Section: Anesthesiology

Original Research Article

COMPARISON OF ORAL GABAPENTIN VERSUS ORAL PREGABALIN FOR ANXIOLYSIS, SEDATION AND ATTENUATION OF STRESS RESPONSE TO LARYNGOSCOPY AND INTUBATION

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Abstract

Background: The aim of the study is to compare the efficacy of oral Gabapentin and Pregabalin as a premedication for studying anxiety, sedation levels and attenuation of stress response to laryngoscopy and intubation in patients undergoing surgeries under general anaesthesia and adverse effects if any. **Materials and Methods:** 100 patients scheduled for elective surgeries under General anaesthesia were enrolled for this prospective, randomized study and allocated into two groups of 50 patients each. Group G received oral Gabapentin 600 mg and Group P received oral Pregabalin 150 mg one hour prior to surgery with sips of water. The above parameters were compared in both the groups. **Result:** Patients in both the groups had significant anxiolysis and sedation but Group P patients were more sedated which was statistically significant. The increase in heart rate, and mean arterial pressure during laryngoscopy and 1minute,3 minutes,5minutes and 10 minutes following intubation were much lesser in Group P patients compared to Group G patients which were statistically significant. Thus Pregabalin provided much better haemodynamic stability during stress of laryngoscopy and intubation. The incidence of headache was higher in Group G patients than Group P whereas the incidence of dizziness was equal in both the groups. No incidences of postoperative nausea ,vomiting and respiratory depression were observed in both the groups. **Conclusion:** Oral Pregabalin 150 mg given one hour prior to surgery provides better anxiolysis, sedation and haemodynamic stability with minimal side effects than oral Gabapentin 600mg.

INTRODUCTION

Preoperative anxiety occurs commonly before any surgery. Anxiety causes increased stress leading to stimulation and activation of autonomic nervous system.[1] and also causes altered pharmacokinetics of anaesthetic agents. In addition laryngoscopy and intubation are noxious stimuli which involve the manipulation of the respiratory tract and further increase these stress responses.[2] The response include tachycardia, hypertension, increased catecholamines, increase in myocardial oxygen demand, dysarrhythmias and even increased intraocular pressure. Arterial pressure starts to increase 5 seconds before laryngoscopy, reaches the peak at approximately 1-2 minutes and decreases to baseline level at 5 minutes.[3] Thus when laryngoscopy duration is prolonged , it causes further elevation of these parameters. While normal patients can tolerate these stress responses, it can increase the morbidity and mortality in patients with hypertension and coronary artery disease.[4] Hence it is of utmost importance to not only alleviate preoperative anxiety but also to suppress the stress responses at the time of laryngoscopy and also during airway manipulation and intubation. Drugs that are commonly used for anxiolysis are benzodiazepines. But they are associated with unpleasant sedation. There are other drugs which are used to attenuate the stress responses are beta blockers[6], narcotics[7], alpha 2 agonists[8], local anaesthetics[9], vasodilators[10] and calcium channel blockers.[11] But the search for the drug which does the same with the minimal side effects still continues. Recently there are studies that focus on GABA analogues namely Gabapentin[12] and also Pregabalin to be not only used for anxiolysis but also to attenuate the effects of airway manipulation and ,laryngoscopy and intubation[13] Gabapentin, a drug

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that is analogous to Gamma Amino Butyric Acid was introduced into the market in 1983. It is neither an agonist nor antagonist. It exerts its action through its ability to bind to α2d subunit of the calcium channels that are voltage gated resulting in decreased release of certain excitatory neurotransmitters. A recent study by Todd et al[14] states that Gabapentin might reduce the release of catecholamines from chromaffin cells of adrenal gland which is mainly responsible for attenuation of stress response. Pregabalin is also analogous to GABA which acts in the similar way as Gabapentin. It was brought into the pharmaceutical industry in 2004 to relieve neuropathic pain and as adjunctive therapy in partial seizures., In addition it produces anxiolysis which is utilized for preoperative anxiolysis. Gabapentin has slow absorption after oral administration. The maximum plasma concentration is attained at 2-3hours and has 60% bioavailability., Pregabalin is absorbed rapidly after oral administration with its plasma concentration peaking at 1 hour with bioavailability is 90%. Both drugs are excreted through renal route. Hence dose adjustment in patients showing altered renal function is required. The adverse effects of these drugs include dizziness, fatigue and somnolence.

