

A Comparative Evaluation of Oral Gabapentin and Oral Clonidine for Attenuating Hemodynamic Responses to Laryngoscopy and Tracheal Intubation

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Abstract

Introduction: Laryngoscopy and endotracheal intubation (L and I) is associated with rise in blood pressure (BP), heart rate (HR), leading to adverse cardiological outcome especially in susceptible individuals. To compare the BP, HR during L and I as well as to evaluate the preoperative sedation status between oral clonidine and oral gabapentine as premedication for the patients undergoing major surgery under general anesthesia.

Objectives

- 1) To compare & assess the efficacy of oral clonidine and oral gabapentin premedication for attenuation of hemodynamic responses during laryngoscopy and tracheal intubation and
- 2) To compare the side effects, if any.

Material and Methods: The study was conducted at Gandhi Medical College and Hamidia Hospital, Bhopal on patients admitted for elective surgery under general anaesthesia, after obtaining ethics committee clearance. The time frame of the study was from March 2017 to August 2018. A total of 60 patients of either sex enrolled in the study were randomly divided into two groups of 30 each. Group A patients received oral clonidine 200 µg and

Group B patients received oral gabapentin 900 mg, 120 mins prior to induction of anesthesia.

Results: Both groups were matched for age, sex weight and intubation time. Anxiety score and sedation scores before induction were significantly better in Group A as compared with Group B. Heart rate rise was obtunded in Group A except at 1 min, as compared with Group B in which tachycardia persisted even at 3 and 5 min following intubation. Mean arterial pressure was maintained below baseline at all times in Group A as compared with Group B in which high significant ($P < 0.001$) was seen at 1 min after intubation.

Conclusion: Oral gabapentin provided good attenuation of hemodynamic response to laryngoscopy and intubation as compared with oral clonidine.

Keywords: Oral gabapentin, oral clonidine, laryngoscopy, intubation

Introduction

Laryngoscopy and tracheal intubation are frequently associated with exaggerated hemodynamic responses due to reflex sympathetic discharge caused by stimulation of the upper airway¹, The cardiovascular changes associated with laryngoscopy and tracheal intubation are hypertension, tachycardia, dysarrhythmias and increased

myocardial oxygen consumption^{2,3}, In addition to there may be transient increase in intraocular pressure and intracranial pressure⁴. Healthy individuals may not be significantly affected by this transient rise in blood pressure and pulse rate, but those associated cardiovascular diseases like hypertension, myocardial insufficiency, dysarrhythmias and with hypertension, myocardial insufficiency and cerebrovascular diseases which are common in elderly individuals may face deleterious effects⁵. Hence in such individuals there is a necessity to blunt this response. Several techniques like deepening the plane of anaesthesia, intravenous and topical lignocaine⁶, sodium nitroprusside⁷, opioids^{8,9,10}, calcium channel blockers^{11,12,13}, beta blockers^{14,15,16}, clonidine¹⁷, dexmedetomidine, gabapentin an antiepileptic and LMA or I gel have been used to attenuate the pressure response following laryngoscopy and tracheal intubation which have variable effectiveness and some of them have undesirable side effects like sedation, drowsiness, dizziness etc. Although clonidine, an alpha-adrenoceptor agonist, was introduced into clinical practice as an antihypertensive medicine, its use has been limited due to untoward side effects including sedation, drowsiness, dizziness, bradycardia and hypotension. However these properties have been beneficial when it is used as an adjunct to anaesthesia and lead to the use of this drug in anaesthesia. It has recently been shown to be effective for preoperative sedation, analgesia and perioperative hemodynamic stability. Many workers have found that clonidine has prevented cardiovascular stress response to laryngoscopy and intubation¹⁸. Some studies have found that it prevented cardiovascular stress response to laryngoscopy and intubation.^{19,20} In the recent times there are few studies which have shown that it is useful for

