COMPARISON OF GABAPENTIN AND LORAZEPAM AS PREMEDICATION TO ATTENUATE THE PRESSOR RESPONSE TO INTUBATION IN CARDIAC PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFT SURGERY; A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Objective: To determine the efficacy of Gabapentin and Lorazepam as premedication to reduce the presser response to intubation in cardiac patients undergoing CABG surgery.

Study Design: Randomized control trial.

Place and Duration of Study: Adult cardiac anesthesia department of Armed Forces Institute of Cardiology, Rawalpindi, from Nov 2017 to Feb 2018.

Material and Methods: This double blinded randomized clinical trial was carried out on 110 patients scheduled for elective CABG under general anesthesia with endotracheal intubation. Patients were divided into two equal groups, where group A patients received 300mg of Gabapentin (Gabix) R in one dosage and group B received 2mg of Lorazepam (Ativan) R in one dosage, 4 hours before shifting to OT. Patient's hemodynamic parameters including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded before induction of anaesthesia (baseline) and at 1, 5 and 10 minutes after tracheal intubation.

Results: There was no significant difference in the baseline hemodynamic parameters of the patients in two groups, the inter-group comparison showed significantly higher HR, SBP, DBP and MAP at 1, 5 and 10 minutes after tracheal intubation in group B (lorazepam) patients ($p<0.05$).

Conclusion: Premedication with 300 mg of oral Gabapentin four hour before surgery better attenuates the hemodynamic response to laryngoscopy & intubation in comparison to 2mg of oral Lorazepam.

Keywords: CABG, Endotracheal intubation, Premedication.

INTRODUCTION

Hypertension and tachycardia, accompanied by increased sympathetic nervous system activity, may guide to an imbalance between myocardial oxygen demand and supply. This may lead to myocardial ischemia in patients who have coronary artery disease or in those with risk of ischemic heart diseases[1,2]. Myocardial ischemia increases the risk of myocardial infarction, which is a serious peri operative complication with an associated mortality rate of 17–42%[3] and may compromise patients' functional status[1,4]. Perioperative myocardial ischemia during elective coronary artery bypass graft (CABG) can occur in the pre bypass period, during bypass and in the post bypass period. Reperfusion of the myocardium after an ischemia stimulates myocardial apoptosis and resultant increase in infarct size through the reperfusion injury, despite the restoration of coronary blood flow[5,6]. To minimize the myocardial ischemia during CABG, multiple strategies are often employed by the perioperative team. Myocardial protection is an area which is being widely researched currently to prevent or reduce the incidence of PMI. Laryngoscopy & intubation are related with cardiovascular changes like hypertension, tachycardia, dysrhythmia and even myocardial ischemia. These responses may be hazardous in individuals with coronary artery insufficiency, vascular anomalies or intracranial disease[4]. Variety of medications have been

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suggested to control these hemodynamic responses and prevent hemodynamic instabilities[7,8].

Gabapentin, a structural analogue of gamma-amino butyric acid, has revealed to have multi-modal effects which make it a potentially useful drug for premedication in adults, providing postoperative analgesia and preoperative anxiolysis while preventing chronic postsurgical pain, postoperative nausea and vomiting and delirium[9]. In addition, the drug has also been reported to successfully attenuate the cardiovascular responses to tracheal intubation. This beneficial effect of Gabapentin is probably due to inhibition of membrane voltage gated calcium channels, an action similar to calcium channel blockers. Two recent randomized controlled trials have shown that oral Gabapentin premedication attenuated the hemodynamic changes following tracheal intubation[10,11]. On the other hand, benzodiazepines used as sedative and anxiolytic medications, are routinely administered to mechanically ventilated (MV) patients 12 in ICU but have been associated with prolonged mechanical ventilation and ICU length of stay (LOS).

As there is no contemporary data documenting the comparison of the effects of Gabapentin and Lorazepam on reduction of presser response in cardiac surgical patients, we conducted this study to evaluate the effects of premedication dose of oral Gabapentin (Gabix) 300 mg and premedication dose of oral Lorazepam (Ativan) 2mg in patients undergoing coronary artery bypass grafting (CABG) surgery.

