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Original Research Article

Attenuation of Haemodynamic Changes during Laryngoscopy and Endotracheal Intubation with Oral Gabapentin versus Oral Clonidine

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ABSTRACT

INTRODUCTION
During the administration of general anesthesia, the procedures of direct laryngoscopy and endotracheal intubation result in a significant rise in heart rate, arterial pressure, and dysrhythmias in around 90% of patients. These modifications can provide a significant risk to patients with brain or coronary diseases. The aim of present study is to assess the attenuation of hemodynamic changes during laryngoscopy and endotracheal intubation with oral gabapentin versus oral clonidine.

MATERIAL AND METHODS
The present double blind randomized controlled trial was conducted among patient undergoing elective surgeries under general anesthesia at Govt. Mohan Kumaramangalam Medical College, during the study period of one year. 90 patients were distributed to three groups using sealed envelope technique. Group A of patients received single dose oral 150 µg clonidine, Group B of patients received single dose oral 200 µg clonidine and Group C patients received single dose oral 800 mg gabapentin . Hemodynamic parameters were noted at different time interval and results were analyzed.

RESULTS
The mean age of subjects was between the age group of 40-50 years and male were higher in number as compared to female. The heart rate was higher in the clonidine 200 group as compared to other two but results were non-significant with (P>0.05). No Significant difference in mean SBP, DBP and MAP was observed at all time intervals. (p>0.05).

CONCLUSION
Oral clonidine and gabapentin reduce direct laryngoscopy haemodynamics. Gabapentin has fewer adverse effects than clonidine. Compared to -200mcg, 150mcg has no adverse effects.

KEYWORDS
Arterial Pressure, Blood Pressure, Diastolic, Haemodynamic, Laryngoscopy, Systolic

INTRODUCTION

Laryngoscopy and endotracheal intubation are powerful stimuli that can cause a rise in sympathetic activity, resulting in elevated heart rate, high blood pressure, and abnormal heart rhythms. It can cause harmful effects on the respiratory, neurological, and cardiovascular systems.[1,2] These reactions are particularly pronounced in persons with hypertension.[3,4] Transient alterations in patients with coronary artery disease, leaking abdominal aneurysm, intracranial aneurysm, and recent myocardial infarction might have potentially harmful implications, including myocardial ischemia, left ventricular failure, and cerebral haemorrhage.[5,6]

Vasodilators, including nitroprusside, hydralazine, and nitroglycerine, have been employed to reduce these hemodynamic reactions with different levels of effectiveness. Calcium channel blockers, beta blockers, and opioids such as alfentanil, fentanyl, and remifentanil have been utilised in various dosage regimens to reduce the hemodynamic response to laryngoscopy and intubation.[7]

Clonidine, the original medicine of the α2 agonist category, is a specific partial agonist for α-adrenoreceptors, with a ratio of around 200:1 (α to α). The antihypertensive effects of this medication result from its ability to reduce sympathetic outflow both centrally and peripherally, as well as activate noradrenergic imidazoline preferring receptors centrally. It also reduces the minimum alveolar concentration (MAC) of halothane and the amount of narcotics needed to prevent reflex cardiovascular response to laryngoscopy and endotracheal intubation. Additionally, it possesses strong analgesic properties in humans. These qualities indicate that clonidine could be a beneficial addition to the anaesthetic management of individuals who already have hypertension.[8] While clonidine can cause dose-dependent adverse effects such hypotension and drowsiness, as well as idiosyncratic adverse effects like bradycardia, it does not cause significant respiratory depression. It only slightly enhances the respiratory depression caused by opioids.[9,10] Clonidine, a medication that stimulates α adrenoreceptors, has the ability to lower blood pressure, induce sedation, and provide pain relief.

Gabapentin, a chemical compound that closely resembles γ-aminobutyric acid, is employed as a medication to prevent seizures.[11] Gabapentin administered before to treatment can effectively inhibit the onset of hyperalgesia.[12] Furthermore, gabapentin specifically targets the nociceptive pathway associated with central sensitization.[13] Gabapentin is a recently developed medication initially used as an antiepileptic. However, it has also demonstrated effectiveness in managing neuropathic pain. The treatment is highly tolerable with little side effects, in contrast to previous antiepileptic medications like carbamazepine.[14]

The aim of present study is to assess the attenuation of haemodynamic changes during laryngoscopy and endotracheal intubation with oral gabapentin versus oral clonidine.

