

Comparison of Gabapentin and Esmolol in Reducing Haemodynamic Response to Laryngoscopy and Intubation: A Randomised Clinical Trial

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ABSTRACT

Introduction: Haemodynamic stress response to direct laryngoscopy and endotracheal intubation have been well established. Both gabapentin and esmolol facilitates in attenuating this stress response through different mechanisms.

Aim: To compare the efficacy of gabapentin and esmolol in reducing the haemodynamic stress response to laryngoscopy and intubation.

Materials and Methods: The present single centre, randomised clinical trial was conducted at Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India, from May 2022 to August 2022 among 90 American Society of Anaesthesiologist (ASA) I and II patients. The patients were divided into two groups, group G and group E. In group G, tablet gabapentin 800 mg was given three hours before surgery while injection normal saline 10 mL intravenously was given two minutes prior to induction. Group E received tablet placebo three hours before surgery and injection esmolol 1.5 mg/kg diluted upto 10 mL was given intravenously two minutes prior to induction. The baseline Heart Rate (HR), Systolic Blood

Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP) and the change at 1, 2, 5 and 10 minutes after laryngoscopy and intubation was observed. Comparison of continuous variables between two groups was done using independent t-test and comparison of percentages between two or more groups was done using Chi-square test.

Results: The mean age of group G and group E was 41.52±9.87 years and 38.54±10.06 years, respectively. Male to female ratio in group G and group E was 20:25 and 21:24, respectively. There was no significant difference in haemodynamic response to intubation between both gabapentin group and esmolol group. However, the esmolol group had more falls in all haemodynamic parameters such as HR, SBP, DBP and MAP (<20%) intraoperatively.

Conclusion: Both esmolol and gabapentin were effective in attenuating the stress response to laryngoscopy and endotracheal intubation when used as premedication. But there was more decrease in HR and blood pressure intraoperatively, when injection esmolol was used.

Keywords: General anaesthesia, Premedication, Stress response

INTRODUCTION

Laryngoscopy and intubation are an essential part of general anaesthesia for patients undergoing surgeries. Laryngoscopy and intubation is well known to invoke haemodynamic response. Stress response to laryngoscopy and intubation occurs due to catecholamine (epinephrine and norepinephrine) release [1]. Epinephrine and nor epinephrine levels may continue to rise for 4-8 minutes after laryngoscopy and intubation while increase in beta endorphins suggest rise in endocrine stress [2].

In the past anaesthesiologists have studied as well as used many drugs like fentanyl, lignocaine, dexmedetomidine, nitroglycerine and nifedipine to attenuate the haemodynamic response to laryngoscopy and intubation [3-6]. Every drug has variable efficacy in attenuating haemodynamic response to laryngoscopy and intubation and unique side-effect profile.

Gabapentin is a newer antiepileptic drug which is also used to treat neuropathic pain [7]. Gabapentin has been shown to reduce haemodynamic response to intubation [8]. It is also used perioperatively to reduce postoperative nausea and vomiting and was shown to be effective in decreasing postoperative nausea and vomiting, reduction of postoperative delirium and postoperative analgesic consumption [9-11]. Gabapentin acts by decreasing the synthesis of neurotransmitter glutamate and by binding to $\alpha 2\delta$ subunit of voltage dependent calcium channels [12]. It was found to be safe in doses of 600-1200 mg in various studies [13-15].

Beta blockers have been used to reduce stress response to laryngoscopy and intubation. Esmolol is a short acting beta1 selective blocker, so have less side-effects and its beta blockade action effectively attenuates stress response [16]. Esmolol has peak action within 1-2 minutes and has elimination half-life of 9 minutes [17]. It was found effective and safe, in doses of 100-200 mg [18].

Aim of the study was to compare the efficacy of gabapentin and esmolol in reducing the haemodynamic stress response to laryngoscopy and intubation. Primary outcome was to compare change in Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP) at 1, 3, 5 and 10 minutes of laryngoscopy and intubation after premedicating the patient with either gabapentin or esmolol. Secondary outcome was to observe any side-effects postoperatively related to esmolol and gabapentin.