attenuation of hemodynamic responses to laryngoscopy and intubation. Hence, this study is planned to compare the effects of clonidine and Gabapentin for attenuating hemodynamic effects on laryngoscopy and intubation. So the present study was designed as Comparative, observational and hospital based study to investigate the effect of clonidine and gabapentin on changes in heart rate and blood pressure, observed during laryngoscopy and tracheal intubation, side effects if any and postoperative sedation score. More recently gabapentin has been used in randomized controlled trials to treat acute post operative pain^{21,22}, to reduce post operative opioid requirement²³ and also in attenuation of pressure response^{24,25} to laryngoscopy and intubation like Increased heart rate, blood pressure, myocardial oxygen demand and dysarrhythmias which usually last for short duration and are well tolerated by healthy individuals but sometime it may lead to severe complications like left ventricular failure, myocardial infarction, increased intracranial tension, cerebral hemorrhage and different types of arrhythmias in patients with pre-existing hypertension, coronary artery disease and other cardiovascular diseases.

Material and methodology

The study was conducted at Gandhi Medical College and Hamidia Hospital, Bhopal on patients admitted for elective surgery under general anaesthesia, after obtaining ethics committee clearance. The time frame of the study was from March 2017 to August 2018

Study design: The study was conducted as a Comparative, observational and hospital based study.

Study population: Patients posted for elective surgery at Gandhi Medical College and Hamidia Hospital, Bhopal

Inclusion criteria

- Patients of ASA Grade I and II.
- Age group 20 year to 50 year of both sexes.

Exclusion criteria: Following patients were excluded from the study

- Age group <20 years or > 50 years.
- Known History of allergy or sensitivity reaction to clonidine or gabapentin.
- History of
 - Cerebrovascular disease
 - Neurological disease
 - Respiratory disease
 - Ischemic heart disease
 - Myocardial Infarction
 - Renal disease and Hepatic dysfunction.

Patients with difficult airway, hypertension, pheochromocytoma and diabetes mellitus, patient on beta blockers, anti convulsant or anti-psychotics.

The study was conducted in 60 patients, divided randomly into 2 groups of 30 patients each. In the statistical analysis of our study, continuous variables were presented as mean for parametric data and median if the data was non parametric or skewed. Student-t test was applied for calculation of statistical significance. Categorical variables were expressed as frequencies and percentages. P <0.05 was taken to indicate a statistically significant difference.

Observation and Results

This study was conducted as a comparative, observational and hospital based study on 60 patients, divided into two groups of 30 each as Group G (Gabapentin group and Group C (Clonidine group) to compare hemodynamic responses to laryngoscopy and tracheal intubation.

Table 1: Mean heart rate

Heart rate(bpm)	Group G	Group C	P value
Baseline	75.7±4.62	78.3±5.478	=0.0592
1 minute	84.77±4.614	95.8±9.94	<0.0001
3 minutes	80.13±4.637	89.37±9.036	<0.0001
5 minutes	76.3±4.97	83.1±7.28	<0.0001
10 minutes	71.6±4.818	75.1±6.02	=0.0158

Gabapentin group showed a mean baseline heart rate (+/-SD) of 75.7±4.62. At 1 minute, 3 minute, 5 minute and 10 minute, the mean heart rates were 84.77±4.614, 80.13±4.637, 76.3±4.97, and 71.6±4.818 respectively. Clonidine group showed a mean baseline heart rate (+/-SD) of 78.3±5.478. At 1 minute, 3 minute, 5 minute and 10 minute interval, the mean heart rates were 95.8±9.94, 89.73±9.03, 83.1±7.28 and 75.1±6.02 respectively. As compared to the baseline mean heart rate, both the groups showed an increase in the mean heart rate at 1 min and then a gradual fall at subsequent time intervals. At each observation, the attenuation of heart rate in response to laryngoscopy and intubation in the Gabapentin group was clinically more than Clonidine group and statistically highly significant (p<0.0001) at 1minute, 3 minute ,5 minute and significant at 10 minute (p=0.0158).

