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HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION USING GABAPENTIN

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ABSTRACT:

Laryngoscopy and Intubation provoke cardiovascular responses that include hyperten sion, Tachycardia, Dysarrhythmias leading to myocardial ischemia and Heart failure.

Objective: This randomized, double-blind study was conducted to evaluate the effect of gabapentin pretreatment on the hemodynamic response to laryngoscopy and endotracheal intubation.

Material and Methods: A total of 60 cases aged 18-65 years, undergoing elective surgery under general anesthesia with endotracheal intubation, were randomly allocated into two groups(Gabapentin and Placebo). Gabapentin group (30 cases) patients received Oral Gabapentin capsules 3 times i.e., at 18:00hrs and 24:00hrs (night before surgery) and 06:00hrs (on the morning of surgery). Placebo group (30cases) received oral Placebo capsules at the same timings as that of Gabapentin group. Anesthesia was induced with midazolam, glycopyrrolate, propofol, rumefentanyl and succinyl choline with preoxygenatio. Patients' heart rate (HR), systolic blood pressure (SBP), Diastolic blood pressure (DBP) and electrocardiography (ECG) changes were recorded prior to induction, after induction, and at 0 minutes, 1 minute, 3 minutes, 5 minutes, and 10 minutes after intubation.

Results: The Heart Rate showed difference at all time intervals between the 2 groups. However this difference between the 2 groups was statistically significant only at the time of post induction. SBP showed difference at all time intervals between the 2 groups which were statiscally significant only at the time of Zero minute. DBP showed difference at all time intervals between the 2 groups which were statistically significant at the time of Zero minute. The mean arterial pressure (MAP) showed difference at all time intervals between the 2 groups which were statiscally significant at the time of Zero minute.

Conclusion: Gabapentin given as premedicant in three divided doses before surgery attenuated the pressor response to laryngoscopy and intubation in patients undergoing elective non-cardiac surgeries.

Key Words: Laryngoscopy, Endotracheal intubation, Gabapentin

INTRODUCTION

Laryngoscopy and endotracheal intubation provoke cardiovascular responses that include hypertension,tachycardia and dysarrhythmias.These haemodynamic changes due to catecholami ne release have no consequences in normal patients who are considered to be ASA I, but they may be associated with myocardial ischemia,myocardial failure in patients with coronary artery disease, valvular heart disease, geriatric and critically ill patients and cerebral haemorraghe in head injury patients with raised intracranial taension. Thus these transient haemodynamic changes can alter the mortality and morbidity.

Various techniques and drugs were adopted to attenuate or abolish these responses, ranging from premedication with betablockers, calcium channel blockers, vasodilators such as nitroglycerine, using additional doses of narcotics, deepening anaesthesia before laryngoscopy, gentle and single attemot laryngoscopy, repeated injections of intravascular induction agents,increasing the concentration of the inhalational agents (e.g; Sevoflurane), preservative free lignocaine 90 sec before intubation and oral clonidine 2 hrs prior to intubation.

Gabapentin is a relatively new drug which was introduced as antiepileptic but proved to be effective in controlling neuropathic pain. The drug is well tolerated with minimalside effects as compared with other antieileptics such as carbamazepine. More recently gbapentin has been used in randomized controlled trilas to treat acute postoperative pain and to reduce the poast operative optoid requirements. While performing these studies with gabapentin, it was observed that some patients were haemodynamically stable. However, only few studies were done previously to check the effect of gabapentin on haemodynamic responses due to laryngoscopy and intubation. These studies have shown that gabapentin was able to attenuate these pressor responses usefully (vide infra, review of the literature), given by different protocols.

Our present study was designed as a prospective, double-blind, randomized,placebo controlled study to investigate the effect og gabopentin on the changes in blood pressure and heart rate observed during laryngoscopy and tracheal intubation when given as premedication in three divided doses on the night before and morning of surgery.

MATERIALS AND METHODS:

The clinical study was carried out to investigate the effect of gabapentin on the hemodynamic responces to laryngoscopy and intubation 60 Subjects were taken of which 30 were study group and 30 were control group.

Inclusion Criteria: 60 adult patients of ASA grade I within the age group of 18-65 years and scheduled for different types of elective non-cardiac surgeries. They were allocated randomly either to the gabapentin or control group who were planned as first on the respective theatre lists.

Exclusion Criteria: Patients with

1. Anticipated difficult intubation
2. ASA physical status III or greater.
3. Hiatus Hernia and GERD
4. Body weight more than 20% of the ideal body weight.
5. Age greater than 65 years and less than 18 years.
6. H/o consumption of Antihypertensive, sedatives, hypnotics etc.
7. Laryngoscopy greater than 15 seconds and more than one attempt.

Ethical Issues: The study was approved by the Hospital Ethics Review Committee, S.V.Medical College and Hospital, Tirupathi

Statistical analysis

Data was analyzed using Epi information statiscal software (version: 3.3.2). Data was presented as mean±S.D. All categorical variables were analyzed using chi-square test. Haemodynamic changes within each group at different time intervals and also between 2 groups were analyzed using ANOVA test. P value <0.05 was considered to be statistically significant. Haemodynamic variables between the two groups at different time intervals were compared using interaction F-ratio.

