Research Paper

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# Comparative study of tablet Gabapentin 600 mg and tablet Gabapentin 1000 mg to attenuate the pressor response to laryngoscopy and tracheal intubation

Medical Science

**KEYWORDS :** Gabapentin, Laryngoscopy, Placebo, Tracheal intubation

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## ABSTRACT

*Background and objectives: Aim of this study was to compare the efficacy and safety of different doses of tab. gabapentin 600 mg, 1000 mg and oral placebo (control) to attenuate the pressor response to laryngoscopy and tracheal intubation and to compare the side effects with the use of it's different dosages.*

*Method: 90 patients, age 18-60 yrs of either sex belonging to ASA I or ASA II posted for elective surgery under general anaesthesia were selected and divided into three equal groups of 30 each. Group I (Control group) received oral placebo. Group II and Group III (Study groups) received 600 mg and 1000 mg of tab. gabapentin respectively 90 mins prior to surgery with a sip of water.Vital parameters such as PR,, NIBP, RR, EtCO2, SpO2 and side effects were noted at the interval of 1, 3, 5, 10 and 15 mins after laryngoscopy and tracheal intubation..*

*Result: Oral gabapentin 1000 mg attenuated the increase in SBP, DBP and MAP associated with laryngoscopy and intubation better than 600 mg but caused more side effects like drowsiness and sedation. The increase in heart rate response was not completely eliminated.*

*Conclusion: Oral gabapentin 1000 mg is a better drug as compared to 600 mg to attenuate the pressor responses to laryngoscopy and tracheal intubation but tachycardiac response is not completely attenuated and it causes more drowsiness and sedation. Thus avoid any other sedation drug peri-operatively to prevent excessive drowsiness and sedation, when Gabapentin 1000 mg is used in the pre-medication.*

**Introduction**

Endotracheal intubation and laryngoscopy are very essential tools in the hands of anaesthesiologists in maintaining airway. Endotracheal intubation has become an integral part of the anaesthetic management and critical care of the patient and has been practiced following its description by Rowbothom and Magill in 1921[1]. In1940, Reild and Brace first described haemodynamic response to laryngoscopy and tracheal intubation[2]. Since the inception of general anaesthesia it has been well recognised that laryngoscopy followed by tracheal intubation is a noxious stimulus which can provoke untoward response in the cardiovascular, respiratory and other physiological systems. Significant tachycardia, hypertension and dysrhythmias can occur with tracheal intubation [3].

The magnitude of cardiovascular response is directly related to the force and duration of laryngoscopy [4]. Many studies have reported that 10%– 18% of the patients develop ischaemic ST segment changes during the procedure[5]. Though these undesirable changes are transitory in nature and well tolerated in healthy individuals, it may result in potentially deleterious effects in patients with hypertension, raised intracranial pressure or coronary artery disease etc.

As laryngoscopy followed by endotracheal intubation has become the standard of safe anaesthesia, it has become absolutely necessary to take steps to minimize the adverse cardiovascular effects associated with it.

The haemodynamic responses during laryngoscopy and endotracheal intubation should be abolished to balance the myocardial oxygen supply and demand.

Gabapentin is a newer drug with anti-epileptic & sedative effects. It has been shown to be effective in neuropathic pain, diabetic neuropathy, post herpetic neuralgia & reflex sympathetic dystrophy. Few studies have shown it to be useful for attenuation of intubation responses.

**AIM OF THE STUDY**

To compare the efficacy and safety of different doses of tab. gabapentin 600 mg, 1000 mg and oral placebo (control) to attenuate the pressor responses to laryngoscopy and tracheal intubation and to compare the side effects with the use of it's different dosages.

**MATERIALS AND METHODS**

After approval from IEC and obtaining written informed consent, 90 patients of either sex, ASA I & ASA II, age 18-60 years, posted for elective surgical procedures under general anaesthesia were selected and divided into three groups. In the pre-operative room, vital parameters were noted ($T_1$) and 90 mins prior to surgery drug was given:

**Group I (Control group):** Received oral placebo
**Group II (Study group):** Received tab. Gabapentin 600 mg
**Group III (Study group):** Received tab. Gabapentin 1000 mg

After shifting the patient to operation theatre, monitors such as Pulse oxymeter, NIBP and ECG were connected to the patient, iv line was secured & a Ringer lactate infusion was started. Base line vital parameters were recorded ($T_2$).