MATERIAL AND METHODS

The present double blind randomized controlled trial was conducted among patient undergoing elective surgeries under general anaesthesia at Govt. Mohan Kumaramangalam Medical College, Salem during the study period of one year. Ethical clearance was taken from institutional ethics committee before commencement of study. Patients were asked to sign an informed consent form after explaining them the complete procedure.

90 Patients undergoing elective surgeries under general anaesthesia in various surgical disciplines were choosed randomly for the study and were distributed to three groups using sealed envelope technique.Group A of patients received single dose oral 150 µg clonidine, Group B of patients received single dose oral 200 µg clonidine and Group C patients received single dose oral 800 mg gabapentin [2 hrs before induction of general anesthesia]. Patients were selected on the basis of inclusion and exclusion criteria-

Inclusion criteria

1. Age range 18-60 of both sex
2. ASA grade I & II
3. Mallampatti class I &II

Exclusion Criteria

1. Age<18 & >60yrs
2. ASA grade III & IV
3. Mallampatti class III & IV
4. Uncontrolled hypertension, cardiac, renal, hepatic & cerebral diseases and diabetes mellitus.
5. Emergency surgeries
6. Pregnant females
7. More than one attempt of intubation
8. Duration of laryngoscopy and intubation > 30sec

After 2 hrs patient was shifted to the operation table & multichannel monitor was attached. HR, SBP, DBP, MBP, respiratory rate, were recorded, I.V. infusion was started with ringer lactate. After 5 min preoxygenation with 100% O_2, premedication was given with inj. glycopyrrolate 4 µg/kg, Inj. fentanyl 2 µg/kg. Induction with Inj. thiopentone sodium 5 mg/kg and intubation was done with Inj. succinylcholine 1.5 mg/kg and cuffed endotracheal tube of appropriate size. Haemodynamic changes - Heart rate (HR), systolic blood pressure (SBP) Mean Blood Pressure (MBP) & Diastolic Blood Pressure (DBP) were recorded during Laryngoscopy and Intubation, 1 min, 3 min, 5 min, 7 min, and 10 min after Laryngoscopy and Intubation and throughout procedure. Anaesthesia was standardized in all three groups.

Statistical analyses were necessary to evaluate the study data in electronic format. The data were compiled using appropriate software, such as Excel and SPSS. Following the collection of data, it was subjected to statistical analysis using SPSS software version 25.0. In order to assess the reduction in hemodynamic stress response across the three groups, the normality assumption was first verified. Subsequently, either the Chi-square test, ANOVA, or paired t-test was employed. The significance level was set at a 95% confidence level ($P<0.05$). The data were presented as a frequency distribution, expressed as a percentage, as well as in terms of the mean ± standard deviation (SD). The data were displayed using appropriate statistical graphs.

RESULTS

Demographic data, when analyzed, did not show any significant difference in age, weight, height & sex ratio among three groups as shown in table 1.

Variable	Group A	Group B	Group C	P value
Mean age (years)	45.12±3.2	46.24±4.1	44.56±2.9	0.213
Sex ratio (m:F)	17:13	18:12	16:14	0.097
Mean Weight (kg)	67.12±3.6	65.36±2.1	66.78±4.3	0.109
Mean height (ft)	5.6±1.1	5.7±1.9	5.55±2.1	0.079

Table 1: Demographic data of patients

The heart rate was higher in the clonidine 200 group as compared to other two but results were non-significant with (P>0.05) as shown in table 2 and figure 1.

