e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(8); 195-199

Original Research Article

A Comparison of Three Different Doses of Gabapentin for Attenuation of the Hemodynamic Response to Laryngoscopy and Tracheal Intubation in General Anaesthesia

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Received: 14-06-2023 / Revised: 11-07-2023 / Accepted: 03-08-2023
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Conflict of interest: Nil

Abstract:

Background and Objectives: Endotracheal intubation is the gold standard for airway management. It is the mostly important measure taken during induction of general anesthesia (GA) to safeguard the airway from gastric content aspiration and to provide positive pressure ventilation. To evaluate and compare the effects of different doses of gabapentin on haemodynamic response to laryngoscopy and endotracheal intubation. To find the safe and adequate dosage of gabapentin required to suppress the haemodynamic responses during laryngoscopy and endotracheal intubation.

Methods: This prospective study was conducted at operation theatres of different surgical discipline in Darbhanga Medical College and Hospital, Laheriasarai, Bihar during the period of January 2018-June 2019.

Conclusion: A single oral dose of Gabapentin 600 mg or 900 mg given one hour before induction of GA can significantly attenuate the pressor responses associated with laryngoscopy and tracheal intubation.

Keywords: Endotracheal Intubation, Laryngoscopy, Hypertension.

Introduction

Endotracheal intubation is the gold standard for airway management.[1] It is the mostly important measure taken during induction of general anesthesia (GA) to safeguard the airway from gastric content aspiration and to provide positive pressure ventilation. It is an integral part of anesthesiologists' contribution to patient care. Conventionally direct laryngoscopy is done to facilitate endotracheal intubation which is noxious as well as invasive stimulus.[2,3] In 1940, Reid and Brace were first to propose haemodynamic changes is response to laryngoscopy and endotracheal intubation in a person during GA.[4] There is a reflex discharge from sympathetic system due to stimulation of epipharynx and laryngopharynx during laryngoscopy and endotracheal intubation which results in increase level of circulating catecholamines.[3] This produces hemodynamic changes such as tachycardia, hypertension, dysarrythmia and subsequent increase in myocardial oxygen demand resulting in myocardial ischemia.[2] The intensity of haemodynamic response increases in proportion with force and duration of laryngoscopy.[5] A typical pressor response starts within 5 seconds, reaches peak in 1-2 minutes and comes back to base level within 5 minutes of laryngoscopy.[6] Laryngoscopic response can result in 40-50% increase in blood pressure, a 20% increase in heart rate, and a rise in both epinephrine an norepinephrine level.[7] A variety non-pharmacological and pharmacological measures were tried to attenuate the haemodynamic response to laryngoscopy and endotracheal intubation with smooth and gentle intubation along with shorter duration of laryngoscopy (<15 seconds), insertion of laryngeal mask airway (LMA) in place of endotracheal tube, deepening of anaesthesia[2] and blocking glossopharyngeal and superior laryngeal nerves etc. The mechanism by which gabapentin attenuates presser response to laryngoscopy and intubation is yet to be established. Its action resembles that of calcium channel blockers.[8] The inhibition of calcium influx in muscle cells with a resultant inhibition of smooth muscle contraction might explain its role in attenuation of the haemodynamic response to laryngoscopy. A large number of randomized clinical trials had been conducted to assess the role of gabapentin in attenuation of haemodynamic response to laryngoscopy and intubation with variable result. The purpose of our study is to evaluate the adequate dose of gabapentin and compare the effects of different doses of the same to attenuate the hemodynamic response laryngoscopy and intubation.

Objectives

- To evaluate and compare the effects of different doses of gabapentin on haemodynamic response to laryngoscopy and endotracheal intubation.
- To find the safe and adequate dosage of gabapentin required to suppress the haemodynamic responses during laryngoscopy and endotracheal intubation.

Materials and Methods

This prospective study was conducted at operation theatres of different surgical discipline in Darbhanga Medical College and Hospital, Laheriasarai, Bihar during the period of January 2018-June 2019. In was a prospective randomised double-blind comparative controlled clinical study.

