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Original Research Article

Effect of clonidine and gabapentin as oral premedication on hemodynamic response to laryngoscopy and tracheal intubation

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ABSTRACT

Background: Laryngoscopy and endotracheal intubation causes stimulation of symphatho-adrenal system resulting in increase in blood pressure and heart rate. The present study compared oral clonidine, gabapentin and placebo premedication in attenuating haemodynamic response to laryngoscopy and endotracheal intubation.
Methods: About 90 adult patients of ASA grade I and II patients in age group of 18-60 yrs, of either sex posted for surgery under general anaesthesia were randomly divided into three groups (30 patients in each group). The study drugs were given orally 90minutes before induction. Group 1 and Group 2 were pre treated with oral clonidine (0.2mg) and gabapentin (800mg) respectively and Group-3 received placebo. The HR, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were recorded before induction of anesthesia and 1, 3, 5, 10min after laryngoscopy and intubation.
Results: It was found that both clonidine and gabapentin reduces HR, SBP, DBP, MAP than placebo group at lminute, 3minutes, 5minutes and 10minutes after intubation. But reduction is more with clonidine as compared to gabapentine and difference was statistically significant (P = <0.0001).
Conclusions: Both oral clonidine and gabapentine attenuate hemodynamic response to laryngoscopy and endotracheal intubation but effect is better with clonidine than oral gabapentine.

Keywords: Clonidine, Gabapentin, Hemodynamic response, Intubation, Laryngoscopy

INTRODUCTION

Laryngoscopy and endotracheal intubation are an integral part of anesthesiologists to patient care. But both laryngoscopy and endotracheal intubation are noxious stimuli leading to hemodynamic fluctuations, higher myocardial oxygen demand and cardiac arrhythmias. This is a concern in all patients particularly in patients with heart disease and cerebro-vascular disease. The adverse cardiovascular effects should be minimized so as to balance the myocardial oxygen supply and demand which is a key note in the safe conduct of anaesthesia. Laryngoscopy and tracheal intubation (L and I) are a strong stimulus for cardiovascular system under light anesthesia.[1]

The magnitude of response varies directly with increasing force and duration of laryngoscopy.[2] Such hemodynamic changes can result in myocardial ischemia, especially in patients with pre-existing cardiovascular disease.[2] To attenuate the hemodynamic response, many techniques have been tried but none is ideal. Different methods to attenuate the hemodynamic changes to laryngoscopy and intubation are increasing the depth of anaesthesia, use of volatile anesthetic agents, large doses of fentanyl, application of local anaesthetics, B blockers like labetalol

and esmolol.[3,4] Still there is search for newer drugs to attenuate the pressure response.

Gabapentin, 1-(aminomethyl) cyclohexane acetic acid, is a structural analogue of the neurotransmitter, gaba amino butyric acid (GABA) was introduced in 1993 as an adjuvant antiepileptic drug for the treatment of refractory partial seizure.[5] It is also effective in treating postherpetic neuralgia, other neuropathic pain, post poliomyelitis neuropathy, reflex sympathetic dystrophy, diabetic neuropathy.[6-10] It has also antinociceptive, antihyperalgesic, and antiallodynic properties.[11] More recently, it has been used to attenuate the stress response to laryngoscopy and Intubation.

Clonidine, a centrally acting α_2 agonist was introduced in 1966 for treatment for hypertension. It also used for premedication to reduce sympathetic activity, to reduce incidence of shivering, to decrease anesthetic and analgesic requirement and to minimize post-operative pain, nausea, and vomiting.

The present study was designed to evaluate the efficacy of oral gabapentin (800mg) versus oral clonidine (200µg) as premedication, in comparison with a placebo, for blunting the hemodynamic response to direct laryngoscopy and intubation.

The aim of my study was to compare the attenuation of hemodynamic response to laryngoscopy and intubation between oral clonidine, oral gabapentin and placebo in patients undergoing elective surgery under general anaesthesia. The parameters studied are heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and to assess any side effects of the drug used.

METHODS

This is a prospective randomized double blind study was carried out in the Department of Anaesthesiology, MKCG Medical College and Hospital, Berhampur, between 2015 and 2018.