Percentage Change in HR from Baseline to	Clonidine 150 – Mean±Std	Clonidine 200 Mean±Std	Gabapentin Mean±Std	P-Value
Pre-Laryngoscopy	-.355±7.199	.0487±6.267	-.737±6.288	0.932
0'	19.213±18.591	23.171±19.218	15.024±11.678	0.318
1’	14.859±19.599	15.281±18.845	7.930±12.048	0.322
3’	11.691±19.905	12.174±18.533	3.410±12.729	0.208
5’	6.430±17.524	6.861±17.196	-1.214±11.355	0.193
7’	.5767±13.258	2.234±13.894	-5.7252±10.378	0.118
10’	-3.006±11.144	.609±14.260	-8.8498±8.103	0.058

Table 2: Comparison of mean Heart Rate across study groups

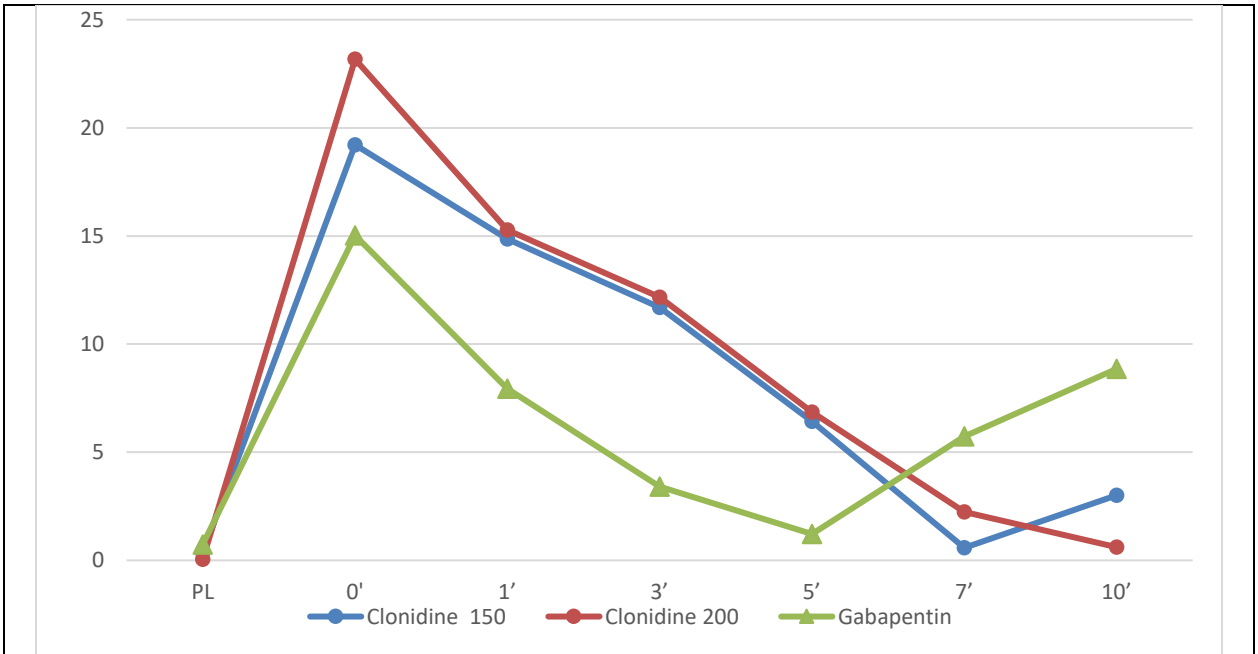

Figure 1: Comparison of mean Heart Rate across study groups

No Significant difference in mean SBP was observed at alltime intervals. In clonidine 200 group shows better control in SBP than the other two groups (P>0.05) as shown in table 3, figure 2.

Percentage Change in SBP from Baseline to	Clonidine 150 Mean±Std	Clonidine 200 Mean±Std	Gabapentin Mean±Std	P-Value
Pre Laryngoscopy	-0.741±5.195	-2.107±7.006	-0.505±4.670	0.635
0'	22.537±11.479	16.434±12.455	21.570±8.002	0.168
1’	6.387±10.988	9.711±6.996	7.519±10.753	0.552
3’	-0.537±11.834	1.949±7.964	1.074±7.306	0.691
5’	-2.023±8.557	-1.742±6.468	-5.056±7.813	0.324
7’	-4.799±7.665	-5.615±6.130	-6.787±6.849	0.660
10’	-2.475±10.190	4.082±14.491	-5.738±10.049	0.053