MATERIALS AND METHODS

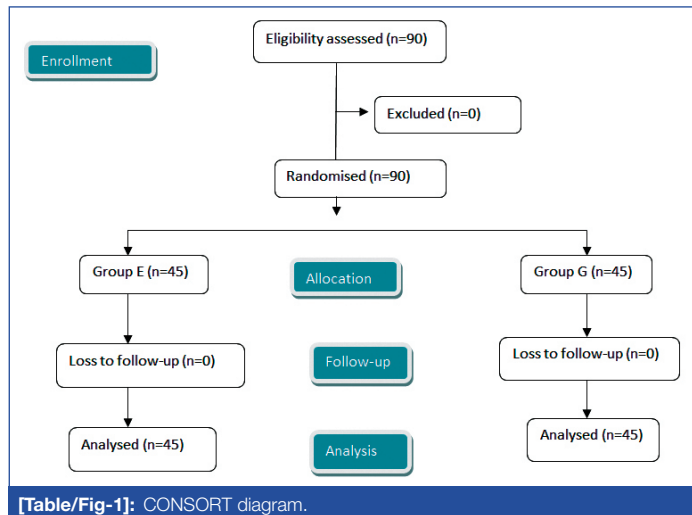
This single centre, randomised clinical was conducted at Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India, from May 2022 to August 2022. Clinical Trials Registry-India (CTRI) number for this trial was CTRI/2022/05/042618. Ethical clearance was obtained from Institutional Ethical Committee (No- BREC/22/26, dated 19th April 2022).

Inclusion criteria: Patients of either sex, age from 18-50 years, belonging to American Society of Anaesthesiologist (ASA) physical

status I and II, scheduled to undergo surgery under general anaesthesia, who were able to understand the study protocol were included in the study.

Exclusion criteria: Patients who had history of cervical spine instability, neurosurgery and patients who were on drugs effecting central nervous system, had difficult airway, had more than one intubation attempt, upper airway anatomical deformity, trauma or tumour, obstetric patients, having Body Mass Index (BMI) ≥ 35 Kg m^{-2} , had history of obstructive sleep apnoea and who were not willing to give consent were excluded from the study.

Sample size calculation: The sample size was calculated using previous study conducted by Shrestha GS et al., [13]. In their study, mean HR after induction in gabapentin group was 92.50 ± 11.92 and in esmolol group was 84.44 ± 14.51 . The sample size was estimated to be 42.55 for each group. Assuming the drop out of few patients, a total number of 90 patients were enrolled for the study. Informed and written consent was taken from all the recruited patients. Patients were randomly allocated in two groups using sealed envelopes [Table/Fig-1]. Total subjects were divided into two groups namely, group G and group E. Group G received tablet gabapentin 800 mg three hours before surgery while injection normal saline 10 mL i.v. two minutes prior to induction. Group E received tablet placebo three hours before surgery and inj. esmolol 1.5 mg/kg diluted upto 10 mL was given i.v. two minutes prior to induction.



[Table/Fig-1]: CONSORT diagram.

Study Procedure

On arrival in operation theatre baseline vital parameters were recorded (HR, SBP, DBP and MAP). After giving general anaesthesia using standard technique, one of the attending anaesthesiologist, who have ≥ 5 years of experience and was blinded to the drugs given, performed the laryngoscopy. A Macintosh number 3 or number 4 laryngoscope blade was used. The patient was intubated with endotracheal tube of appropriate size. HR, SBP, DBP and MAP were measured at 1, 2, 5 and 10 minutes after intubation and anaesthesia care was provided as per standard anaesthesia protocol. In the postoperative period any side-effects related to esmolol and gabapentin like sedation, respiratory depression, headache, anxiety, blurred vision, nausea and vomiting were noted.

STATISTICAL ANALYSIS

Data was entered, cleaned and coded in Microsoft (MS) Excel spreadsheet. Analysis of data was performed using Statistical Package for the Social Sciences (SPSS) software version 20.0. Continuous variables were expressed as mean and standard deviation if normally distributed and as median and interquartile range if not normally distributed. Categorical variables were expressed as percentages. Comparison of percentages between two or more groups was done using Chi-square test while, comparison of continuous variables between two groups was done

using independent t-test and between three or more groups was done using one-way Analysis of Variance (ANOVA). The p-value < 0.05 was considered statistically significant.