After obtaining clearance from institutional ethics committee and written informed consent from each patient, this study was conducted with ninety patients (n=90) of either sex, aged between 18 and 60 years, of ASA physical status I and II undergoing elective surgery under general anaesthesia. Patients on beta blockers, anticipated difficult airway, grossly obese, with history of drug abuse potential, with history of allergy to study drugs were excluded from study.

After preanaesthetic check-up all patients included the study group were advised to take tab alprazolam (0.5mg) and one tab of ranitidine night before surgery. In the morning of surgery patients were randomly divided to three equal groups according to a computerized random table of 30 patients in each group.

- Group 1= patients received 0.2mg clonidine (0.1mg x 2 tablets),
- Group 2= patients received 800mg gabapentin (400mg x 2 tablets),
- Group 3= patients received placebo (antacid 2 tablets).

To make the study bias free, all the tablets were kept in envelops of same size and color by a separate anaesthesiologist who was blind to the study. Each of the envelop was randomly selected and patient were advised to take it orally with a sip of water 90min before induction. Both the patient and the investigator were unaware of the assigned drugs. In the operation table, patients were attached to essential monitors like pulse oxymeter, non-invasive blood pressure monitor (NIBP), electrocardiography (ECG). Baseline parameters of heart rate (HR), systolic BP, diastolic BP and mean arterial pressure (MAP), ECG finding and SP02 were noted.

Procedure

Intravenous cannula secured and infused with ringer lactate solution. Patients premedicatated with 0.2mg glycopyrrolate, 0.5mg/kg pentazocine and 0.03mg/kg midazolam intravenously then pre-oxygenated for 3minutes with oxygen 100%. All patients were induced with Propofol 2mg/kg. inj vecuronium (0.1mg/kg) given for muscle relaxation. After three minutes of IPPV, under direct laryngoscopy intubation done with appropriate size cuffed PVC endotracheal tube. After confirmation of tube position it was connected to ventilator and anaesthesia was maintained with 33% O_2: 66% N_2O with intermittent doses of vecuronium. Patients where more than 2 attempts were required for laryngoscopy and intubation were excluded from the study. After completion of surgery and return of the spontaneous respiratory effort patients were reversed with inj myopyrolate and extubated after return of protective reflexes.

Collection of data heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MAP) were recorded before induction of anesthesia and 1, 3, 5, 10min after laryngoscopy and intubation. Data were tabulated in Microsoft excel sheet and compared statistically by using SPSS. Data were represented as mean with standard deviation. Data were compared among study groups by one way analysis of variance (ANOVA) for numerical variables and Chi-square test for categorical data. A P value less than 0.05 was considered as statistically significant.

RESULTS

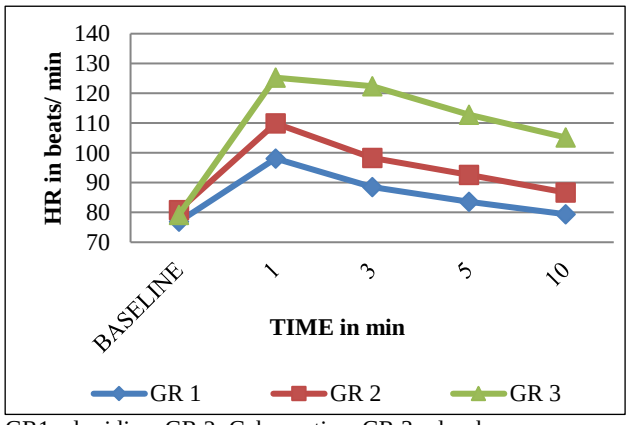
The demographic profiles of patients were depicted in Table 1. Study showed that there is no significant difference in demographic profile between three groups (Table 1).

Table 1: Demographic profile of study participants (n=90).

Characteristics	GR 1	GR 2	GR 3	P value
Gender				
Male	17	16	10	0.5
Female	13	14	20	
Age (in years) [Mean±SD]	32.88±8.57	30.72±7.59	34.96±9.51	0.2
Body weight (in kg) [Mean±SD]	67.88±11.25	71.32±10.68	67.12±14.65	0.4

* GR1: clonidine, GR 2: Gabapentine, GR 3: placebo

Figure 1 shows comparison of mean Heart rate of participants among three groups. The baseline mean heart rate (HR) was comparable between the 3 groups. Post-intubation heart rate increased in all the groups, rise was highest in group 3 (placebo) and lowest in group 1 (clonidine). The mean HR measured at 1minute, 3minute, 5minute and 10minutes post-intubation were higher in group 2 (gabapentine) than group 1 (clonidine) and the difference was statistically significant (Figure 1).