Results:

In the present study 60 ASA grade I and II patients (n=60) of either sex and aged between 18-65 years were selected and randomly allocated into 2 groups of 30 patients each i.e., Gabapentin group (GBP) and Placebo group (Table-1).

Table 1:Group of patients

Group	Type of capsules received by the patient	No. of patients
GBP group	Gabapentin	30
Placebo	Placebo	30
	Total	60

Patient characteristics with regard to age, sex and body weight were comparable in both groups. This data was analyzed by Chi-square test (Table-2)

Table:2 Age, Sex and Body weight in both groups

Group	Gabapentin group(n=30)	Placebo group (n=30)	P value
Mean Age (Years)±SD	40.03±12.65	40.60±12.40	0.86 NS
Sex (M+F)%	15+15 (50% + 50%)	16+14 (53.3% + 48.3%)	0.60 NS
Mean weight±SD	60.03±11.69	58.06±7.68	0.44 NS

The mean duaration of laryngoscopy in gabapentin group was 11.03±1.80 seconds and in placebo group was 0.50±2.38 seconds. The difference in the duration was not found statistically significant (p value = 0.33) Table-3

Table 3: Direct laryngoscopy in study subjects

Group	Mean duration of Laryngoscopy	P Value
Gabapentin group	11.03±1.80	0.33 NS
Placebo	10.50±2.38	0.34 NS

Haemodynamic changes:

All heamodynamic changes were analyzed by student t test and ANOVA test. Heart rate at post induction, 0 min, 1 min, and 3 min after laryngoscopy and intubation was considered to be statiscally significant (p values = 0.009, 0.0016, 0.004 and 0.021) between the 2 groups. SBP at 0 min, 1 min, and 3 min after laryngoscopy and intubation was considered to be statiscally significant (p values = 0.001, 0.001 and 0.02) between the 2 groups. DBP at 0 min, 1 min, and 3 min after laryngoscopy and intubation was considered to be statiscally significant (p values = 0.0025, 0.0003 and 0.11) between the 2 groups.MAP at 0 min, 1 min, and 3 min after laryngoscopy and intubation was considered to be statiscally significant (p values = 0.0002, 0.001 and 0.04) between the 2 groups (Table 4,5,6)

There were no adverse effects observed with the study drug. Gabapentin is able to attenuate the pressor response due to laryngoscopy and intubation successfully.

Table4: Heamodynamic changes in SBP

Group	Baseline	Pre-induction	Post-induction	0 min	1 min	3 min	5 min	10 min
Gabapentin	128.80±13.10	135.66±16.94	117.20±16.43	132.30±17.03	136.23±20.12	123.33±14.29	115.56±10.88	110.80±9.77
Placebo	129.33±15.00	137.33±17.68	117.60±15.66	157.46±24.49	162.23±21.43	134.06±20.01	118.13±16.28	111.80±10.96
Statistical significance	t=0.14 p=0.88 NS	t=0.37 p=0.71 NS	t=0.09 p=0.92 NS	t=4.60 p<0.001 S	t=4.84 p<0.001 S	t=2.39 p=0.02 S	t=0.71 p=0.47 NS	t=0.37 p=0.71 NS
ANOVA test and significance	F ratio with duration of time = 40.20; p<0.001;NS F ration between groups of patients=31.05; p<0.001; S Interaction F ratio=6.65; p<0.001;S							

Table 5: Changes in DBP

Group	Baseline	Pre-induction	Post-induction	0 min	1 min	3 min	5 min	10 min
Gabapentin	75.53±11.76	79.23±11.62	117.20±16.43	68.53±10.32	81.03±13.60	74.40±11.72	70.10±10.98	65.30±9.40
Placebo	72.96±9.18	76.43±10.12	65.90±8.64	89.36±15.66	94.13±13.06	79.10±11.32	67.63±10.67	63.03±7.94
Statistical significance	t=0.94 p=0.35 NS	t=0.99 p=0.32 NS	t=1.07 p=0.28 NS	t=3.16 p=0.0025 S	t=3.80 p=0.0003 S	t=1.57 p=0.11 NS	t=0.88 p=0.38 NS	t=1.00 p=0.31 NS
ANOVA test and significance	F ratio with duration of time = 31.40; p<0.001;S F ration between groups of patients=3.90; p=0.048; S Interaction F ratio=5.38; p<0.001;S							

Table 6: Changes in Mean Arterial Pressure (changes in heart rate)