**The level of sedation was assessed by four point score**

- 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.

Pre-medication was done with inj. glycopyrollate (0.004mg/kg), inj. fortwin (0.3mg/kg) iv. All patients were pre-oxygenated with 100% of $O_2$ for 3 minutes. Induction was done with inj. propofol (2mg/kg) given slowly till the patient was induced and vital parameters were recorded again ($T_3$).

Muscle relaxant inj. rocuronium (0.6 mg/kg) was given & vital parameters were recorded again ($T_4$).

Laryngoscopy and tracheal intubation was done, followed by recording of the vital parameters ($T_5$). Surgery was allowed to proceed.

The periodic monitoring of the vitals was carried out at 1, 3, 5, 10 and 15 mins after laryngoscopy and tracheal intubation. Anaesthesia was maintained with 66% $N_2O$ & 33% $O_2$ along with isoflurane 0.8%-1% with Bain's circuit and controlled ventilation with intermittent doses of inj.rocuronium.

Replacement of fluid was done with crystalloids or colloids and if blood loss was excessive blood transfusion was done. At the end of surgery, patient was reversed with inj. neostigmine methyl sulphate (0.05 mg/kg body wt.) & inj.glycopyrrolate (0.008mg/kg body wt.) iv. Patient was extubated and vital parameters were noted. The patient was then shifted to recovery room and sedation score was assessed.

At the end of study, all results obtained were statistically analysed and compared using ANOVA and Chi-square test. Probability less than 0.05 was considered significant.

**RESULTS:**

In the present study, 90 ASA grade I and II patients of either sex and aged between 18 and 60 years were selected and randomized into two groups, Group I (control group Received oral placebo), Group II ( study group received tablet Gabapentin 600 mg) and Group III (study group received tablet Gabapentin 1000 mg) of 30 in each. three groups were comparable with respect to age, weight, height, sex and ASA grading (table 1).

**Table 1: Demographic Data**

| | GROUP I **Mean ± SD (n=30)** | GROUP II **Mean ± SD (n=30)** | GROUP III Mean ± SD (n=30) | P VALUE |
|---|---|---|---|---|
| AGE (years) | 35.67 ± 12.55 | 38.77 ± 14.19 | 37.57 ± 13.28 | > 0.05 |
| HEIGHT (cm) | 152 ± 8.5 | 157 ± 7.6 | 155 ± 8.1 | > 0.05 |
| WEIGHT (kg) | 57.57 ± 6.04 | 57.30 ± 6.02 | 58.1 ± 6 | > 0.05 |
| ASA GRADING (I / II) | 24 / 6 | 25 / 5 | 23 / 7 | > 0.05 |
| SEX (MALE/ FEMALE) | 19 / 11 | 17 / 13 | 18 / 12 | > 0.05 |

Figure 1: Post intubation 0 min to 15 min stages, there was statistically highly significant difference in the mean pulse rate between three groups (P<0.0001). There was no attenuation of the mean pulse rate by any of the groups.

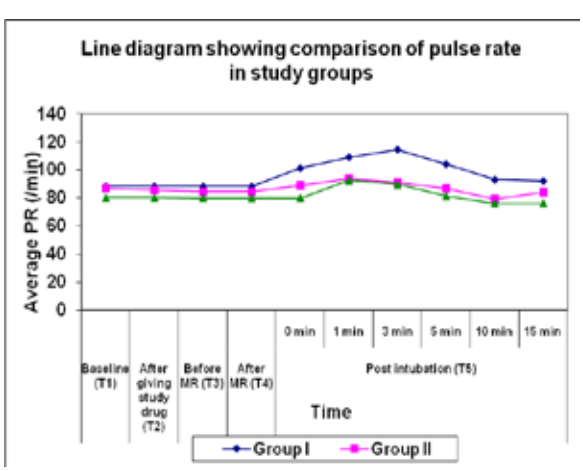



**FIG: 5**

**Baseline to 15 min stages, the difference in the Systolic blood pressure between three groups was statistically significant. Max attenuation of SBP was shown by Group III.**