GR1: clonidine, GR 2: Gabapentine, GR 3: placebo.

Figure 1: Comparison of mean heart rate of participants among three groups.

Table 2 comparison of systolic blood pressure among participants of three groups. All the three groups had comparable baseline systolic blood pressure (SBP).

After intubation, SBP was significantly high in group 3 (placebo) compared to group 1 (clonidine) and group 2 (gabapentin). The reflex rise in SBP was less in clonidine group compared to gabapentin group and the difference was statistically significant.

Table 3 shows comparison of diastolic blood pressure among three groups. The baseline diastolic blood pressure (DBP) was comparable between the three groups. After intubation, DBP increased in all the three groups. The rise in DBP was significantly less in group 1 and group 2 compared to group 3. Post-intubation, clonidine group showed significantly less DBP than gabapentin group.

Figure 2 shows comparison of mean arterial pressure (MAP) among three groups. The baseline mean arterial blood pressure (MAP) was comparable between three groups. After intubation MAP increased in all the groups. The rise was lowest in clonidine group compared to gabapentin group at all points of time, the difference being statistically significant.

Table 2: Comparison of systolic blood pressure among participants of three groups (n=90).

Parameter	GR 1 (Mean±SD)	GR 2 (Mean±SD)	GR 3 (Mean±SD)	P Value		
Systolic blood pressure				GR1 and 2	GR2 and 3	GR 1 and 3
baseline	112.50±7.82	114.90±9.41	118.73±10.59	0.286	0.144	0.012
1 min	129.90±8.77	141.67±8.64	160.33±11.39	<0.0001	<0.0001	<0.0001
3 min	120.03±7.77	134.10±9.75	151.40±10.10	<0.0001	<0.0001	<0.0001
5 min	110.70±8.21	123.27±10.36	137.83±10.80	<0.0001	<0.0001	<0.0001
10 min	102.10±6.87	107.37±7.67	131.23±8.67	<0.0001	<0.0001	<0.0001

Table 4 depicted the comparison of incidence of side effects of drugs among three groups. The incidence of side effects like drowsiness was seen more in clonidine group than in gabapentin group, whereas dizziness was seen only in the gabapentin group.

Table 3: Comparison of diastolic blood pressure among three groups (n=90).

Parameter	GR 1 (Mean±SD)	GR 2 (Mean±SD)	GR 3 (Mean±SD)	P Value		
Diastolic blood pressure				GR1 and 2	GR2 and 3	GR 1 and 3
Baseline	72.23±6.24	74.50±8.55	77.33±11.23	0.245	0.276	0.034
1 min	85.43±8.18	88.66±5.09	106.90±4.17	0.042	<0.0001	<0.0001
3 min	79.36±7.48	84.40±6.09	94.83±7.62	0.0058	<0.0001	<0.0001
5 min	73.53±5.79	79.20±6.40	89.97±5.67	0.0007	<0.0001	<0.0001
10 min	68.16±4.33	71.53±8.51	79.30±2.87	0.0482	<0.0001	<0.0001

Table 4: Comparison of incidence of side effects of drugs among three groups (n=90).

Side effects	GR 1		GR 2		GR 3	
	No.	%	No.	%	No.	%
Dry mouth	0	0	1	3.33	0	0
Headache	0	0	1	3.33	1	3.33
Drowsiness	6	20	4	13.33	0	0
Dizziness	0	0	2	6.67	0	0
Nausea/vomiting	0	0	0	0	1	3.33
Pruritus	0	0	0	0	0	0

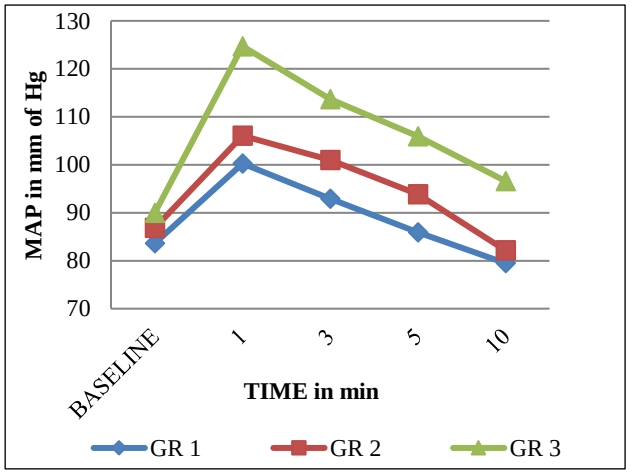


Figure 2: Comparison of mean arterial pressure (MAP) among three groups.

