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Comparison of Oral Gabapentin Versus Control on Hemodynamic Response to Direct Laryngoscopy for Tracheal Intubation in Patients Undergoing Elective Surgery

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ABSTRACT

Introduction: Endotracheal intubation is indicated in many clinical scenarios e.g. cardiopulmonary arrest, respiratory failure, life threatening airway obstruction, patients at risk of aspiration and for elective procedures required general anesthesia. Gabapentin is known as an anti-epileptic drug. It is also used to relieve pain and attenuate hemodynamic changes in normotensive patients during laryngoscopy and intubation. **Aims & Objectives:** To compare the mean hemodynamic response (Heart Rate (HR), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) with oral gabapentin versus control in normotensive patients undergoing elective surgeries under general anesthesia with direct laryngoscopy for endotracheal intubation. **Place and duration of study:** The study was conducted in Department of Anesthesia, Shaikh Zayed Hospital, Lahore from September 2016 to September 2017. **Material & Methods:** It was a randomized placebo controlled trial. 108 normotensive patients were divided into two groups. One group was treated with oral gabapentin and other group received placebo capsule (Control group). Hemodynamic response (Heart Rate (HR), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)) was also noted in elective surgeries (hysterectomy, hernioplasty, thyroidectomy and laparoscopy) under general anesthesia. Statistical analysis was done on SPSS v23.0. Independent sample t-test was applied to compare the hemodynamic response between two groups. **Results:** In this study, the mean age of the oral gabapentin group was 41.67±9.37 years and mean value in control group was 40.9±9.1 years. Comparison of HR, SBP and DBP at baseline and 10 minutes after endotracheal intubation showed statistically significant attenuation in the gabapentin group when compared to placebo. **Conclusion:** Oral gabapentin 400mg b.d once at bed time and once in the morning just prior to surgery significantly blunted the hemodynamic response in normotensive patients undergoing elective surgery under general anesthesia with direct laryngoscopy and endotracheal intubation.

Key words: *Endotracheal Intubation, Surgery, General Anesthesia, Laryngoscopy, Gabapentin*.

INTRODUCTION

Endotracheal intubation is indicated in many clinical scenarios like cardiopulmonary arrest, respiratory failure, and life threatening airway obstruction, patients at risk of aspiration and for elective procedures required general anesthesia. Direct laryngoscopy for endotracheal intubation is one of the most painful procedure carried out on human body which is associated with acute hemodynamic response, lasting at least for ten minutes.[1,2]

Various techniques are present for attenuating hemodynamic response of tracheal intubation and laryngoscopy including various drugs e.g calcium channel blockers, opioids, beta blockers, sodium channel blockers, vasodilators and alpha agonists. All have been employed with some degree of success.[3,5]

Gabapentin is a structural analog of the neurotransmitter 3-aminobutyric acid and is used to prevent and control seizures. It is also used to treat chronic painful conditions like complex regional pain syndrome, post herpetic neuralgia, tension type headache, cancer pain. Furthermore, the potential role of this drug has been studied on pre-operative anxiolytic and sedation, post-operative analgesia, prevention of post-operative nausea and vomiting and post-operative delirium. Mechanism of Gabapentin to blunt the hemodynamic response to direct laryngoscopy and intubation might be similar to the action of calcium channel blockers.[6,7] In this regard different studies conducted on Gabapentin have produced variable data.[8,9]

There is paucity of literature on Gabapentin for attenuating presser response to laryngoscopy and endotracheal intubation in Pakistan.

The purpose of present study was to compare mean hemodynamic response to oral gabapentin versus placebo in normotensive patients undergoing elective surgery with general anesthesia using direct laryngoscopy for tracheal intubation. Our data will enable us to determine future usefulness of Gabapentin in reducing hemodynamic stress response to laryngoscopy for tracheal intubation with potential benefits to Patients, health care professionals and planners.

Inclusion criteria: Age 25-60 years, normotensive, either gender undergoing elective surgery (hysterectomy, hernioplasty, thyroidectomy and laparoscopy) under general anesthesia.