Group	Baseline	Pre-induction	Post-induction	0 min	1 min	3 min	5 min	10 min
Gabapentin	93.28±10.66	98.04±12.05	84.75±11.45	96.25±12.11	99.4±14.5	90.71±11.27	85.25±9.90	80.46±8.56
Placebo	91.75±9.56	96.73±11.30	83.13±9.32	112.06±17.71	116.83±15.10	97.42±13.61	84.46±11.47	79.28±8.31
Statistical significance	t=0.58 p=0.56 NS	t=0.43 p=0.66 NS	t=0.60 p=0.54 NS	t=4.03 p=0.0002 S	t=4.56 p<0.001 S	t=2.07 p=0.04 S	t=0.28 p=0.77 NS	t=0.54 p=0.59 NS
ANOVA test and significance	F ratio with duration of time = 41.75; p<0.001;S F ration between groups of patients=14.74; p<0.001; S Interaction F ratio=7.00; p<0.001;S							

Discussion:

Our results showed that gabapentin attenuated the pressor response to tracheal intubation, as systolic, diastolic, mean arterial pressures and heart rates were significantly lower in the gabapentin vs control group.

The cardiovascular responses to laryngoscopy and tracheal intubation are well known and linked with increasing catecholamine blood levels. Shribman and colleagues found that laryngoscopy alone or followed by tracheal intubation increases arterial pressures and catecholamine levels while intubation significantly increases heart rate. Our results are consistent with its findings, but we did not measure catecholamine levels.

Several techniques have been proposed to attenuate such responses. Nitroglycerine administered intranasally attenuated the hypertensive response to laryngoscopy and intubation but tachycardia was observed in both the nitroglycerine and the control group. Also topical lignocaine spray applied before or after induction of anaesthesia prevented the increase in mean arterial blood pressure but had no affect on the heart rate.

Beta blockers and calcium channel blockers have also been used successfully to prevent the haemodynamic responses to tracheal intubation. Drugs with rapid onset and short duration of action similar to the beta blocker esmolol and the opioid remifentanil are particularly useful for the induction-intubation period. The most recent studies regarding prevention of haemodynamic changes after laryngoscopy and tracheal intubation investigate the effect of remifentanil, an opioid with very rapid onset and very short time of action.

Remifantanil 1µg/kg followed by 0.5 µg/kg/min attenuated the pressor response to intubation but was associated with bradycardia and/or hypotension. Other workers found that remifantanil 0.5µg/kg did not prevent hypertension and trachycardia during rapid sequence induction. However, remifentanil 1µg/kg was effective while 1.25µg/kg in some patients caused hypotension.

When assessing the techniques to ameliorate the cardiovascular responses to intubation the drugs used to induce anaesthesia may influence these results. We induced anaesthesia with Propofol which would cause some hypotension and barycardia. But before giving propofol we also gave midazolam does not alter the heart rate on their own, but tramadol reduces heart rate and succinyl choline also produces similar effects i.e;sinus bradycardia. The bradycardia after propofol is nullified by glycopyrrolate. Now in our patients we observed increase in heart rate which is attributed solely due to laryngoscopy and intubation only, and gabapentin was found to suppress the increase in heart rate. We counteracted the fall of blood pressure seen after propofol with infusion of crystalloid solution. None of our patients exhibited hypotension after induction, so the attenuation of hypertensive response seen after gabapentin could be solely due to the gabapentin only and this suppression was not seen after placebo.

We premedicated our patients with three doses of gabapentin in this study, unlike Fassolaki et al who used four doses of gabapentin. Our three doses were administered at 18:00 hrs, 24:00 hrs(on the night before surgery) and 6:00 hrs on the day of surgery. We omitted the 12:00 hrs(on the day before surgery) dose because of non availability of theatre lists by this time. Another reason was that we also wanted to see if only three doses of gabapentin are sufficient to produce adequate blood

levels which would attenuate the haemodynamic responses. A review of the literature of pharmacology of gabpentin shows that sufficient antiepileptic effect could be achieved even with three doses.

We studied patients up to 65 years only, as elderly patients take more often drugs such as antidepressants, hypotics and anti hypertensives.Older patients also exhibit increased sensitivity to drugs and the cardiovascular effects of gabapentin are not studied in them extensively.Aged patients should comprise a different group with doses of gabapentin duly adjusted to age.

The exact mechanism by which gabapentin attenuates the pressor response to laryngoscopy and intubation is unknown. The drug inhibits membrane voltage gated calcium channels blockers. Another explanation for its attenuation of pressor response may be that gabapentin was shown to slightly reduce the release of several monoamine neurotransmitters,from mammalian brain tissues in vitro.

Preclinical data gathered early in the development of gabapentin showed anxiolytic effects in several animal modes.Isolated anecdotal reports emerged over the years and indicated the successful use of gabapentin to treat anxiety symptoms.This may be be another explanation for attenuation of pressor response.To our knowledge no randomized controlled trial has the cardiovascular effects of gabapentin as primary aim.As gabapentin is recently used as adjuvant for acutepostoperative pain. Studies on its haemodynamic effects will be more than welcome.

Conclusion:

It is concluded that gabapentin given as premedicant in 3 divided doses before surgery attenuated the pressor response to laryngoscopy and intubation in patients undergoing elective non-cardiac surgeries.

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