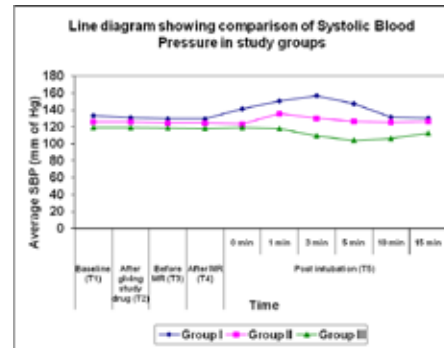



**FIG: 6**

**Baseline to 15 min stages, the difference in the Diastolic blood pressure between three groups was statistically significant. Max attenuation of DBP was shown by Group III.**

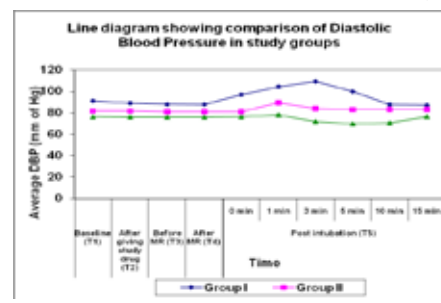



**FIG: 7**

**Baseline to 15 min stages, the difference in the Mean arterial pressure between three groups was statistically significant. Max attenuation of Mean arterial pressure was shown by Group III.**

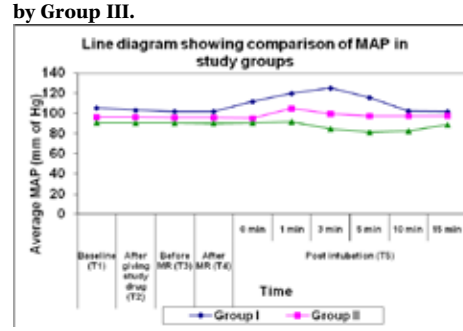
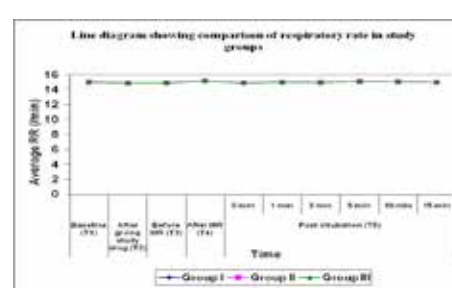



**FIG: 8**

**From baseline to 15 min post intubation, there was no statistically significant difference in the RR between three groups.**



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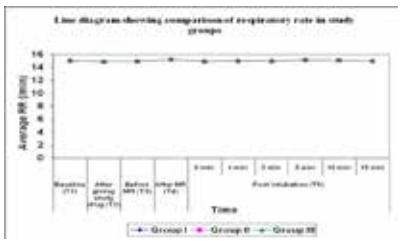

**FIG:9**
**Mean sedation score was statistically very highly significant (P<0.0001). Max sedation score was shown by Group III.**

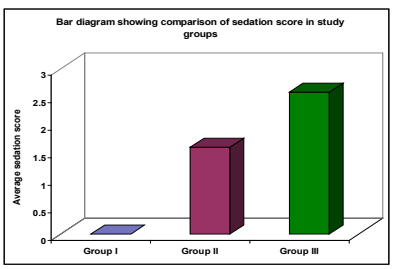


**FIG: 10**

**In group I, no side effects observed. In group II, 2 (2.22%) cases had dizziness and drowsiness respectively and in group III, 2 (2.22%) cases had dizziness and 15(16.65%) cases had drowsiness, statistically highly significant (P<0.0001).**