Aim Of the Study

The aim of this study is to compare the efficacy of oral Gabapentin and Pregabalin as a premedication for anxiolysis, sedation and attenuation of stress response to laryngoscopy and intubation in patients undergoing surgeries under general anaesthesia and also monitored for post operative complication such as dizziness, headache, nausea and vomiting.

MATERIALS AND METHODS

After obtaining institutional ethical committee approval and written informed consent from all the patients, this prospective, comparative and randomized study was conducted in Coimbatore Medical College Hospital, Coimbatore from July 2016 to September 2017.Randaomization was done by sealed envelope method. 100 patients of 20 to 60 years scheduled for elective surgeries under General anaesthesia with ASA PS I and II after thorough pre anaesthetic check up and airway assessment were enrolled in this study. Those patients with anticipated difficult intubation, history of cardiac hypertensive, pulmonary diseases, elevated renal parameters, allergy to drugs, those taking sedatives ,hypnotics and second attempt at intubation were excluded from the study. They were then randomly allocated into 2 groups -

Group G (Receiving Oral Gabapentin 600mg)

Group P (Receiving Oral Pregabalin 150mg)

Patients were given their allocated drugs 1 hour prior to surgery with sips of water. Baseline parameters such as pulse rate, blood pressure, respiratory rate and oxygen saturation were recorded. The patient's level of anxiety , sedation and vitals were recorded1 hour after premedication, After shifting into the theatre, patient was connected to the monitors and intravenous fluids were started. Patients were then premedicated with Inj. Midazolam 1mg iv, Inj. Glycopyrrolate 0.2mg iv and Inj, Fentanyl 2µg/kg. Patient was then preoxygenated with 100% oxygen for 3 minutes. Induction done with Inj. Propofol 2 mg/kg. Inj. Succinyl choline is given at a dose of 2 mg/kg to facilitate laryngoscopy and intubtion. Anaesthesia was maintained with Nitrous oxide 60% in oxygen, Desflurane and Inj. Vecuronium at an initial dose of 0.1 mg/kg followed by 0.01 mg/kg for supplemental muscle relaxation. After completion of surgery the residual muscle blockade reversed by Inj. Neostigmine 0.05 mg/kg and Inj. Glycopyrrolate 0.01 mg/kg. After adequate respiratory efforts, patient was extubated following thorough suctioning. The duration of laryngoscopy was recorded with a stopwatch. The heart rate and mean arterial pressure were then recorded before and, during laryngoscopy 1 minute, 3 minutes, 5 minutes and 10 minutes following intubation. Intraoperatively, all the parameters were continuously monitored. and hypotension defined as Systolic BP less than 90mmHg, bradycardia (Heart rate < 60/min), hypoxemia and arrhythmias were watched for and postoperatively for any adverse effects dizziness, headache, nausea and vomiting and treated appropriately.

Scores Used in Our Study

Table 1: Anxiety score

Anxiety score	Patient response
0	Quiet and Comfortable
1	Uneasy
2	Worried or Anxious
3	Very worried or Very Upset

Table 2: Sedation score

Sedation Score	Patient response
1	Wide Awake
2	Sleeping Comfortably but responding to verbal commands
3	Deep Sleep but Arousable
4	Deep Sleep but not Arousable

Values signify the score in both the tables.

Statistical Analysis

The collected data was analysed using IBM.SPSS (STATISTICAL PACKAGE FOR SOCIAL SCIENCES) statistics software 23.0 Version. For continuous variables, mean and standard deviation were used. Chi-square test was used to find significant difference in categorical data. P value ≤ 0.05 was considered to be significant.

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RESULTS

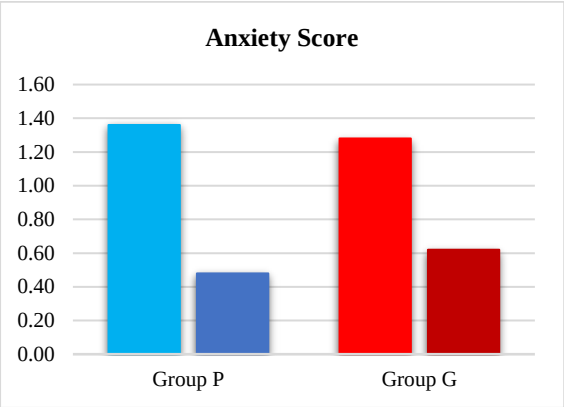

Figure 1: Anxiety Score before and after premedication

Patients were compared in terms of anxiety, sedation levels and stress response to laryngoscopy and intubation by their heart rate and mean arterial pressure and at 1 minute, 3 minutes, 5 minutes and 10 minutes after that. There were no significant difference between the age, Gender, ASAPS, duration of laryngoscopy and surgery.