Table 3: Comparison of systolic blood pressure across study groups

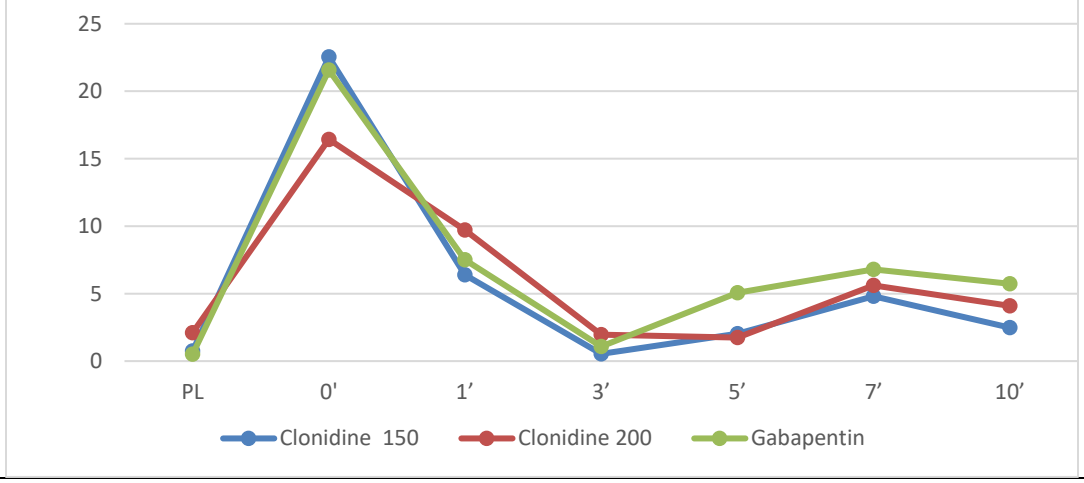

Figure 2: Comparison of systolic blood pressure across study groups

No Significant difference in mean diastolic blood pressure was observed at all time intervals. In clonidine 150 group shows better control in diastolic pressure than the other two groups (P>0.05) as shown in table 4, figure 3.

Percentage Change in DBP From Baseline to	Clonidine 150 - Mean±Std	Clonidine 200 Mean±Std	Gabapentin Mean±Std	P-Value
Pre Laryngoscopy	-.952±7.54004	.9877±6.92199	-2.0257±6.36013	0.388
0'	22.427±16.35424	22.5073±16.19497	18.1265±10.14700	0.555
1’	9.3841±13.46975	14.4128±14.9185	6.1883±8.96738	0.128
3’	5.276±11.53596	5.6989±13.26442	-1.2383±6.67965	0.086
5’	-2.592±9.80884	-2.0967±11.9252	-6.0118±8.60710	0.423
7’	-3.689±12.95139	-6.3016±13.2030	-9.1250±9.39036	0.363
10’	-2.82±19.50624	1.6618±20.76676	-10.8531±9.2188	0.076