DISCUSSION

The present study was carried out with oral premedication with clonidine (0.2mg), gabapentin (800 mg) and placebo 90minutes before surgery to compare the attenuated hemodynamic response following laryngoscopy and endotracheal intubation. Authors used oral formulation of the drugs, as it is a noninvasive route and gabapentine does not have any intravenous preparation. We used clonidine 90minutes before surgery as clonidine is well absorbed after oral administration and its bioavailability is nearly 95%. The peak concentration in plasma and the maximal hypotensive effect are observed 1 to 3hours after an oral dose.[12]

Clonidine produces a fall in heart rate and blood pressure due to decreased cardiac output but no effect on peripheral resistance. It stimulates central nervous system α receptors and found to have some beneficial premedicating effects like sedation, reduction of dose of induction agent, attenuation of laryngoscopic stress response.[13-15] The exact mechanism of gabapentin in controlling this hemodynamic response remains unknown. Since, gabapentin inhibits membrane voltage gated calcium channels (VGCCs); it is possible that it may have a similar action to calcium channel blockers. Possible pharmacologic targets of gabapentine are selective activation of GABA B receptors, enhancements of N methyl D aspartate (NMDA) currents, blocking AMPA receptor mediated neurotransmission in the spinal cord. Gabapentine does not affect nociceptive threshold but has a selective effect on nociceptive process involving central sensitization which also help in post op pain control.[16]

Memis et al, compared 800mg gabapentin with 400mg 1hour before induction and found 800mg suppress hemodynamic responses at laryngoscopy and intubation.[17] Serhat et al, also observed the same results.[18] Bafina et al, compared the different doses of gabapentin to attenuate the hemodynamic response to laryngoscopy and intubation and found significant result with 1000mg dose.[19] Comparing all these we choose 800mg gabapentin and administered it 90minutes before surgery.

For clonidine oral dose as premedication in our study corroborated with the study of Filos et al, who compared two doses of clonidine 150µg with 300µg given 90 minutes before surgery and found 150µg as effective as 300µg.[20] Study of Yu et al, also confirmed that oral clonidine preserves heart rate effectively after pneumoperitonium.[21] Gupta et al, compared intravenous Lignocaine with oral clonidine for attenuation of hemodynamic response to laryngoscopy and intubation.[22] Fassoulaki et al, studied the effect of gabapentin on pressure response to laryngoscopy and intubation and their results corroborated with our results.[23] Kayan et al, studied the effect of preoperative gabapentin 800mg, given 2h before surgery and found attenuation of increase in the MAP but not the HR.[24] Marashi et al, used 900mg

gabapentin and 200µg clonidine, 2hours before surgery and concluded that both gabapentin and clonidine have effective role in blunting the hemodynamic responses to laryngoscopy and intubation.[25] Comparative study between oral clonidine and gabapentine for attenuation of hemodynamic response to laryngoscopy and intubation by Mojtaba et al, matches to this study.[26] Montazeri et al, compared the efficacy of oral gabapentin (800mg) and clonidine (0.3mg) premedication for controlling the pressure responses to laryngoscopy and tracheal intubation and the study results comparable with our results.[27] Majumdar et al, also compared the blunting hemodynamic response by pre-medicating the patients with oral clonidine (200µg) and gabapentin (800mg) 2h prior to surgery and the results matches with our results.[28]

Stress mediators like endogenous plasma catecholamine or cortisol values were not studied. Pediatric and geriatric patients were excluded from study. Sample size was small.

CONCLUSION

From this study, authors concluded that both oral clonidine (0.2mg) and oral gabapentin (800mg) given 90minutes prior to laryngoscopy are safe and effective prophylactic measures for attenuating hemodynamic response to laryngoscopy and tracheal intubation. Oral clonidine (0.2mg) is better as compared to gabapentin (800mg) premedication, in attenuating the hemodynamic response to laryngoscopy and intubation; if given sufficient time before the procedure. However, further studies are required to confirm our findings.

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