Exclusion criteria: Patients having anticipated difficult Intubation (Mallampati >II), ASA III or IV, Patients having allergy to Gabapentin (medical record), Renal disease (creatinine>1.2mg/dl), liver disease (AST>40IU, ALT>40IU) and Patients having history of ischemic heart disease (on medical record).

MATERIAL AND METHODS

The study was conducted in Department of Anesthesia, Shaikh Zayed Hospital, Lahore from September 2016 to September 2017. The study design was randomized placebo controlled trial.

A total of 108 normotensive patients fulfilled the inclusion criteria, were included in the study. Demographic data like name, age, gender and surgical procedure was noted.

Group 1 patients received 400 mg of Oral Gabapentin at 11pm night before surgery and 400mg at 6am in the morning of surgery while group 2 patients received matching placebo capsule orally containing starch as an ingredient. Patients prepared for surgery and baseline (Pre-induction) heart rate, SBP and DBP was recorded. Patients were given injection Tramadol 1 mg/kg around 5 minutes before intubation. Initiation of general anesthesia was done with injection Propofol 2.5 mg/kg and injection Atracurium 0.5 mg/kg. Patients were ventilated via facemask and bag for three minutes and then intubated via direct laryngoscopy by a qualified anesthesiologist.

Hemodynamic response was seen at baseline and after 10 minutes of intubation. Readings were taken directly from the attached monitor.

Statistical analysis:

Data were analysed by SPSS v23.0. Categorical variables like gender; surgical procedure was described as frequencies and percentages. Quantitative variables like age, heart rate, systolic, and diastolic blood pressure were described as mean and standard deviation. Both groups compared for mean heart rate, systolic blood pressure and diastolic blood pressure by independent sample *t* test. Data was stratified for gender, age, American Society of Anesthesiologists (ASA) and surgical procedure. For post-stratification, t-test was applied. A p-value ≤ 0.05 was taken as significant.

RESULTS

In current study, 108 normotensive patients were selected. The mean age of the oral gabapentin group was 41.67±9.37 years and its mean value in control group was 40.93±9.12 years. In this study 14(12.96%) patients were male and 94(87.04%) patients were female. 0.15:1 was the male to female ratio of the patients.

In this study, the male patients were fourteen, in which nine were on oral gabapentin group and 5 were on placebo group. Female patients were 94 in number, out of which 45 were on oral gabapentin group and 49 were in placebo group. In our study, 105 patients were ASA type I out of which 52 were from oral gabapentin group and 53 were from placebo group, similarly 3 patients were from ASA

II group out of which 2 were from oral gabapentin group and 1 was from placebo group.

Laparoscopic cholecystectomy was done in 16 cases, mesh Hernioplasty in 47 cases, open Cholecystectomy in 25 cases, thyroidectomy in 13 cases, total abdominal hysterectomy in 5 cases and lobectomy in 2 cases.

The mean value of heart rate at baseline of the oral gabapentin group was 74.94±10.83 per minute and its mean value in control group was 84.41±11.01 per minute. There was significant difference between groups with heart rate at baseline of the patients i.e, p =0.001. In this study, the mean value of HR at 10 minutes of the oral gabapentin group was 74.07±8.68 per minute and its mean value in control group was 88.11±12.91 per minute with a p-value of 0.001 which is statically significant.

The mean value of SBP at baseline of the oral gabapentin group was 114.11±13.84 mmHg and its mean value in control group was 127.26±8.61 mmHg. There was significant difference between groups with SBP at baseline of the patients i.e, p =0.001. The mean value of SBP at 10 minutes of the oral gabapentin group was 111.35±8.82 mmHg and its mean value in control group was 130.96±11.74 mmHg with a p-value of 0.001 which is statically significant.

The value of DBP at baseline of the oral gabapentin group was 77.56±6.39 mmHg and its mean value in control group was 68.50±8.87 mmHg. There was significant difference between groups with DBP at baseline of the patients i.e, p =0.001. In this study the mean value of DBP at 10 minutes of the oral gabapentin group was 81.63±9.21 mmHg and its mean value in placebo group was 65.87±8.78 mmHg with a p-value of 0.001 which is significant.

