Original Article

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Comparative Evaluation of Oral Gabapentin versus Oral Pregabalin Premedication for Anxiolysis, Sedation, and Attenuation of Pressor Response to Endotracheal Intubation

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Abstract

Background: Hemodynamic responses of laryngoscopy and tracheal intubation and pre-operative Anxiety due to surgical stress are major problems for patients under General Anesthesia, which should be attenuated by appropriate premedication. The aim of the present study was to compare the effects of Oral Gabapentin versus Oral Pregabalin as premedicants for alleviating anxiety, producing sedation, and Attenuating pressor response to laryngoscopy and tracheal intubation.

Materials and Methods: In this prospective, randomized double-blind study, 60 consented adult patients of ASA Grade I and Grade II, aged between 25 and 55 years of both genders, undergoing elective surgeries requiring intubation, were randomized into 2 groups of 30 patients each as Group G and Group P. Group G received single oral dose of gabapentin 600 mg and Group P received single oral dose of pregabalin 150 mg with sips of water 1 h before surgery. Anxiety and sedation scores were assessed before administration of drugs and 1 h later. Homonymic parameters like heart rate (HR), mean arterial pressure (MAP) were recorded at baseline, after premedication, after induction, during laryngoscopy (0 min) and 1, 3, 5, and 10min after intubation.

Results: In both the groups, there was significant increase in HR and MAP at 0, 1, 3, and 5minutes after intubation, but attenuation of HR and MAP was significantly high in Group P when compared to Group G ($P < 0.001$). The degree of sedation and anxiolysis was significantly high in Group P than Group G ($P < 0.001$).

Conclusion: 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.

Key words: Anxiety, Gabapentin, Pregabalin, Pressor response, Sedation

INTRODUCTION

Pre-operative anxiety due to surgical stress is a major problem for patients posted for various surgeries under general anaesthesia.[1] Laryngoscopy and tracheal intubation is also associated with abnormal hemodynamic responses which may cause Tachycardia, hypertension, and arrhythmias due to neuroendocrinal stress response.[2] It is very much essential to alleviate anxiety, attenuate these abnormal pressor responses to noxious stimuli during anesthesia and surgery.[3]

Several pharmacological agents like benzodiazepines, opioids, local anesthetics, calcium channel blockers, beta blockers, alpha agonists etc., have been used to reduce anxiety, produce sedation and attenuate pressor responses.[4,5] Each agent has its own merits and demerits.

Recently, gamma-amino butyric acid (GABA) analogs pregabalin and gabapentin have gained prominence in various

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clinical studies, in not only alleviating peri-operative pain but also effective in attenuating pressor response to intubation and in producing peri-operative sedation and anxiolysis.[6]

In this prospective, randomized, double-blinded and comparative study, we aimed to compare the efficacy of oral gabapentin versus oral pregabalin as premedicant drugs for alleviating anxiety, producing sedation, and attenuating hemodynamic response to laryngoscopy and Endotracheal intubation.

MATERIALS AND METHODS

This study was undertaken in orthopedic operation theatre in a tertiary care Government General and Teaching Hospital between May 2014 and January 2015. After obtaining Institutional Ethical Committee approval and written, informed consent, 60 adult patients of ASA Grade I and II, aged between 25 and 55 years were included in the study.

Inclusion Criteria

- Weight between 40 and 70 kg
- Both genders
- Airway: Mallampatti Grade I and Grade II only
- Normotensive patients
- Orotracheal intubation only.

Exclusion Criteria

- H/o allergy to study drugs
- Anticipated difficult intubation
- Laryngoscopy exceeding 20 s with normal airway
- Second attempt for intubation in a normal airway
- Patients on sedatives, hypnotics, and analgesics for chronic pain.

Patients were randomized into 2 groups of 30 each as Group G and Group P. Randomization was done by computer-generated random numbers.

Group G: Patients received Gabapentin 600 mg ($n = 30$).
Group P: Patients received Pregabalin 150 mg ($n = 30$).