RESULTS

Both the groups were comparable with respect to demographic characteristics such as age, sex, height, weight and BMI [Table/Fig-2]. Preintubation baseline values of HR, SBP, DBP and MAP were comparable between two groups.

Variables	Group G (Mean±SD)	Group E (Mean±SD)	p-value
Age (years)	41.52±9.87	38.54±10.06	0.160
Sex (M:F)	20:25	21:24	0.84
Height (cm)	61.39±9.88	61.47±11.41	0.970
Weight (kg)	167.52±7.81	165.73±7.05	0.260
Body mass index (in Kg/sqm)	21.87±3.21	22.36±3.91	0.520

[Table/Fig-2]: Comparison of demographic profile (N=90).

There was no significant difference between the two groups with respect to change in HR after intubation at 1, 2, 5 and 10 minutes. A maximum variation of 8.89% HR from baseline level was observed in group G while 8.31% in group E was seen after induction [Table/Fig-3].

Heart Rate (HR)	Group G (Mean±SD)	Group E (Mean±SD)	Group G (% change)	Group E (% change)	p-value
Baseline	84.39±17.16	85.81±14.72	-	-	0.674
at 1 min	82.32±13.91	82.22±15.21	-2.45	-4.18	0.974
at 2 min	80.45±13.17	79.95±15.7	-4.67	-6.83	0.870
at 5 min	79.15±12.72	77.97±13.97	-6.21	-9.14	0.677
at 10 min	76.89±13.06	78.68±13.08	-8.89	-8.31	0.518

[Table/Fig-3]: Comparison of heart rate between the two groups.

There was no statistically significant difference in the values of SBP after intubation between the two groups. There was a maximum variation of 15.09% in SBP from baseline value in group G and 14.31% in group E [Table/Fig-4].

Systolic BP	Group G (Mean±SD)	Group E (Mean±SD)	Group G (% change)	Group E (% change)	p-value
Baseline	133.76±19.2	133.86±15.97	-	-	0.978
At 1 min	120.36±14.51	125.63±12.66	-10.02	-6.15	0.071
At 2 min	113.91±13.99	119.04±14.71	-14.84	-11.07	0.093
At 5 min	113.58±12.87	114.7±15.75	-15.09	-14.31	0.713
At 10 min	114.34±11.79	115.75±14.58	-14.52	-13.53	0.617

[Table/Fig-4]: Comparison of systolic BP between the two groups.

There was no statistically significant difference in DBP between the two groups. There was variation of maximum 15% in group G from baseline DBP values while 13% in group E was observed [Table/Fig-5].

No statistically significant difference was observed in MAP after intubation between two groups. Maximum variation of 15% in MAP from baseline value was seen in group G and 13% in group E [Table/Fig-6].

Diastolic BP	Group G (Mean±SD)	Group E (Mean±SD)	Group G (% change)	Group E (% change)	p-value
Baseline	85.8±14.2	82.2±12.09	-	-	0.200
at 1 min	78.69±12.99	79.18±11.61	-8.29	-3.67	0.852
at 2 min	74.21±10.72	74.47±10.74	-13.51	-9.40	0.909
at 5 min	72.89±11.41	71.38±10.03	-15.05	-13.16	0.509
at 10 min	74.52±11.32	71.45±9.61	-13.15	-13.08	0.170

[Table/Fig-5]: Comparison of diastolic BP between the two groups.

Mean Arterial Pressure (MAP)	Group G (Mean±SD)	Group E (Mean±SD)	Group G (% change)	Group E (% change)	p-value
Baseline	103.73±14.84	102.45±13.12	-	-	0.665
at 1 min	93.52±12.59	96.2±11.78	-9.84	-6.10	0.300
at 2 min	88.82±11.96	91.56±12.65	-14.37	-10.63	0.294
at 5 min	88.02±11.43	88.15±13.17	-15.15	-13.96	0.958
at 10 min	88.89±10.37	88.31±11.72	-14.31	-13.80	0.806

[Table/Fig-6]: Correlation between Basal Metabolic Index (BMI) (Kg/m²) and Modified MMSE Score among cases (n=65).

