at 5 min). Heart rate continued to remain lower in the Gabapentin group after 10 minutes too.

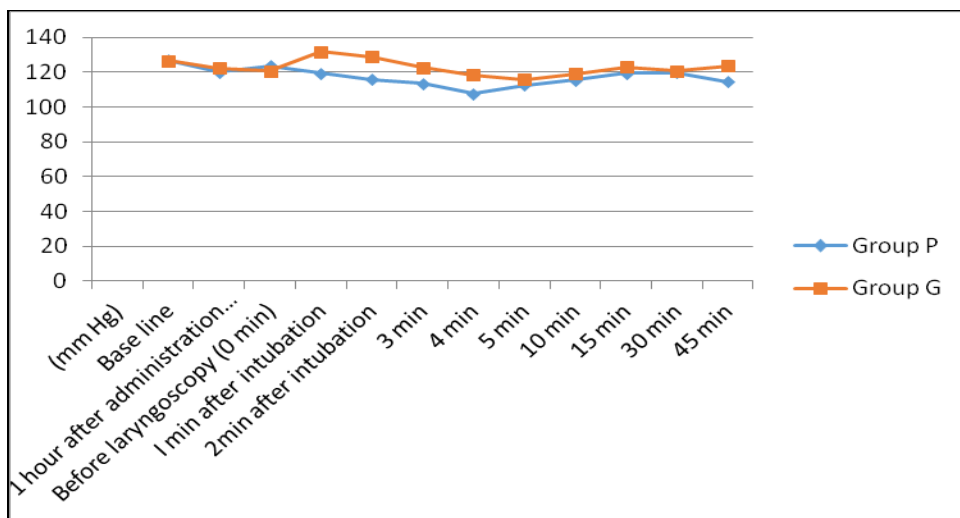


Figure 2: Comparison of SBP (mm Hg) distribution in two groups of patients studied

This difference in SBP between the two groups is significant, hence Pregabalin is more effective in suppressing the rise in SBP compared to Gabapentin up to 15

minutes following intubation ($p < 0.006$ at 1 min, 0.003 at 2min, 0.027 at 3min, 0.035 at 4 min and 0.397 at 5 min).

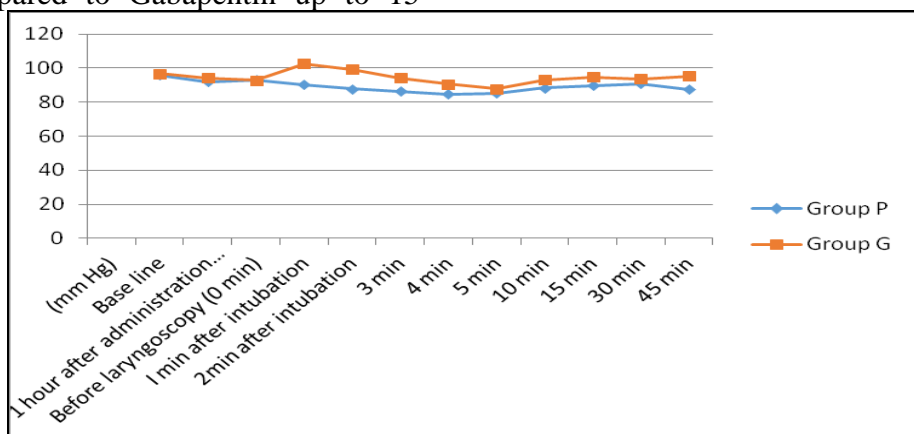


Figure 3: Comparison of DBP (mm Hg) distribution in two groups of patients studied

In our study, the mean DBP of patients in the Pregabalin group was 77.43 ± 12.10 and the mean DBP of patients in Gabapentin group was 78.33 ± 8.82 . Hence the mean DBP of the patients in both the groups were comparable at baseline ($p = 0.743$).

In the Group G, there was an increase in the mean DBP of the patients at 1, 2, minutes and after that the DBP was maintained below the baseline. Whereas in the Group P, there was no rise in mean

DBP compared to the baseline right from the 1st minute of intubation.

This difference in DBP between the two groups is significant, hence Pregabalin is more effective in suppressing the rise in DBP compared to Gabapentin following intubation ($p < 0.0001$ at 1, 2, $P = 0.017$ at 3 min, $P = 0.028$ at 4 min, $P = 0.239$ at 5 min and $P = 0.137$ at 10 min, $p = 0.095$ at 15 min, $p = 0.099$ at 30 min and $p = 0.001$ at 45 min).