Both the drugs are given with sips of water 1 h before surgery. Patients of both the groups are not premedicated with any sedative drugs before surgery. The observer Anesthesiologist who did the peri-operative observations was unaware of the study drugs.

In the pre anesthetic room, all the Baseline parameters like heart rate (HR), blood pressure, Respiratory Rate, and oxygen saturation are recorded. Exactly, 1 h after the study drug premedication, anxiety, and sedation were assessed in all the patients using appropriate scoring systems.

After shifting the patients to operation theater room, standard anesthetic regimen was administered for patients of both the groups, with in. Glycopyrrolate 10 μg/kg intravenous (IV), in. Ondansetron 0.1 mg/kg IV, in. Tramadol 1 mg/kg IV as premedication prior to induction. After preoxygenation for 3 min with 100% oxygen, all patients were induced with in. Thiopentone sodium 5 mg/kg IV, intubated with succinylcholine 1.5 mg/kg IV, maintenance of anesthesia was done with in. Vecuronium 0.1 mg/kg IV, with 60% N20 and 40% O_2 and isoflurane 0.4-0.6%. Laryngoscopy and intubation were performed by an experienced anesthesiologist who was blinded to the study protocol. The following parameters were recorded.

- Duration of laryngoscopy in seconds
- HR and mean arterial pressure (MAP) at baseline (before premedication)
- HR and MAP After premedication and after induction
- HR and MAP at 0 min (during laryngoscopy)
- HR and MAP at 1 min (after intubation)
- HR and MAP at 3 min (after Intubation)
- HR and MAP at 5 min (after Intubation)
- HR and MAP at 10 min (after Intubation).

Thereafter, HR and MAP are monitored every 5 min intervals till the completion of surgery. At the end of the surgery, all the patients were reversed with In. neostigmine 0.05 mg/kg and In. glycopyrrolate 0.01 mg/kg and extubated. All the patients were monitored for any other complications throughout the intraoperative period.

Anxiety and Sedation levels are assessed as per the following clinical scores:

4 - Point anxiety score	4 - Point sedation score
0 - Quiet and comfortable	1 - Wide awake
1 - Uneasy	2 - Sleeping comfortably but responding to verbal commands
2 - Worried or anxious	3 - Deep sleep but arousable
3 - Very worried or very upset	4 - Deep sleep but not arousable

Statistical Analysis

Statistical analysis was done using GraphPad.com software. Data were analyzed and compared using student's *t*-test and chi-square test. Data were represented as mean and standard deviation. $P < 0.05$ was considered statistically significant.

RESULTS

Totally, 60 patients were included in the study. All the patients completed the study successfully.

Demographic characteristics like age, weight, ASA physical status, Mallampatti grading, duration of laryngoscopy were comparable between both the groups $P > 0.05$ (Table 1).

The degree of anxiety, before and after premedication was assessed and compared using 4-point anxiety score. There was alleviation of anxiety in both the groups when compared with baseline values. The reduction in anxiety was highly significant in group P when compared to Group G. ($P = 0.01$ in Group G vs. 0.001 in Group P) (Table 2).

Both the groups were sedated after premedication, but the degree of sedation was significantly higher in Group P when compared to Group G ($P = 0.017$ in group G vs. 0.001 in Group P) (Table 3).

There was no significant difference in baseline HR and MAP values among both the groups ($P = 0.533$). 1 hour, after premedication and immediately after induction also, there was no significant difference in the HR and MAP in both the groups. 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 ($P = 1.000$) (Tables 4 and 5, Figures 1 and 2).

Complications such as headache and dizziness occurred in few cases of both the groups. In group P, the incidence of headache and dizziness is less when compared to Group G. The incidence of headache is (Group P 3.33% vs. 13.33% Group G) and dizziness is (Group P 3.33% vs. 6.66% Group G). They subsided without any treatment. No other side effects such as somnolence, blurred vision, and peripheral edema were reported in this study (Table 6).