There were no other adverse effects like sedation, pruritis, headache, ataxia, respiratory depression were observed in the postoperative period in both groups.

DISCUSSION

Several drugs have been used in past to attenuate the haemodynamic response of laryngoscopy and intubation. Gabapentin is an antiepileptic drug and esmolol is a short acting beta blocker. They have been used to reduce stress response to laryngoscopy. Primary aim of the study was to compare change in HR, SBP, and DBP and MAP at 1, 3 and 5 and 10 minutes of laryngoscopy and intubation after premedicating the patient with either gabapentin or esmolol. There was no significant difference in above haemodynamic parameters in response to intubation between both gabapentin group and esmolol group.

Shrestha GS et al., compared gabapentin, esmolol or their combination to attenuate haemodynamic response to laryngoscopy and endotracheal intubation. They concluded that the combination of gabapentin and esmolol better reduces both the pressure and tachycardiac response to laryngoscopy and intubation [13].

Tiwari AB et al., studied the efficacy of gabapentin and esmolol against haemodynamic response during intubation and laryngoscopy. On the basis of their study they concluded that blood pressure and HR was better controlled in esmolol group as compared to gabapentin group following laryngoscopy and endotracheal intubation [15].

To the best of authors knowledge above two are the only studies comparing esmolol with gabapentin in attenuating stress response to laryngoscopy and intubation till now. In the study conducted by Shrestha GS et al., only 18 patients were enrolled so, results can not be generalised. While in second study conducted by Tiwari AB et al., tablet gabapentin was given at the time of laryngoscopy. As we know peak action of gabapentin comes in 2-3 hours so it should have been given atleast two hours prior to induction. This study was conducted with greater number of patients and tablet gabapentin was given three hours prior to surgery. No statistically significant difference was found in haemodynamic parameters after intubation in both groups. Both esmolol and gabapentin were effective in attenuating stress response to laryngoscopy and intubation.

Tamaskar A et al., found that esmolol 1.5 mg/kg given 3 minutes before intubation is highly useful in reducing the haemodynamic stress response of laryngoscopy and intubation [19]. These results were similar to the present study group esmolol. Fassoulaki A et al., found that premedication with gabapentin 1600 mg attenuated the haemodynamic pressor response to laryngoscopy and intubation of the trachea but had no effect on change of HR [20].

Bala I et al., concluded that gabapentin 800 mg in a single (morning of surgery) or double dose (morning plus night before surgery) given in group 2 and 3 was equally effective in reducing the hypertensive response to laryngoscopy and tracheal intubation in controlled hypertensive patients [14]. Similarly in this study, 800 mg gabapentin given three hours before surgery was effective in attenuating stress response.

Secondary objective of this study was to observe any side-effects postoperatively related to esmolol and gabapentin like sedation, pruritis, headache, ataxia, respiratory depression. No such side-effects were noted in any of the study group. Similarly, Shrestha GS et al., Tiwari AB et al., and Tamaskar A et al., did not observe any side-effects pertaining to esmolol and gabapentin in their study [13,15,19].

Limitation(s)

This study was done in ASA I and ASA II patients, effect of esmolol and gabapentin in ASA III patients is unknown. Also, type of hypertensive drug in ASA II controlled hypertensive patients was not taken account, which might have affected the haemodynamic response. Tablet gabapentin should be given atleast 2-3 hours before surgery for its onset of effect so can't be used in emergency surgeries.

CONCLUSION(S)

Both esmolol and gabapentin are equally effective in attenuating the stress response to laryngoscopy and intubation. Provided injection esmolol 1.5 mg/kg given two minutes before intubation and tablet gabapentin 800 mg given three hours before surgery. Esmolol caused greater fall in haemodynamic parameters intraoperatively (although <20% of baseline levels), so should be used cautiously in hypovolemic and hypotensive patients.

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