MATERIAL AND METHODS

This study was double blind randomized control trial conducted at Armed Forces Institute of Cardiology/NIHD from between November 2017 and February 2018. After approval of the hospital ethics committee, consecutive 110 patients scheduled for elective CABG, were randomly allocated in two groups A and B using computer generated random number tables. After taking informed consent from the patient and a day before surgery, when the patients were listed up for surgery, the in-charge nurse of the pre-operative ward was informed by the investigator to allocate the patient in either of the two groups. Neither the patient nor the anaesthetist planned to be conducting the surgery next day, did not know what premedication the patient had received, Patients in group A (n=55) received 300mg of Gabapentin, 4 hours before shifting to OT with a sip of water, and patients in group B (n=55) received 2mg of Lorazepam, 4 hours before shifting to OT with a sip of water. All patients were induced with standard intravenous induction drugs including propofol 1mg/kg, fentanyl 3ug/kg, midazolam 2mg and sevoflurane 4%. An anesthesiology resident who was blinded to the study recorded baseline parameters of patients including heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP), mean arterial pressure (MAP) immediately before intubation (baseline), and at

Table-I: Patient's characteristics of both groups.

Variable	Gebapentin (N=55)	Lorazepam (N=55)	*p*-value
Age (Mean ± SD)	59.1 ± 8.3	62.3 ± 7.9	0.03
BMI (Mean ± SD)	24.3 ± 2.0	24.3 ± 1.6	0.83
Gender			
Male	42 (76.3%)	33 (60.0%)	
Female	13 (23.6%)	22 (40.0%)	0.10
Hypertension	46 (83.6%)	51 (92.7%)	0.11
Diabetes	33 (60.0%)	35 (63.6%)	0.84
Smokers	20 (36.3%)	14 (25.4%)	0.30

1, 5 and 10 minutes after tracheal intubation. Patients of both genders and age between 25 to 65 years, undergoing elective CABG surgery were included in the study. Patients with emergency CABG, uncontrolled hypertension, patients with missed dose of beta blockers and with severe renal dysfunction with serum creatinine level >2micromole/L and/or Creatinine clearance <40ml/min. were excluded from our study.

RESULTS

The results were available for all 110 patients. There was no significant difference between the demographics including age, gender, body mass index (BMI) and co-morbids like hypertension and diabetes in the patients of two groups, except the Gabapentin group had more smokers than the Lorazepam group (table-I).

The baseline hemodynamic variables including SBP, DBP, MAP, and HR were all similar in the two groups (p>0.05). Although, there were similar trend in the hemodynamic response to tracheal intubation in both groups, i.e. a rise in SBP and DBP at 1 and 5 minutes interval, post-intubation and returning towards baseline at 10 minutes, these hemodynamic changes were significantly pronounced in patients of group B (receiving Lorazepam) as shown in tables-II & III.

Table-II: Comparing mean arterial pressure and Heart rate between the Gebapentin and Lorazepam groups at different time points of intubation.

Variable	Gebapentin (n=55)	Lorazepam (n=55)	*p*-value
MAP baseline	111.7 ± 15.3	109.4 ± 10.8	0.38
MAP after 1minute of intubation	100.0 ± 16.7	114.6 ± 10.1	<0.001
MAP after 5 minute of intubation	89.5 ± 14.8	103.3 ± 10.3	<0.001
MAP after 10 minute of intubation	84.9 ± 12.0	93.5 ± 10.0	<0.001
HR baseline	83.6 ± 11.7	74.2 ± 11.2	<0.001
HR after 1minute of intubation	78.6 ± 14.7	82.6 ± 13.1	0.132
HR after 5 minute of intubation	71.6 ± 12.1	74.2 ± 9.4	0.182
HR after 10 minute of intubation	68.8 ± 9.5	66.8 ± 9.9	0.298

Table-III: Comparing systolic and diastolic blood pressure between the Gebapentin and Lorazepam groups at different time points of intubation.