None of the patients had Respiratory depression in the immediate post-operative period and post-operative SpO_2

Table 1: Demographic data

Parameters	Mean±SD (*n*=30)		*P* value
	Group G	Group P	
Age in years (mean±SD)	35.20±6.95	35.83±7.91	0.744
Weight in kgs (mean±SD)	51.46±4.01	51.73±4.31	0.802
Sex (male/female) (*n*)	18:12	21:9	0.588
ASA I/II	26:4	24:6	0.730
Mallampatti (I:II)	23:7	21:9	0.771
Duration of scopy (sec)	16.13±1.65	16.43±1.56	0.472

Data expressed as mean (SD) or ratio or absolute numbers, *Fischer's exact test, SD: Standard deviation

Table 2: Comparison of anxiety score

Groups	Anxiety score (Mean±SD (*n*=30))		*P* value
	Before premedication	1 h after premedication	
Group-G	1.16±0.83	0.63±0.85	0.017*
Group-P	1.26±0.82	0.53±0.81	0.001**

Student-*t*-test, SD: Standard deviation, *Statistically significant, **Statistically highly significant

Table 3: Comparison of sedation score

Groups	Sedation score (Mean±SD (*n*=30))		*P* value
	Before premedication	1 h after premedication	
Group-G	1	1.13±0.34	0.04
Group-P	1	1.33±0.54	0.001**

Student-*t*-test, SD: Standard deviation, **Statistically highly significant *p* value - 0.001

Table 4: Comparison of heart rate (BPM)

Parameters	Mean±SD (*n*=30)		*P* value
	Group G	Group P	
Baseline	79.20±4.52	78.50±3.87	0.522
After premedication	79.93±5.47	78.96±4.52	0.459
After induction	81.53±5.06	80.86±5.07	0.612
During laryngoscopy (0 min)	89.83±6.28	85.13±3.32	0.001**
1 min	88.36±5.79	84.26±3.26	0.001**
3 min	86.93±5.17	82.96±3.51	0.001**
5 min	85.13±4.38	81.96±2.32	0.001**
10 min	78.28±4.52	78.28±2.94	1.000

SD: Standard deviation, **Statistically highly significant

Table 5: Comparison of MAP (mmHg)

Parameters	Mean±SD (*n*=30)		*P* value
	Group G	Group P	
Baseline	89.30±2.74	88.80±3.08	0.509
After premedication	88.72±3.91	87.49±3.89	0.226
After induction	87.41±3.7	86.19±2.84	0.158
During laryngoscopy (0 min)	99.86±2.28	96.28±1.72	0.001**
1 min	97.80±2.52	94.9±2.80	0.001**
3 min	95.20±2.74	92.50±2.10	0.001**
5 min	93.60±2.40	90.17±2.84	0.001**
10 min	88.18±4.30	88.18±2.70	1.000

Student-*t*-test, SD: Standard deviation, **Statistically highly significant, MAP: Mean arterial pressure

Table 6: Comparison of side effects

Side effects	*n*=30 (%)	
	Group G	Group P
Dizziness	2 (6.66)	1 (3.33)
Somnolence	-	-
Blurred vision	-	-
Headache	4 (13.33)	1 (3.33)
Peripheral edema	-	-

Data expressed in absolute numbers

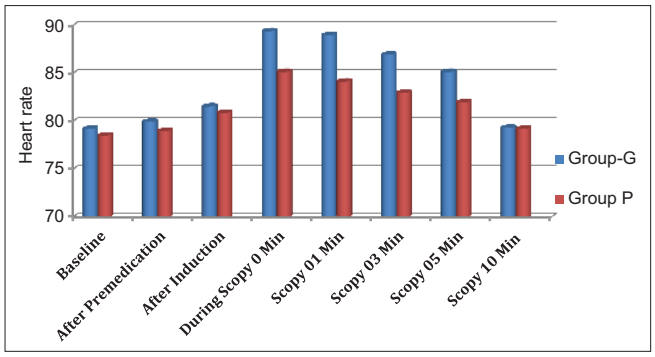

Figure 1: Comparison of heart rate (BPM)