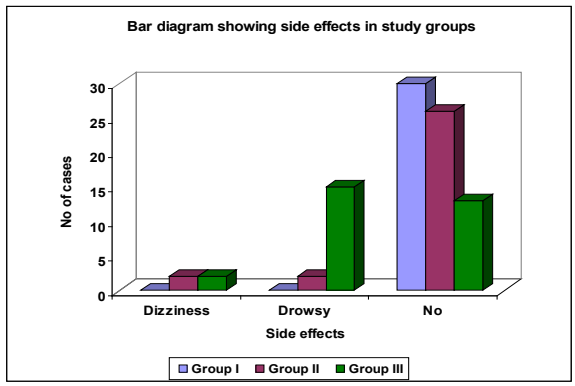


**FIG :11**

**Table: 1**

| Pulse rate at Mean | | Group I | | Group II | | Group III | | F Value | P Value |
|---|---|---|---|---|---|---|---|---|---|
| | | SD | Mean | SD | Mean | SD | | | |
| Baseline (T1) | | 88.27 | 13.41 | 87.07 | 14.66 | 80.2 | 12.69 | 3.07 | >0.05 |
| After giving study drug (T2) | | 88.27 | 13.41 | 85.6 | 14.42 | 80.17 | 12.68 | 2.79 | >0.05 |
| Before MR (T3) | | 88.2 | 13.33 | 84.57 | 14.19 | 80.03 | 12.64 | 2.79 | >0.05 |
| After MR (T4) | | 88.2 | 13.33 | 84.43 | 14.35 | 79.93 | 12.71 | 2.83 | >0.05 |
| Post intubation (T5) | 0 min | 101.2 | 11.04 | 89.03 | 15.03 | 80.03 | 12.45 | 20.21 | <0.0001 |
| | 1 min | 109.13 | 10.46 | 93.93 | 15.08 | 92.57 | 13.65 | 14.55 | <0.0001 |
| | 3 min | 114.6 | 10.08 | 91.13 | 14.18 | 89.73 | 14.05 | 35.11 | <0.0001 |
| | 5 min | 104.1 | 8.83 | 86.93 | 10.83 | 81.23 | 11.99 | 37.60 | <0.0001 |
| | 10 min | 92.97 | 6.65 | 79.27 | 9.66 | 76.13 | 9.99 | 30.42 | <0.0001 |
| | 15 min | 92.1 | 6.58 | 84.2 | 9.42 | 76.33 | 9.92 | 24.28 | <0.0001 |

**Table: 2**

| SBP (mmHg) at Mean | | Group I | | Group II | | Group III | | F Value | P Value |
|---|---|---|---|---|---|---|---|---|---|
| | | SD | Mean | SD | Mean | SD | | | |
| Baseline (T1) | | 133.37 | 10.47 | 125.67 | 11.85 | 119.57 | 12.68 | 10.47 | <0.0001 |
| After giving study drug (T2) | | 131.13 | 10.51 | 125.67 | 11.85 | 119.33 | 12.54 | 7.69 | <0.001 |
| Before MR (T3) | | 129.83 | 10.42 | 124.6 | 12.07 | 119 | 12.72 | 6.35 | <0.005 |
| After MR (T4) | | 129.73 | 10.45 | 124.6 | 12.07 | 118.63 | 12.78 | 6.64 | <0.005 |
| Post intubation (T5) | 0 min | 141.4 | 11.26 | 123.37 | 10.47 | 119.3 | 12.65 | 31.41 | <0.0001 |
| | 1 min | 150.73 | 10.8 | 135.63 | 14.47 | 118.47 | 10.63 | 53.45 | <0.0001 |
| | 3 min | 156.97 | 8.91 | 130.23 | 12.17 | 110.03 | 10.66 | 146.28 | <0.0001 |
| | 5 min | 147.4 | 8.6 | 126.37 | 10.21 | 104.2 | 11.87 | 131.58 | <0.0001 |
| | 10 min | 131.87 | 8.5 | 125.47 | 7.59 | 106.53 | 9.85 | 68.85 | <0.0001 |
| | 15 min | 130.6 | 7.43 | 126.33 | 8.01 | 112.87 | 9.15 | 37.95 | <0.0001 |