Variable	Gebapentin (n=55)	Lorazepam (n=55)	*p*-value
Systolic BP baseline	159.2 ± 18.6	156.7 ± 15.8	0.43
Systolic BP after 1 minute of intubation	138.5 ± 23.4	161.0 ± 15.5	<0.001
Systolic BP after 5 minute of intubation	120.7 ± 19.8	144.8 ± 15.6	<0.001
Systolic BP after 10 minute of intubation	113.7 ± 14.5	128.6 ± 14.8	<0.001
Diastolic BP baseline	89.1 ± 14.0	86.1 ± 10.3	0.20
Diastolic BP after 1minute of intubation	81.8 ± 14.9	91.6 ± 9.7	<0.001
Diastolic BP after 5 minute of intubation	73.8 ± 13.6	83.3 ± 9.9	<0.001
Diastolic BP after 10 minute of intubation	70.1 ± 12.9	88.8 ± 96.0	0.158

DISCUSSION

Hemodynamic response to tracheal intubation remains a sore point for the practicing anaesthesiologists all across the world. A lot of work has been done in patients undergoing cardiac as well as non-cardiac surgeries using different drugs and comparing their effects on patients.

In our study it was found that the changes in hemodynamic variables (i.e. the rise in HR, SBP, MAP and DBP) were present in both groups, but the measures of these indicators were significantly lower in Gabapentin group at all time points. Review of recent literature had

similar results and is comparable with our study. The hemodynamic presser response during laryngoscopy and intubation occurs frequently[14]. Shribman et al reported that laryngoscopy increases the blood pressure and catecholamine levels, while intubation significantly increases heart rate which could lead to dangerous sequelae[13,14]. Though various agents have been used to prevent these pressure responses, but still the search for ideal agent continues[15-18]. Our study shows that the presser response to intubation does occur after premedication with Gabapentin, but the severity is much less as compared to the patients receiving Lorazepam.

Our study concurs with the study conducted by Rastogi et al who found that 150 mg of pregabalin successfully attenuated the hemo-dynamic response to airway instrumen-tation[19]. However, unlike other studies our study did not note any significant difference in the heart rate between the two groups following intubation. The probable reason could be the dose and type of different premedication and induction agents used in other studies.

Our study also confers to the study done by Chaudhary et al who did a comparative study between pregabalin and clonidine. They observed that pregabalin was equally efficacious in stabilizing the hemodynamics during laryngo-scopy. However, pregabalin premedication was associated with higher mean heart rate values after intubation as compared to the clonidine group[20-24].

In another comparative study, Raichurkar et al concluded that 200µg clonidine and 150mg pregabalin given 90 minutes before surgery and noted that pregabalin was better in attenuating hypertensive response to airway instrumentation while heart rate was better attenuated by clonidine premedication[25].

The present study is comparable with other similar studies that has obtained some powerful evidence indicating that the use of oral gabapentin, even hours before tracheal intubation can be successful for attenuation of the hemodynamic response to laryngoscopy and intubation[26-28]. The mechanism of hemodynamic response attenuation following preoperative gabapentin administration is already unknown. One of the anticipated mechanisms is inhibition of membrane voltage-gated calcium channels that is similarly identified following use of calcium channels blockers. In fact the non strychnine site of NMDA receptor and two subunits of voltage-sensitive calcium channels have been indicated as the binding sites of gabapentin, thus can mediate hemodynamic indices stability by gabapentin[29-31]. In another study, decreasing the synthesis of some neurotransmitters such as glutamate has been suggested as the mechanism of hemodynamic stability following gabapentin administration[29]. Besides, it has been shown that the change in arterial pressure usually occurs the following laryngoscopy while the maximum increase in heart rate can occur during endotracheal intubation[31]. On the other hand, gabapentin mechanism of action in attenuating heart rate and blood pressure response to tracheal intubation might be different[32], and more studies in this field are needed.

CONCLUSION

We conclude that premedication with 300 mg of oral gabapentin four hours before surgery better attenuates hemodynamic response to laryngoscopy & intubation along with acceptable levels of sedation in comparison of 2mg of lorazepam.

ACKNOWLEDGEMENT

We thank research and develpoment department AFIC/NIHD staff specially Shahzaib Arshad and Nazma Latif for helping in data collection and entry.

CONFLICT OF INTEREST

This study has no conflict of interest to be declare by any author.

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