The study was conducted in one hundred forty (140) patients of ASA grade I from both sexes, aged between 19-60 years undergoing various surgery under GA. Total 140 (35 in each group) The sample size was decided in consultation with the statistician, and was based on previous studies, which indicated that approximately 2-23 patients should be included in each group in order to ensure a power by 10-20% in HR and SBP. Alpha error was assumed to be 0.05. WINPEPI (Software) version 11.48, Abreamson, JH. (WINPEPI updated computer programmes for epidemiologists and their teaching potential. Epidemiologic prospective and innovations. 2011;8:1)

The study was conducted after approval from the ethical committee of the institution. A written informed consent was obtained from all the patients participating in the study before the day of surgery. The criteria for selection and exclusion of the patients for this study were as follows:

Inclusion Criteria

- Informed written consent.
- ASA Status I
- Age group 18-60 years
- Both sexes
- Weighing 40-80 kg
- Orotracheal intubation only
- Mallampatti 1 and 2

Exclusion Criteria

- Patient Refusal
- Hypertension (controlled and Uncontrolled both)
- Systolic blood pressure less than 90 mm Hg
- Heart rate less than 60 beats/minute
- Coronary artery disease
- COPD and asthma

All patients were visited in the evening prior to surgery and a brief account of the anaesthetic procedure was explained to them.

The patients were subjected to detailed clinical examination and routine investigations to exclude any pre-existing systemic disorder. ECG and chest X-ray were also assessed. The patients having no disease other than the pathology necessitating surgery were included in this study.

- Results were represented as, ratio.
- Repeated measure ANOVA was used for intragroup comparison of changes from baseline to different time intervals during the study period which was done separately for each group. This was followed by post hoc Bonferroni test.
- One-way ANNOVA was used for multiple group comparisons followed by Post hoc Tukey's test for intergroup comparisons.
- Chi-square test was used for categorical data (gender)
- A "P" value of 0.05 or less was considered for statistical significance.

Results

One hundred and forty patients belonging to ASA I were enrolled in the study and allocated into four groups of 35 patients each randomly. The study group included the patients receiving Gabapentin 300 mg in group B, Gabapentin 600mg in group C, Gabapentin 900 mg in group D. The control group that is group A comprised of patients receiving placebo. After the completion of study, all the groups were compared statistically for their demographic characteristics i.e., age, sex and weight, The demographic data of the patients comprising of age sex and weight are shown in table-1. The patients accepted for the study were in the age group of 18-60 yrs. The mean age in the control group (Group A) was 38.714±9.028, in Group B it was 34.828±6.331. there was no significance difference among the groups in terms of age (P=0.0825). All the four groups were found to be comparable in respect of male female ratio as the P value of sex ratio among the group was 0.7988. The weight of the patients varied between 40 kg to 80 kg in Group A with a mean of 57.57±10.598,45 kg with a mean of 55.628±6.544 in Group B,37 kg to 75 kg with a mean of 54.485±9.733 in Group C and 43 kg to 65 kg with a mean of 54.057±6.111 in Group D. the groups were comparable in terms weight as the P value of the groups was 0.3113.

Table 1: Demographic characters of studied patients

	Group A	Group B	Group C	Group D	P value
Number of cases	35	35	35	35	-
Age (y)	34.714±9.028	34.828±6.331	38.685±10.070	39.114±11.331	0.0825
Sex (male/female)`	15/20	18/17	14/21	16/19	0.7988@
Weight(kg)	57.571±10.598	55.628±6.544	54.485±9.733	54.057±6.111	0.3113

Data were expressed as mean±SD

[@]Data were expressed as ratio, Ξ^2 test was used

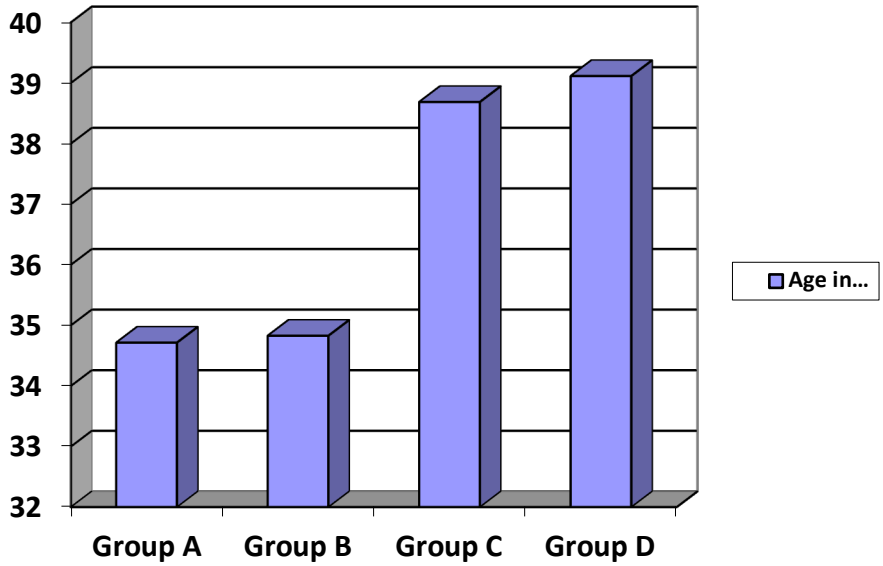

Figure 1:

In the present study the drug Gabapentin was given one hour prior to induction of anaesthesia. Haemodynamic changes observed just before giving the drug (i.e., one hour before induction o GA) and at 0 min, 1min, 3 min and 5 min after laryngoscopy and intubation.

Heart rate comparison

Heart rate of all the four groups (Group A-patients receiving placebo, Group B- patients receiving Gabapentin 300 mg, Group C- patients receiving Gabapentin 600 mg and Group D- patients receiving Gabapentin 900 mg) were compared. Base line HR recorded just before giving the placebo/drug (i.e, one hour before induction. Table-2, shows the heart rate of all the four groups at various intervals. Base line heart rate of all the four groups were found to be comparable without significant difference (P>0.05). In all the four groups there were significant rise in heart rate at the time of laryngoscopy compared to base line. Heart rate consistently remained substantially higher compared to the base line at 0 minute and 1 minute following laryngoscopy and intubation (P<0.001) in all the four groups. Heart rate appeared to decrease with regard to time in all the four groups. At 3minute after laryngoscopy and intubation heart rate non-significantly varied with baseline (P>0.05) in all the four groups. Heart rate at 5 minute following laryngoscopy and intubation showed no statistically significant difference among the groups (P>0.05).

Table 2: Heart beat/minute at various intervals

	Group A	Group B	Group C	Group D	P value
Base line	84.5714±22.170	87.66±6.980	83.3714±11.204	88.8±7.959	0.6065
0 minute	104.8285±19.56***	98.2±17.352***	102.3428±16.132***	98.057±7.050***	0.2060
1 minute	95.8857±14.929***	96.2857±16.309	96.9428±12.574***	94.2±6.650***	0.8983
3 minute	87.2571±12.777#	89.4571±13.691#	89.8±12.936#	89.7714±6.131#	0.7714
5 minute	80.5714±12.074#	83.3142±15.076	86.514±11.176	82.7714±7.272***	0.2097
P value<	0.0001	0.0001	0.0001	0.0001	

SBP of all the four groups (Group A- patients receiving placebo, Group B- patients receiving Gabapentin 300 mg, Group C-patients receiving Gabapentin 600mg and Group D- Patients receiving Gabapentin 900mg) were compared Base line SBP recorded just before giving the placebo/drug (i.e, one hour before induction of GA) and then at 0,1,3 and 5 minutes after laryngoscopy and intubation. Table -3 shows the mean SBP of all the four groups at various intervals. The base line SBP were similar in all the four groups (P=0.6437). In Group A and Group B there were extremely significant rise in the SBP at 0 minutes when compared to base line (P<0.001). SBP remained higher than base line at following 0,1,3 and 5 minutes after laryngoscopy and intubation in Group A and Group B. In Group C and Group D SBP remains substantially lower than the base line at 0, 1,3, and 5 minutes after laryngoscopy nad tracheal intubation (P value<0.001).

Inter-group comparison showed significantly higher SBP in Group A and B following laryngoscopy and tracheal intubation at 0,1,3 and 5 minutes. Increase in SBP in Group A and B were similar(P>0.05). In Group C and D SBP remained significantly low at 0,1,3 and 5 minutes after laryngoscopy and tracheal intubation. There was extremely Comparison of diastolic blood pressure (DBP), DBP of all the four groups (Group A-patients receiving placebo, Group B-patients receiving Gabapentin 300 mg, Group C-patients receiving Gabapentin 600 mg and Group D patients receiving Gabapentin 900 mg) were compared. Base line DBP recorded just before giving the placebo/drug (i.e., one hour before induction of GA) and then at 0,1,3 and 5 minutes after laryngoscopy and intubation. Table-4, shows the mean DBP of all the four groups at various intervals. The base line MAP was found to be comparable among all the four groups (P=0.3920). In group A and Group B there was statistically significant increase in the MAP at 0,1 and 3 minutes after laryngoscopy and intubation when compared to base line (P<0.001). At 5 minute after laryngoscopy and intubation MAP returned to the base line both Group A and Group B (P<0.005). In Group D as well MAP was statistically significantly lower at 0,1,3 and 5 minutes (P value <0.001, P value<0.001,P<0.001).Intergroup comparison showed no statistically showed no statistically significant difference in MAP of Group A and Group B at0,1,3 and 5 minutes(P>0.05). Group C and Group D showed statistically significant lower map at 0,1,3,5 minutes compare to Group A (P<0.001).