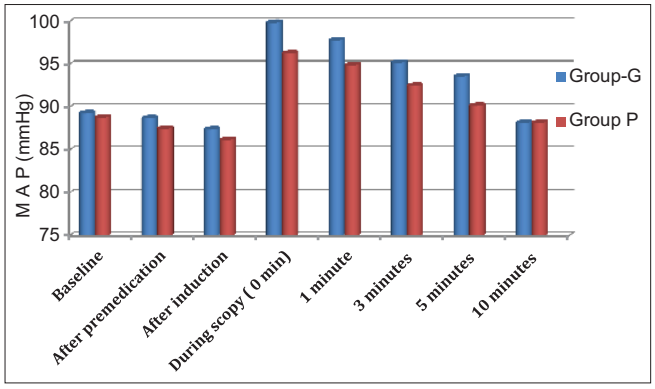

Figure 2: Comparison of mean arterial pressure (mmHg)

values did not fall to <95% in any of the patients in this study. No cases of delayed recovery were reported, and all the patients were extubated successfully on the table immediately after surgery.

DISCUSSION

Attenuation of the hemodynamic response to laryngoscopy and intubation, anxiolysis and peri-operative sedation require different pharmacological agents for each individual action.[7] GABA analogs such as pregabalin and gabapentin are known for their multimodal effects like anxiolysis, sedation peri-operative analgesia, attenuation of hemodynamic responses to laryngoscopy and intubation etc., in various clinical studies.[8,9]

Gabapentin is a structural analogue of neurotransmitter GABA, which acts by selective activation of GABA-B receptors and enhancement of NMDA receptors thus producing the desired pharmacological actions.[10] Pregabalin is also structurally related to GABA but inactivates GABA receptors and acts by decreasing the synthesis of the neurotransmitter glutamate. Thus, it acts as an analgesic, anxiolytic, anticonvulsant, and maintains hemodynamic stability throughout peri-operative period.[11]

Oral bioavailability of Pregabalin (90%) is more than that of gabapentin (60%). As GABA analog performs multiple actions with a single oral dose, we selected these drugs for this study. In both the study groups, there was a significant reduction in anxiety and significant attenuation of pressor response. But the attenuation of pressor response was more significant with pregabalin (150 mg) than gabapentin (600 mg) due to its more sedative effect.[12]

The results of our study correlated with the study of Namratha. S. Urs, Shobha D, who compared oral gabapentin and pregabalin premedication for attenuation of Pressor Response to Endotracheal Intubation. But they did not assess sedation and Anxiety in their study.[13]

De-Paris *et al.* demonstrated that gabapentin attenuated anxiety associated with simulated public speaking in volunteers, which is related to the pre-operative anxiety state.[14] Gabapentin has advantage of decreasing anxiety without causing amnesia.[15]

Anju Ghai *et al.* evaluated the effect of pregabalin 300 mg and gabapentin 900 mg on preoperative anxiety and sedation and concluded that they cause a significant reduction in preoperative anxiety and produce sedation without producing significant side effects.[16] These observations also correlated with our study, but the difference is, they used higher doses when compared to our study.

Kumkum Gupta *et al.* performed a placebo-controlled study with oral pregabalin 150 mg and demonstrated that pregabalin effectively attenuates hemodynamic pressor response to Laryngoscopy and intubation while maintaining hemodynamic stability.[17] In their study, pregabalin was given 60-75 min prior to surgery, as in our study.

Memiş, *et al.* demonstrated that patients receiving 800 mg of oral Gabapentin 1 h prior to surgery had significant reduction in the MAP and HR during the first 10 min after endotracheal intubation compared with 400 mg of oral Gabapentin or placebo.[18] The observations of Memiş, study correlated with our study except that the dose of Gabapentin we used is 600 mg.

Rastogi Bhawan, *et al.* in their study proved that Oral pregabalin 150 mg effectively attenuated the hemodynamic response to orotracheal intubation at the first attempt which is very much useful in patients with cardiovascular diseases.[19,20] The findings of this study were similar to our study.

CONCLUSION

We conclude 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.

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