Table 4: Comparison of mean Diastolic BP across study groups

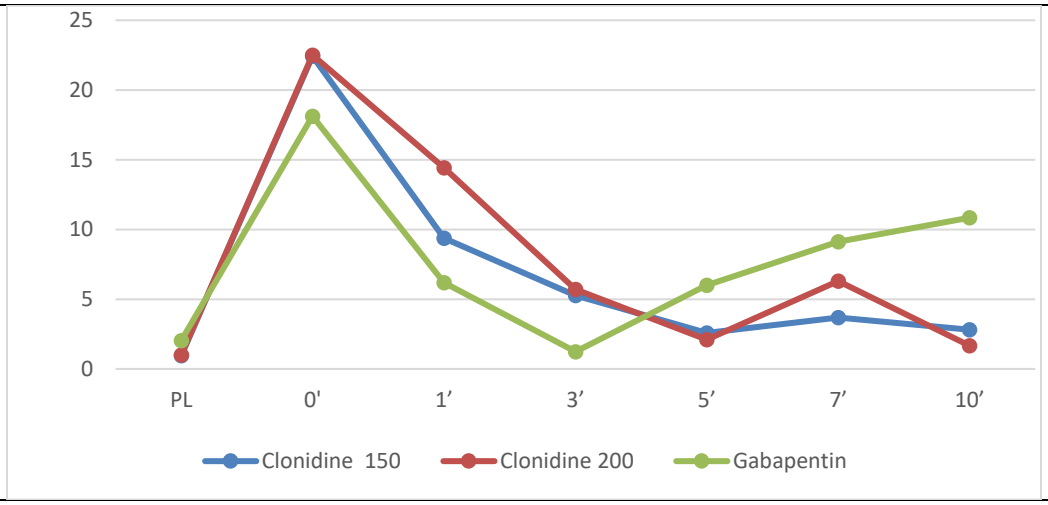

Figure 3: Comparison of mean Diastolic BP across study groups

No Significant difference in mean arterial pressure was observed at alltime intervals (P>0.05) as shown in table 5, figure 4.

Percentage Change in Map From Baseline to	Clonidine 150 - Mean±Std	Clonidine 200 Mean±Std	Gabapentin Mean±Std	P-Value
Pre laryngoscopy	-1.2981±4.24058	-.6522±5.70741	-2.3366±4.3545	0.540
0'	21.6956±14.012	18.5361±10.99720	20.0726±7.5130	0.672
1’	8.9171±12.32563	10.6665±10.88608	7.6589±9.78995	0.690
3’	2.1434±7.62034	2.9729±9.24363	-.8814±4.68380	0.233
5’	-3.0802±8.67240	-3.1095±8.99317	-6.5346±6.3540	0.307
7’	-4.8184±9.89187	-7.0060±8.43837	-9.2112±6.4897	0.262
10’	-3.4125±14.4127	1.1789±14.95540	-9.1917±7.5136	0.063

Table 5: Comparison MAP across study groups

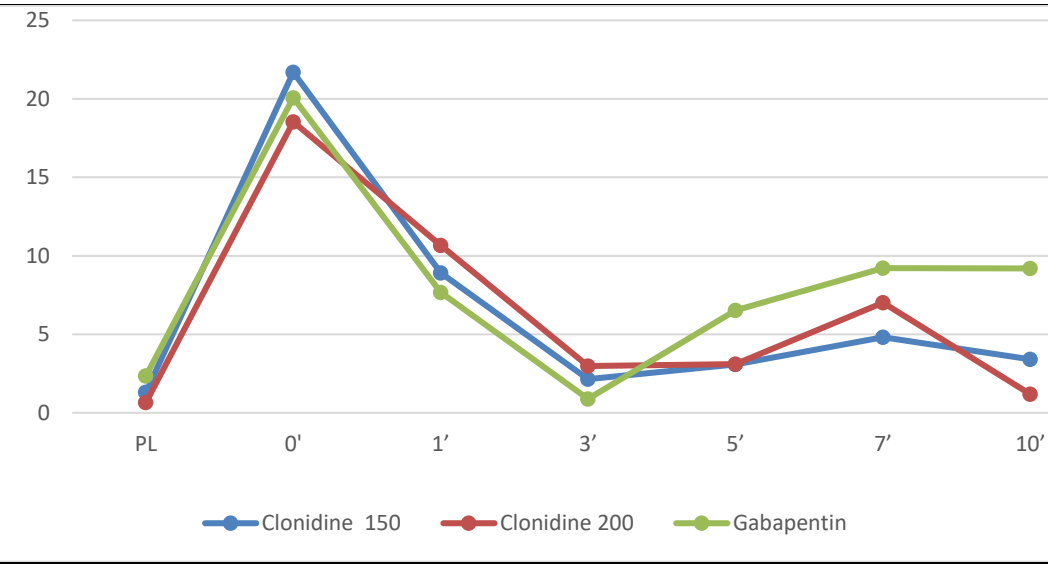

Figure 4: Comparison MAP across study groups

DISCUSSION

Laryngoscopy and tracheal intubation lead to sympathoadrenal activation, resulting in an increase in arterial blood pressure, tachycardia, and dysrhythmias.[3,4] Attaining a seamless induction with minimum reflexive changes in blood flow during laryngoscopy and endotracheal intubation is a crucial objective in anaesthesia. Various techniques have been developed to mitigate this unfavorable hemodynamic response to laryngoscopy and endotracheal intubation, but each approach has its own benefits and drawbacks.[15]