**Table: 3**

| DBP (mmHg) at Mean | | Group I | | Group II | | Group III | | F Value | P Value |
|---|---|---|---|---|---|---|---|---|---|
| | | SD | Mean | SD | Mean | SD | | | |
| Baseline (T1) | | 91.13 | 8.16 | 81.63 | 5.44 | 76.23 | 5.35 | 41.05 | <0.0001 |
| After giving study drug (T2) | | 89 | 8.36 | 81.63 | 5.44 | 76 | 5.64 | 29.15 | <0.0001 |
| Before MR (T3) | | 87.77 | 8.34 | 80.97 | 5.71 | 75.93 | 5.79 | 23.36 | <0.0001 |
| After MR (T4) | | 87.73 | 8.35 | 80.97 | 5.71 | 75.93 | 5.79 | 23.19 | <0.0001 |
| Post intubation (T5) | 0 min | 96.9 | 7.07 | 81.13 | 8.09 | 76.23 | 5.35 | 72.86 | <0.0001 |
| | 1 min | 104.33 | 5.87 | 89.3 | 12.58 | 78.1 | 7.45 | 62.80 | <0.0001 |
| | 3 min | 109.27 | 5.72 | 83.93 | 6.37 | 71.63 | 7.97 | 242.40 | <0.0001 |
| | 5 min | 99.8 | 3.58 | 82.93 | 4.31 | 69.73 | 8.91 | 184.41 | <0.0001 |
| | 10 min | 87.67 | 5.85 | 83.2 | 5.49 | 70.47 | 7.79 | 57.35 | <0.0001 |
| | 15 min | 87.13 | 5.53 | 83.2 | 5.49 | 76.47 | 8.03 | 20.94 | <0.0001 |

**Table: 4**

| MAP (mmHg) at Mean | | Group I | | Group II | | Group III | | F Value | P Value |
|---|---|---|---|---|---|---|---|---|---|
| | | SD | Mean | SD | Mean | SD | | | |
| Baseline (T1) | | 105.21 | 8.48 | 96.31 | 6.03 | 90.68 | 6.86 | 30.81 | <0.0001 |
| After giving study drug (T2) | | 103.04 | 8.58 | 96.31 | 6.03 | 90.44 | 6.93 | 22.59 | <0.0001 |
| Before MR (T3) | | 101.79 | 8.52 | 95.51 | 6.39 | 90.29 | 7.05 | 18.36 | <0.0001 |
| After MR (T4) | | 101.73 | 8.53 | 95.51 | 6.39 | 90.17 | 7.1 | 18.26 | <0.0001 |
| Post intubation (T5) | 0 min | 111.73 | 6.59 | 95.21 | 8.43 | 90.59 | 6.85 | 67.62 | <0.0001 |
| | 1 min | 119.8 | 5.9 | 104.74 | 11.93 | 91.56 | 7.92 | 76.14 | <0.0001 |
| | 3 min | 125.17 | 4.94 | 99.37 | 7.08 | 84.43 | 8.09 | 271.55 | <0.0001 |
| | 5 min | 115.67 | 3.84 | 97.41 | 5.05 | 81.22 | 9.31 | 209.81 | <0.0001 |
| | 10 min | 102.4 | 5.2 | 97.29 | 4.97 | 82.49 | 7.3 | 90.91 | <0.0001 |
| | 15 min | 101.62 | 4.61 | 97.58 | 5.13 | 88.6 | 7.1 | 40.57 | <0.0001 |

**Table: 5**

| Parameters | Group I | | Group II | | Group III | | F Value | P Value |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD | | |
| Sedation score | 0 | 0 | 1.57 | 0.63 | 2.57 | 0.63 | 192.16 | <0.0001 |

**Table: 6**

| Side effects | Group I (%) | Group II (%) | Group III (%) | Total (%) |
|---|---|---|---|---|
| Dizziness | 0 | 2 (2.22) | 2 (2.22) | 4 (4.44) |
| Drowsy | 0 | 2 (2.22) | 15 (16.65) | 17 (18.87) |
| No | 30 (33.33) | 26 (28.89) | 13 (14.46) | 69 (76.69) |
| Total | 30 (33.33) | 30 (33.33) | 30 (33.33) | 90 (100) |

SPO2 was almost similar in all the three groups.