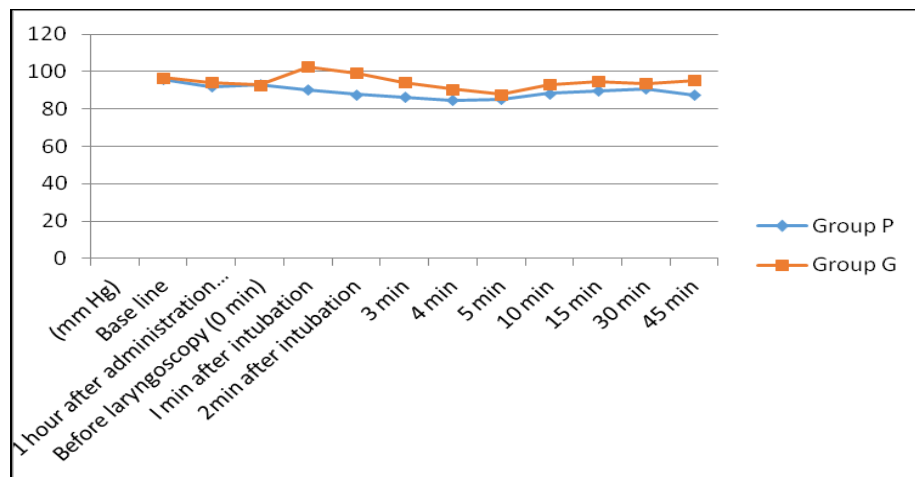


Figure 4: Comparison of MAP (mm Hg) distribution in two groups of patients studied

The difference in MBP between the two groups was significant, hence Pregabalin was more effective in suppressing the rise in MBP compared to Gabapentin following intubation ($p < 0.0001$ at 1 and 2 min, $p = 0.013$ at 3 min, $p = 0.046$ at 4 min, $p = 0.443$ at 5 min and $p = 0.129$ at 10 min).

Discussion

Ali et al [2] demonstrated that administration of Gabapentinoids did not affect basal plasma catecholamine (epinephrine and norepinephrine) concentrations before intubation, failed to attenuate the catecholamine response to intubation and conversely, enhanced the increase of plasma norepinephrine concentration. The results of this study also showed that despite higher plasma concentration of norepinephrine in patients receiving Gabapentin than in the control group after intubation, the increase in mean arterial pressure and heart rate was lower in the Gabapentin group during the study period. The cardiovascular response to catecholamines may be attenuated by Gabapentinoids without affecting their secretion. The important determinant of the level of arterial pressure to tracheal intubation may be reactivity to norepinephrine and not the plasma concentration.

Ayya Syama Sundar et al [3] conducted a study on 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. They compared single preoperative dose of Pregabalin 150mg to a placebo.

The study showed that a single oral dose of 150 mg Pregabalin given 1 h before surgery attenuated the pressor response to tracheal intubation in adults. So Pregabalin 150 mg was used in our study and the results were similar to our study.

The mean systolic arterial pressure (SBP) and DBP measured during different time periods between the two groups was significantly lower in the Pregabalin group except the baseline diastolic arterial pressure.

Eren et al [4] determined the effect of a single dose of Pregabalin 150 mg, administered 1 h prior to surgery on reducing the cardiovascular response and stated that 150 mg of Pregabalin had significantly decreased the mean arterial pressure and heart rate response to tracheal intubation of the patients undergoing lumbar discal hernia repair under general anesthesia. The results were similar to our study with respect to mean arterial pressure (MAP).

Snehalatha Bhashyam, P Krishna Prasad, B Sowbhagya Lakshmi conducted a study comparing Oral Gabapentin versus Oral Pregabalin Premedication for Anxiolysis, Sedation, and Attenuation of Pressor Response to Endotracheal Intubation. Group G and P respectively received Gabapentin 600mg and Pregabalin 150 mg. According to their study, during laryngoscopy (0 min) and immediately after 1, 3 and 5 min of laryngoscopy and intubation, there was increase in the HR and MAP in both the groups and the rise was significantly high at 0 min, i.e., during laryngoscopy in both the groups. But when comparing both the groups, the attenuation of HR and MAP was significantly high in Group P than Group G ($P < 0.001$). After 5 min, the HR and MAP declined in both the groups. And at 10 min after intubation, HR and MAP values almost reached the baseline values and there was no significant difference in the HR and MAP in both the groups ($P = 1.000$).

They concluded that oral Pregabalin 150 mg and Gabapentin 600 mg given as premedicants 1 h before surgery decreased preoperative anxiety, improved sedation, and effectively attenuated pressor response to intubation. But when compared to Gabapentin 600 mg, Pregabalin 150 mg led to a significant reduction in preoperative anxiety, improved sedation and significantly attenuated hemodynamic response to laryngoscopy and intubation, without significant side effects.

This study concluded that Pregabalin is better in attenuating the increase in the heart rate, Systolic blood pressure and mean arterial pressure ($P < 0.001$) which is similar to our study. Heart rate was less than the baseline.