Clonidine and gabapentin are currently being extensively studied as additional medications to be used alongside anaesthesia in different forms.[16,17] Clonidine was initially developed as a medication to treat high blood pressure, but it also possesses pain-relieving, calming, and anxiety-reducing effects. It enhances the calibre of induction, maintenance, and recuperation from anaesthesia. Through its central sympatholytic activity, it reduces the haemodynamic response to surgical nociceptive stimuli and enhances cardiovascular stability during the perioperative period.[18] The mechanism underlying the prevention of tachycardia during laryngoscopy and endotracheal intubation, as well as the reduction of heart rate caused by clonidine, is complex and shared. The system is composed of various parts. Specifically, the activation of α2 adrenoceptors has two effects: it decreases sympathetic activity in the peripheral nervous system and increases vagally-induced reflex bradycardia. Additionally, stimulation of presynaptic alpha adrenoceptors in the periphery reduces the release of nor epinephrine from nerve endings towards the blood vessels and decreases sympathetic activity towards the heart.[19] Recently, gabapentin has been assessed for its analgesic and anti-hyperalgesic properties during the perioperative period.[20] The role of gabapentin in reducing the haemodynamic response has been emphasised by Fassoulaki et al. and Memiş et al.[15,16] We assessed and compared the efficacy of oral clonidine and gabapentin in eliminating the haemodynamic response to laryngoscopy and endotracheal intubation.

The mean (±SD) baseline pulse rate values in groups A, B, and C were similar in our investigation. An intergroup statistical examination of the pulse rate reveals no significant variations. The results of our study were consistent with the findings of Kaur et al. and Kapse et al.[21,22] Both studies reported that oral clonidine was more effective than oral gabapentin in reducing cardiovascular responses (HR) to laryngoscopy and intubation, with statistical significance ($P<0.001$ and $P<0.05$, respectively). However, gabapentin was found to provide superior sedation compared to clonidine ($P<0.05$).Previous research conducted by Gupta et al,[23] Raichurkar et al,[24] Soni et al[25] and Murari et al[26] found that administering oral clonidine at a dosage of 0.2 mg effectively reduced the sympathoadrenal responses, specifically heart rate, during laryngoscopy and intubation.

The mean (±SD) baseline DP, SP and MAP values in groups A, B, and C were comparable in our investigation. The intergroup statistical analysis of systolic pressure, diastolic pressure, and mean arterial pressure indicates that there are no significant differences. Brijesh et al and Sharma et al conducted a comparative study to assess the effectiveness of clonidine 0.03 mg and gabapentin 900 mg in reducing the haemodynamic response to intubation. The researchers determined that a dosage of 0.3 mg of oral clonidine was more successful in reducing systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) compared to a dosage of 900 mg of oral gabapentin throughout the procedures of laryngoscopy and intubation. This conclusion was statistically significant with a p-value of less than 0.05.[27,28]

The findings were consistent with the research conducted by Mishra et al and Das et al. Similar to our study, they also concluded that both treatments were effective. However, the administration of 0.2 mg of oral clonidine was found to be more effective than 800 mg of oral gabapentin in reducing haemodynamic responses, specifically heart rate, during laryngoscopy and endotracheal intubation ($P<0.05$).[29,30]

In this investigation, we did not monitor the BIS to assess the degree of anaesthesia or the adequacy of muscular relaxation, which can also impact haemodynamic alterations.

CONCLUSION

Both oral clonidine & gabapentin are effective in attenuating the hemodynamic response to direct laryngoscopy. Gabapentin when compare to clonidine has minimal side effects. Clonidine 150mcg when compare to Clonidine -200mcg is free of side effects. One can effectively provide stable hemodynamic conditions during laryngoscopy and endotracheal intubation by using these drugs.

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