Discussion

Finding ideal method of smooth induction of GA by managing noxious stimulus of endotracheal intubation has remained a challenge for anaesthesiologists. Laryngoscopy and tracheal intubation evoke transient but noticeable haemodynamic response due to sympatho-adrenal discharge, which is evident by rise in heart rate and blood pressure following laryngoscopy and intubation.[9] Specific measures should be taken to prevent these changes as hypertension may effect perioperative morbidity through the extent of end organ damage, like myocardial ischemia or cerebral haemorhage.[10] Aronson and Fontes[11] stated that rise in pulse pressure as little as 19 mmHg in both normotensive and hypertensive persons is associated with a 20% or more increased risk of renal failure, coronary events and cerebral stroke. Intraoperative haemodynamic stability, good analgesic property, opioids sparing effects, no respiratory depression makes gabapentin an attractive premedication which can be beneficial in obese, hypertensive and cardiac compromised patients. Gabapentin is already being used effectively in post-operative pain management.[12] Gabapentin exhibits a non-predictable pharmacokinetic profile. Though there are numerous studies establishing its role in post-operative analgesia, studies establishing its role in attenuation are sparse. Although various clinical trails have shown the efficacy of gabapentin in various clinical situations the dose-response relationship has not been studied. Gabapentin has been used preoperatively as a single dose as well as in multiple doses in different clinical settings. Furthermore, variable results obtained in each of the studies with different doses of gabapentin motivated us to conduct this study to evaluate safe and clinically effective dose of gabapentin for attenuation of haemodynamic response to laryngoscopy and tracheal intubation. In most of the studies the effect of gabapentin on heart rate is inconsistent. The haemodynamic results of our study were in agreement with recent results with gabapentin. In the current study, we had taken four groups of 35 patients each, with each receiving either placebo or gabapentin in doses 300mg, 600mg or 900mg oral gabapentin 1 hour prior to induction of anaesthesia. The doses of gabapentin we opted for was chosen after careful consideration of the oral bioavailability of the drug as well as a few previous trials done on similar lines. Gabapentin bioavailability is unpredictable and not dose proportional; that is, as dose increase bioavailability decreases. Bioavailability of gabapentin is approximately 60%, 47%, 34%, 33% and 27% following 900,1200,2400,3600, and 4800 mg/day given in 3 divided doses, respectively.[13 Bioavailability of a 300 mg oral dose would be60% which appeared to be maximum. Similarly, for a dose of 600 mg and 900 mg bioavailability will be 40% and 34%[94] respectively. Serhat et al. commented that significant attenuation of heart rate can be achieved with a combination of daxamethhasone 8 mg intravenously and oral gabapentin 800 mg given 1 hr prior to surgery.[14] Though our present study was not designed to evaluate the effect of gabapentin on intraoperative haemdynamics but we observed that in 600 and 900 mg gabapentin group intraoperative haemodynamic remained stable. However, in 900 mg gabapentin group excessive sedation and dizziness during post-operative period were observed. The bioavailable amount of 600mg gabapentin and 900 mg gabapentin are almost same going by their bioavailability of 40% and 34% respectively. This explains the reasons behind their statistically similar effect on attenuation haemodymanic response to intubation. We had studied patients up to 60 years age as elderly patients more often are on drugs such as antidepressants, hypnotics and antihypertensive. Older patients also exhibit increased sensitivity to drugs and the cardiovascular effects of gabapentin have not been studied extensively. Separate studies are required to study the effect of gabapentin in older age group patients.

Conclusion

However, the incidence of adverse effects like nausea, dizziness, light headedness and somonolence was more among the patient pre-medicated with 900

mg gabapentin. So, a 600 mg dose of gabapentin can be used 1 hour before surgery to attenuate the prssor response to laryngoscopy and trachea intubation without subjecting the patients to any serious side effects. We need to conduct many more studies to verify whether attenuation of haemodynamic changes with oral gabapentin is influenced by alternative anesthetic regimens especially in older age group patients with co-morbidities like hypertension.

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