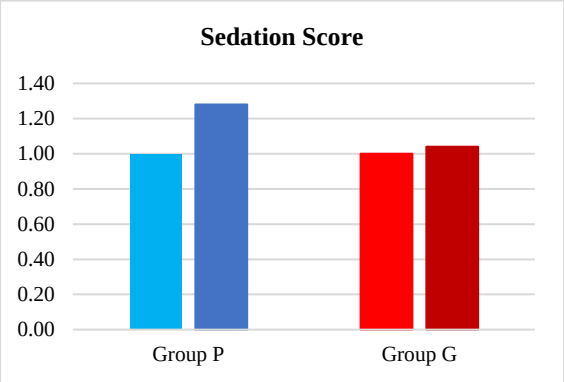

Figure 2: Sedation Score –baseline and after premedication

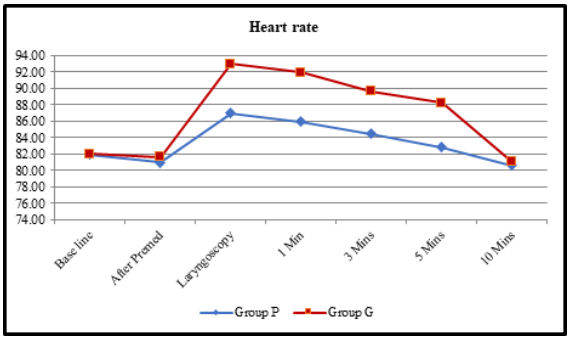

Figure 3: Variations in the heart rate between two groups

Baseline: Heart rates in both the groups were statistically not significant with a p-value of 0.922. After premedication,, it was not statistically significant with a p-value of 0.482.During laryngoscopy, the heart rates in both the groups increased but the increase in Group G was much higher and is statistically significant. At 1, 3 and 5 minutes, the heart rates in both the groups began to decrease but they were still at a higher level compared to their baseline values and the heart rates of group G patients remained at a higher level and it was statistically significant. At 10 minutes, heart rates returned to almost the baseline values in both the groups with insignificant p value.

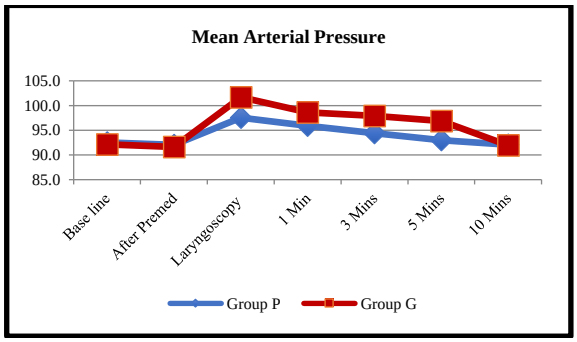

Figure 4: Variations in Mean Arterial Pressure between two groups

Baseline: Mean arterial BP in both the groups were statistically not significant with a p-value of 0.654. After premedication, mean arterial pressure between both the groups were not statistically significant with a p-value of 0.655

During Laryngoscopy: The mean arterial BP in both the groups increased but the increase in Group G was much higher with the significant p value.

At 1, 3 and 5 minutes: The mean arterial BP in both the groups begin to decrease but they are still higher compared to their baseline values in group G patients and it was statistically significant. After 10 minutes, Mean arterial pressure returned to almost the baseline values in both the groups . It was not significant with a p-value of 0.899. Patients in both the groups were observed for adverse effects following administration of the drugs and post operatively. While 2 patients in Group G experienced headache and 1 patient complained of dizziness, only 2 patients in Group P experienced adverse effects. However, this is not significant.

Table 3: Anxiety Score in Both the Groups

	Baseline Score	After Premedication	p-value
GROUP P	1.36	0.48	**0.001**
GROUP G	1.28	0.62	**0.002**

<0.001 is significant

Anxiety scores following premedication proved to be statistically significant.