**DISCUSSION**

In present study we have compared the efficacy and safety of different doses of tab. gabapentin to attenuate the pressor response to laryngoscopy and tracheal intubation.

The difference between the age, sex, weight and ASA grading within the groups was statistically not significant.

Comparison of mean pulse rate was observed among groups at baseline, after giving study drug, before MR, after MR and post intubation at 0 min, 1 min, 3 min, 5 min, 10 min and 15 min. Significant rise in mean pulse rate was observed in group I (placebo) as compared with group II (600 mg gabapentin) and group III (1000 mg gabapentin) in post intubation stage from 0 min to 15 min.In rest of stages the mean pulse rate was statistically not significant among the three groups. (Table: 1 ).

Similar finding was also noted by **Mausumi Neogi, SantanuBasak, Debasis Ghosh,Sandip Mukherjee, Satrajit Dawn, Dhurjoti P Bhattacharjee[6] in 2012** who carried out randomized double-blind placebo-controlled clinical study on the effects of gabapentin premedication on haemodynamic stability during laparoscopic cholecystectomy. Heart rate in group who received gabapentin was significantly lower (P<0.05) after tracheal intubation and pneumoperitoneum and remained lower in comparison to group who received placebo throughout the peumoperitoneum.

Comparison of mean SBP was observed among groups at baseline, after giving study drug, before MR, after MR and post intubation at 0 min, 1 min, 3 min, 5 min, 10 min and 15 min. Significant rise in mean SBP was observed in group I (placebo) as compared with group II (600 mg gabapentin) and group III (1000 mg gabapentin) from baseline to 15 min post intubation stage in the study. Similar results were observed in mean DBP (Table: 2, 3 )

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Similar finding was observed in a study conducted by **Fassoulaki A, Melemeni A, Paraskeva A, Petropoulos G.[7] in 2006** who investigated the effect of gabapentin when given before operation on the haemodynamic responses to laryngoscopy and intubation. Forty-six patients undergoing surgery for benign disease were randomly allocated to receive gabapentin 1600 mg or placebo capsules before surgery. Systolic arterial pressure was significantly lower in the gabapentin vs the control group at 0, 1, 3, 5 and 10 min after intubation. DAP also was lower in the gabapentin group 0, 1, 3, and 10 min after intubation Authors concluded that gabapentin, under the present study design attenuates the pressor response but not the tachycardia associated with laryngoscopy and tracheal intubation.

**TahiraIftikhar, ArshadTaqi, AsiyaSibtain, SuhailAnjum, Iftikhar Awan[8] in 2011** studied the effect of gabapentin 800 mg given orally one hour before surgery on haemodynamic responses to laryngoscopy and tracheal intubation. 60 patients were randomly allocated to one of the two groups with group I receiving 800 mg of gabapentin and group II receiving placebo. Mean SBP with gabapentin was lower compared to placebo but it was significant at 1min, 2min, 10min and 15 min after intubation ($P<0.05$). Mean diastolic BP with gabapentin was significantly lower at 3 min after intubation with $P<0.05$. Mean BP with gabapentin was significantly lower at 2min, 10 min and 15 min after intubation at $P<0.05$.

**GeetaBhandari, K.S. Shahi[9] in 2012** conducted prospective randomized double blind study to compare the effects of gabapentin on arterial pressure and heart rates at induction of anaesthesia and at tracheal intubation. Among forty patients in the study group twenty patients received oral placebo (Group P ), and 20 patients received 900 mg of gabapentin (Group G).DBP was significantly less in group who received gabapentin compared to control group who received placebo. This finding was similar as in the present study.