Namratha. S. Urs, Shobha D [5] conducted a Comparative Evaluation of Oral Gabapentin and Pregabalin Premedication for Attenuation of Pressor Response to Endotracheal Intubation under General Anaesthesia. They had divided the subjects

into three groups. Group A – Control group were given placebo, Group B – Gabapentin group (800mg) and Group C – Pregabalin group (150mg). An increase in heart rate and MAP was seen from the time of laryngoscopy upto 5 minutes after intubation. Maximum heart rate and MAP was seen at 0 min of intubation. The average maximum heart rate in the study Group A-100.56, Group B-90.96 and Group C-86.64 was seen at 0 min and maximum MAP was 106.34, 98.62 and 95.0 in Group A, B and C respectively at 0 min. The difference between the control and the Gabapentin and Pregabalin was found to be highly significant with a p value of <0.001 at 0, 1, 3 and 5 min after intubation.

Thereafter the heart rate and MAP started declining towards baseline by the end of 10min. When compared to Gabapentin, Pregabalin had very slight rise in HR and MAP to laryngoscopy but was not statistically significant.

In the above study they concluded that a single oral dose of 800mg of Gabapentin and 150mg of Pregabalin administered 2 hrs prior to surgery effectively reduces the hemodynamic response to laryngoscopy and endotracheal intubation even though not completely attenuated which is due to its analgesic and sedative effect. So it is a safe, simple and economical technique with good patient comfort and compliance. The results were corresponding to our study with respect to heart rate, SBP and MAP but they have used Gabapentin 800mg whereas we used 600mg.

Dhananjaya Bangalore Daddaiah et al [6] conducted a comparative study of oral Pregabalin and oral Gabapentin in the attenuation of hemodynamic response to laryngoscopy and intubation on one hundred and twenty patients into three groups of forty patients each to receive preoperatively – Group C vitamin capsules, Group G Gabapentin 800 mg,

and Group P Pregabalin 150 mg 90 min before the scheduled surgery.

The above study showed the increase in HR response to laryngoscopy and intubation was minimized by both Gabapentin and Pregabalin when compared with the control group ($P < 0.05$) at baseline and 1 min; however, there was no statistically significant difference between the two study groups ($P > 0.05$). There was statistically significant reduction in SBP, DBP, and MAP at 1 min with $P = 0.026$, 0.014 , and 0.001 and at 5 min with $P = 0.002$, 0.007 , and <0.001 , respectively, in Gabapentin group. In Pregabalin group, there was a reduction in SBP, DBP, and MAP at 1 min following intubation with $P < 0.001$, <0.001 , and <0.001 and at 5 min with $P = 0.001$, <0.001 , and <0.001 , respectively.

They concluded that Both oral Gabapentin 800 mg and Pregabalin 150 mg administered as a premedicant are safe and effective measures in attenuating the hemodynamic responses to laryngoscopy and intubation. However, further studies with different doses and timing of the study drugs need to be assessed. They have not concluded about the difference between the two drugs.

But in our study we found that there is significant difference between Pregabalin and Gabapentin, Pregabalin being better than Gabapentin in attenuating the intubation response. P-value for heart rate <0.001 , SBP <0.006 . Another difference is that they have administered 800mg of Gabapentin whereas 600mg of Gabapentin was used in our study.

Chandrakant Waikar et al [7] conducted a Comparative Study of Oral Gabapentin, Pregabalin, and Clonidine as Premedication for Anxiolysis, Sedation, and Attenuation of Pressor Response to Endotracheal Intubation where they used clonidine 200 μg and Gabapentin 900 mg and Pregabalin 150 mg.

In their study, mean arterial pressure was well attenuated by Pregabalin than others which is similar to our study but the mean heart rate following laryngoscopy and intubation was attenuated by clonidine group significantly.

Our findings were similar to the study conducted by Kumkum Gupta et al. [8] on the effects of Pregabalin on the perioperative stress response which concluded that the Pregabalin was effective in reducing the stress response for laryngoscopy and intubation and good analgesia also. [9]

In Pregabalin group heart rate, systolic and diastolic blood pressure and mean arterial blood pressure were below the baseline values during laryngoscopy and intubation where as in Gabapentin group heart rate, systolic and diastolic blood pressure, mean arterial blood pressure came down to baseline values by the end of 3rd minute from onset of laryngoscopy. So, we can come to a conclusion statistically that oral Pregabalin is better than oral Gabapentin in attenuating the hemodynamic changes after laryngoscopy and intubation.

Conclusion

In Pregabalin group heart rate, systolic and diastolic blood pressure, mean arterial blood pressure and rate pressure product were below the baseline values during laryngoscopy and intubation where as in Gabapentin group heart rate, systolic and diastolic blood pressure, mean arterial blood pressure and rate pressure product came down to baseline values by the end of 3rd minute from onset of laryngoscopy.

Hence from our clinical comparative study we conclude that oral Pregabalin is a better drug for attenuation of hemodynamic stress response to laryngoscopy and intubation compared to oral Gabapentin. However the study has to be done on a larger population and high risk patients.

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