Statistically significant difference was found among HR, SBP and DBP at 10 minutes with groups stratified by age i.e, p<0.05. Statistically significant difference was found among HR, SBP and DBP at 10 minutes with study groups stratified by gender except the HR in male patients at 10 minutes i.e. p-value<0.05.

Statistically significant difference was found among HR, SBP and DBP at 10 minutes with study groups stratified by surgery except HR at 10 minutes in patients with open cholecystectomy i.e, p<0.05.

Surgery	Groups Patient no = n		Total
	Oral Gabapentin	Control	
Laparoscopic Cholecystectomy	7	9	**16**
Mesh Hernioplasty	24	23	**47**
Open Cholecystectomy	16	9	**25**
Thyroidectomy	7	6	**13**
Total abdominal hysterectomy	0	5	**5**
Lobectomy	0	2	**2**
Total	**54**	**54**	**108**

Table-1: Comparison of surgery in groups

	Age (years)	Study Groups		p-value
		Oral Gabapentin	Control	
HR at 10 minutes	≤40	75.12±8.22	91.89±13.37	0.001
	>40	73.11±9.12	84.33±11.47	0.001
SBP at 10 minutes	≤40	109.15±8.41	128.81±13.96	0.001
	>40	113.39±8.84	133.11±8.75	0.001
DBP at 10 minutes	≤40	65.00±7.04	80.07±9.72	0.001
	>40	66.68±10.21	83.19±8.57	0.001

Table-2: Comparison of Heart Rate (HR), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) at 10 minutes in study groups stratified by age

	Gender	Study Groups		p-value
		Oral Gabapentin	Control	
HR at 10 minutes	Male	75.22±8.41	79.60±15.02	**0.492**
	Female	73.84±8.81	88.98±12.53	**0.001**
SBP at 10 minutes	Male	109.89±8.25	131.20±9.04	**0.002**
	Female	111.64±8.98	130.94±12.06	**0.001**
DBP at 10 minutes	Male	67.67±6.61	82.20±6.22	**0.001**
	Female	65.51±9.18	81.57±9.51	**0.001**

Table-3: Comparison of Heart Rate (HR), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) at 10 minutes in study groups stratified by gender

	Surgery	Study Groups		p-value
		Oral Gabapentin	Control	
HR at 10 minutes	**Lap. Cholecystectomy**	71.14±9.44	89.56±10.63	**0.003**
	Mesh Hernioplasty	72.96±6.58	88.52±14.19	**0.001**
	Open cholecystectomy	75.75±11.61	82.00±11.20	**0.204**
	Thyroidectomy	77.00±6.40	93.83±12.01	**0.008**
SBP at 10 minutes	**Lap. Cholecystectomy**	112.14±13.89	135.67±12.15	**0.003**
	Mesh Hernioplasty	112.13±6.97	125.70±12.54	**0.001**
	Open cholecystectomy	110.56±9.85	135.00±8.46	**0.001**
	Thyroidectomy	109.71±7.52	129.83±5.42	**0.001**
DBP at 10 minutes	**Lap. Cholecystectomy**	63.14±10.12	84.33±8.57	**0.001**
	Mesh Hernioplasty	65.04±9.87	80.09±11.40	**0.001**
	Open cholecystectomy	68.94±6.86	83.33±6.021	**0.001**
	Thyroidectomy	64.43±7.02	80.67±8.07	**0.003**

Table- 4: Comparison of Heart Rate (HR), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) at 10 minutes in study groups stratified by surgery

DISCUSSION

This study was conducted in Department of Anesthesia, Shaikh Zayed Hospital, Lahore to compare the mean hemodynamic response with oral gabapentin versus control in normotensive patients undergoing elective surgery under general anesthesia with direct laryngoscopy and endotracheal intubation.

The purpose of endotracheal intubation is to permit air to pass freely to and from the lungs in order to ventilate the lungs with oxygen and protection against aspiration of the gastric contents. Direct laryngoscopy and intubation result in an increase in heart rate and blood pressure that may result in angina, myocardial ischemia, cardiac arrest and cardiovascular events[10]. Various doses of gabapentin have been studied previously to attenuate the hemodynamic response in normotensive patients. Gabapentin is known as an anti-epileptic drug. It has additionally been utilized in the treatment of chronic painful conditions[11] e.g. phantom limb, complex regional pain syndrome, post herpetic neuralgia, cancer pain and restless leg syndrome.