Comparison of Mean arterial pressure was observed among groups at baseline, after giving study drug, before MR, after MR and post intubation at 0 min, 1 min, 3 min, 5 min, 10 min and 15 min. Significant rise in mean arterial pressure was observed in group I (placebo) as compared with group II (600 mg gabapentin) and group III (1000mg gabapentin) from baseline to 15 min post intubation stage in the study. (Table: 4)

Similar finding was observed in a study conducted by **UshaBafna, Vipin K Goyal, Ashish Garg[10] in 2011** who compared the effect of different doses of gabapentin on haemodynamics associated with laryngoscopy and intubation. MAP and HR were significantly increased in patients receiving placebo and 600 mg gabapentin after laryngoscopy and intubation compared to baseline value and group III who received 1000 mg of gabapentin**.**

**Memiş D, Turan A, Karamanlioğlu B, Seker S, Türe M.[11] in 2006** compared the effects of gabapentin on arterial pressure and heart rate at induction of anaesthesia and tracheal intubation in a randomized double-blind study. Patients receiving placebo and 400 mg gabapentin showed a significant increase in BP and HR associated with tracheal intubation compared to baseline levels and group III. There was significant decrease in heart rate and arterial pressure in group III after intubation 1, 3, 5 and 10 min ($P < 0.001$, $P < 0.001$, $P < 0.05$ and $P < 0.05$, respectively) compared to groups I and II.

Comparison of respiratory rate was observed among groups at baseline, after giving study drug, before MR, after MR and post intubation at 0 min, 1 min, 3 min, 5 min, 10 min and 15 min. Mean respiratory rate difference was statistically not significant among group I (placebo), group II (600 mg gabapentin) and group III (1000 mg gabapentin) from baseline to 15 min post intubation stage in the study.

Comparison of sedation score was observed among groups at baseline, after giving study drug, before MR, after MR and post intubation at 0 min, 1 min, 3 min, 5 min, 10 min and 15 min. Significant high sedation score was observed in group III (1000 mg gabapentin) and group II (600 mg gabapentin) compared to group I (placebo) from baseline to 15 min post intubation stage in the study.(Table: 5)

Significantly high sedation score was also reported in a study conducted by **AnjuGhai, Monika Gupta, NehaRana, Raman Wadhera[12] in 2012** who studied that role of premedication with oral gabapentin would produce dose-related reductions in acute (state) anxiety and increase in sedation (sleepiness) before induction of general anaesthesia. Authors concluded that preoperative gabapentin (900 mg) administration 1 hour before surgery led to significant reduction in preoperative anxiety and improved sedation without producing significant side effects.

Side effects among the three groups were studied. Dizziness and drowsiness was significantly more among the groups who received gabapentin. Drowsiness was significantly more with 1000 mg gabapentin compared with 600 mg gabapentin. (Table: 6 **).**

**Jae Ho Lee, Hyun KyuLee, Na Hyung Chun, Yoon So, and Chi Young Lim[13] in 2013** studied post-operative effects of gabapentin after thyroid surgery. Incidence of adverse effects included somnolence, dizziness, headache and nausea with gabapentin. The difference in occurrence of side effects with placebo group was statistically not significant which was contrasting with our study finding.

Similar finding was also noted by **Mausumi Neogi, Santanu Basak, Debasis Ghosh, Sandip Mukherjee, Satrajit Dawn, Dhurjoti P Bhattacharjee[6] in 2012** who carried out randomized double-blind placebo-controlled clinical study on the effects of gabapentin premedication on haemodynamic stability during laparoscopic cholecystectomy. Observed difference in side effects (dizziness, somnolence, nausea and headache) with gabapentin and placebo was statistically not significant.

The percentage saturation ($SpO_2$) was 100% in all the three groups.

**CONCUSION**

Oral gabapentin 1000 mg attenuates the increase in systolic blood pressure, diastolic blood pressure and mean arterial pressure associated with laryngoscopy & intubation better than 600 mg. But the increase in heart rate response is not completely eliminated and it causes more drowsiness and sedation.

When gabapentin 1000 mg is used in the pre-medication, avoid any other sedative drug peri-operatively to prevent excessive drowsiness and sedation since gabapentin itself has got a central sedative action and this property of the drug was utilized in our cases.

## REFERENCE

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