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Table 4: Sedation Score Two Groups

	Baseline score	After premedication	p-value
GROUP P	1.00	1.28	0.001
GROUP G	1.00	1.04	0.157

Group P patients had high sedation scores following premedication when compared to those in Group G and it is statistically significant.

Table 5: Heart rate before and after premedication in two groups

TIME	PREGABALIN	GABAPENTIN	P-VALUE
BASELINE	81.92±4.499	82.02±5.622	0.922
AFTER PREMEDICATION	80.98±4.162	81.66±5.386	0.482
DURING LARYNGOSCOPY	86.96±4.145	93.02±5.957	0.002
1 MINUTE AFTER LARYNGOSCOPY	85.98±4.093	91.98±5.964	0.001
3 MINUTES AFTER LARYNGOSCOPY	84.44±3.980	89.64±5.958	0.001
5 MINUTES AFTER LARYNGOSCOPY	82.86±3.964	88.28±6.064	0.001
10 MINUTES AFTER LARYNGOSCOPY	80.62±3.999	81.04±4.973	0.643

Table 6: Mean Arterial Pressure Before and After Premedication

TIME	PREGABALIN	GABAPENTIN	P-VALUE
BASELINE	92.556±4.9368	92.114±4.9029	0.654
AFTER PREMEDICATION	92.044±4.5719	91.618±4.9155	0.655
DURING LARYNGOSCOPY	97.542±4.6539	101.678±4.5565	0.001
1 MINUTE AFTER LARYNGOSCOPY	95.926±4.4731	98.602±4.8649	0.002
3 MINUTES AFTER LARYNGOSCOPY	94.382±4.3861	97.938±4.7836	0.001
5 MINUTES AFTER LARYNGOSCOPY	92.980±4.1519	96.886±4.6773	0.001

DISCUSSION

The anticipation of surgery increases the anxiety levels in patients undergoing surgery and this when combined with the stress of intubation increases the heart rates and mean arterial pressures of these patients to undesirable levels. Many drugs have been used in attenuation of these stress responses. This study has been undertaken to compare the efficacy of 2 drugs namely Pregabalin and Gabapentin given orally 1 hour prior to surgery in not only attenuating the stress responses to intubation but also to lessen the anxiety levels of the patients and provide sedation. The study subjects include those who were posted for elective surgery to be done under general anaesthesia belonging to either ASA PS I or II between the age groups 18 to 60 years. Both the groups were comparable in terms of age, gender, ASA PS classification, duration of laryngoscopy, duration of surgery, SPO2 level and the p-value between them showed insignificant. The preoperative anxiety levels were comparable in both the groups. Following premedication, the anxiety levels in both the groups decreased and they were found to be statistically significant. While patients in both the groups were sedated, the sedation levels in the patients in Group P was statistically significant.[13] The hearts rates were measured following premedication, during laryngoscopy, at 1 minute, 3 minutes, 5 minutes and 10 minutes following intubation. The heart rates begin to increase during laryngoscopy and in the immediate period after that in both the groups. However, the increase was less in Group P when compared to group G and it was statistically significant during laryngoscopy, 1 minute, 3 minutes and 5 minutes following intubation. At 10 minutes after intubation, the heart rates begin to decrease to near baseline values and it was not statistically significant both the groups.l[12] The mean arterial pressure was calculated from the observed values of systolic and diastolic blood pressures. The baseline mean systolic pressure in Group P and Group G were similar and not statistically significant. The values after premedication were not much different from the baseline values and it was also statistically not significant. During laryngoscopy, 1 minute, 3 minutes and 5 minutes following intubation the mean arterial pressure increased in both the groups. The rise in Group P was significantly lesser than Group G. At 10 minutes after intubation, the mean arterial pressure of the patients in both the groups returned to near baseline values and with a p-value of 0.899, it proved to be statistically not significant study. In this study, the incidence of headache in Group P was 2% and 4% in Group G. The incidence of dizziness in both Group P and Group G was similar at 2%.[13]

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CONCLUSION

This study was done to evaluate the efficiency of oral Pregabalin and Gabapentin given as premedication one hour before General anaesthesia for elective surgeries. Even though both the drugs provide anxiolysis and sedation ,oral Pregabalin gives better and effective anxiolysis and sedation and significantly attenuates the sress response to laryngoscopy and intubation with minimal side effects than oral Gabapentin.It is also cost effective and gives better quality of anaesthesia..

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Competing Interest

There is no competing interest

Authors Contribution

All authors in our study contributed to the data collection of the patients

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