In our study the mean value of heart rate at 10 minutes of the oral gabapentin group was 74.07±8.68 per minute and its mean value in placebo group was 88.11±12.91 per minute, the mean value of SBP at 10 minutes of the oral gabapentin group was 111.35±8.82 mmHg and its mean value in placebo group was 130.96±11.74 mmHg and the mean value of DBP at 10 minutes of the oral gabapentin group was 65.87±8.78 mmHg and its mean value in placebo group was 81.63±9.21 mmHg. In this study oral gabapentin significantly blunted the hemodynamic response to control group in normotensive patients undergoing elective surgery under general anesthesia with direct laryngoscopy and endotracheal intubation.

A study by Tahira Iftikhar et al[10] concluded that oral gabapentin reduces the stress response to intubation and laryngoscopy on Heart rate, Systolic blood pressure and diastolic blood pressure after 2, 10 and 15 minutes; Mean Systolic Blood Pressure with Gabapentin was lesser comparing with placebo except it was significant at 1 minute (136±22vs149±23), 2 minutes (120±21vs136±24), 10 minutes (107±12vs118±16) and 15 minutes (106±13vs116±13) following intubation ($p \leq 0.05$).

Mean Diastolic Blood Pressure with gabapentin was significantly lesser after 3minutes (69±15vs74±17) after intubation with $p \leq 0.05$. Mean Blood Pressure with gabapentin was significantly lesser after 2 minutes (91±18vs103±18), 10 minutes (79±12vs88±13) and 15 minutes (79±14vs86±12)

after intubation at $p \leq 0.05$. Reduce in Heart Rate with gabapentin was significant after 10minutes (92±15vs101±18) and 15 minutes (87±14vs99±16) after intubation ($p \leq 0.05$).

In a similar study, conducted by Deepak et al.,[12] concluded that the mean Systolic Blood Pressure was significantly lesser in gabapentin group as comparing with control group after 0, 1, 3, 5 and 10 minutes after intubation; while, lower Diastolic Blood Pressure and mean Blood Pressures were noted at 0, 1, 3, and 5 minutes after intubation. Heart Rate was lesser in gabapentin group 0, 1 and 3 minutes after intubation. Gabapentin blunted the cardiovascular response to endotracheal intubation and laryngoscopy. The mean SBP was significantly low as compared to control group (108±12 vs. 124±17 mmg), DBP (67±10 vs. 79±12 mmHg) but there is no significant difference in mean HR (75±15 vs. 78±12 bpm) after 10 minutes of intubation.[8]

Another study showed that mean SBP with gabapentin was 117.85±3.67 vs. 126.65±1.83 mmHg ($p<0.05$) as compared to control group but mean DBP was 77.05±2.68 vs. 83.35±1.62 mmHg ($p>0.05$) and also no significant difference in mean HR (73.75±3.09 vs. 78.7±1.61 bpm, $p>0.05$) after 10 minutes of intubation.[9] Memis et al[13] thought about the impact of 400 mg and 800 mg gabapentin on hemodynamic and announced that gabapentin 800 mg, however not 400 mg, was more effective in maintaining the heart rate and blood pressure after tracheal intubation.

Koc et al[14] demonstrated that pretreatment with gabapentin 800 mg prevent the hemodynamic reaction to laryngoscopy and endotracheal intubation. In another examination, Kaya et al[15] revealed that gabapentin 800 mg given 2 hours before surgery effectively reduces the increase in intraocular pressure and mean arterial presseure after tracheal intubation. Bafna et al [16] found that gabapentin 1000 mg given one hour before surgery significantly blunt the hemodynamic reaction to laryngoscopy and intubation.

CONCLUSION

It has been proven in our study that oral gabapentin 400mg b.d once at bed time and once in the morning just prior to surgery significantly reduces the mean hemodynamic response in normotensive patients undergoing elective surgery under general anesthesia with direct laryngoscopy and endotracheal intubation.

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