Table2: Changes in mean systolic blood pressure

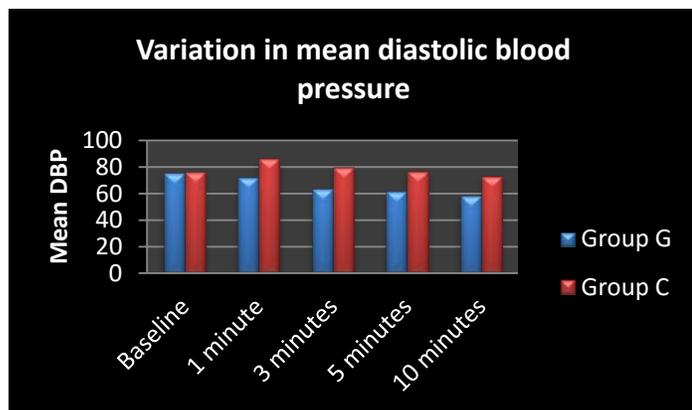
SBP (mm Hg)	Group G	Group C	P value
Baseline	117±4.80	120±7.49	=0.698
1 minute	123.8±4.07	131±6.96	<0.0001
3 minutes	112.8±3.896	126±7.08	<0.0001
5 minutes	109±3.79	119±6.06	<0.0001
10 minutes	106±3.83	112.6±6.345	<0.0001

The baseline mean and standard deviation of systolic blood pressure in group G was 117.6±4.80.The mean systolic blood pressures were 123.8±4.07, 112.8±3.896, 109±3.79 and 106±3.82 at 1minute, 3 minute, 5 minute and 10 minute intervals respectively from onset of

laryngoscopy. The baseline mean and standard deviation of systolic blood pressure in group C was 120 ± 7.49 . The mean systolic blood pressures were 131 ± 6.96 , 126 ± 7.08 , 119 ± 6.06 and 112.6 ± 6.345 at 1 minute, 3 minute, 5 minute and 10 minute intervals respectively from onset of laryngoscopy.

As compared to the baseline systolic blood pressure, both the groups showed an increase in the mean systolic blood pressure at 1 min and then a gradual fall at subsequent time intervals. The mean systolic blood pressure at 1 minute, 3 minute, 5 minute and 10 minute time interval was clinically less in Gabapentin group than in the Clonidine group. At 1, 3, 5 and 10 minutes p value was <0.0001 which was statistically highly significant indicating Gabapentin attenuates the systolic blood pressure response to laryngoscopy and intubation more than Clonidine.

Graph 1: Comparison of diastolic blood pressure (mm of Hg) of two groups



As compared to the baseline mean diastolic blood pressure, both the groups showed an increase in the mean diastolic blood pressure at 1 min and then a gradual fall at subsequent time intervals. The mean diastolic blood pressure at 1 minute, 3 minute, 5 minute and 10 minute time interval was clinically less in Gabapentin group than in the Clonidine group. Base line p value was 0.5476 but at 1, 5 and 10 minutes p value was <0.0001 which was statistically highly significant showing that Gabapentin

attenuates the diastolic blood pressure response to laryngoscopy and intubation more than Clonidine.

Table3: changes in mean arterial blood pressure

MAP(mm Hg)	Group G	Group C	P value
Baseline	89.289 ± 4.4	91 ± 7.294	$=0.2730$
1 minute	89.417 ± 4.442	101.2 ± 6.63	0.0001
3 minutes	80.3 ± 3.80	95.39 ± 6.12	0.0001
5 minutes	77.27 ± 4.163	91.03 ± 6.78	0.0001
10 minutes	74.61 ± 4.24	85.9 ± 6.58	0.0001

The baseline mean and standard deviation of mean arterial pressure in group G was 89.289 ± 4.4 . The mean arterial pressures were 89.41 ± 4.442 , 80.3 ± 3.804 , 77.27 ± 4.163 and 74.61 ± 4.239 at 1 minute, 3 minute, 5 minute and 10 minute time intervals respectively. The mean arterial pressure fell below the baseline value at 3,5 and 10 minutes). The baseline mean and standard deviation of mean arterial pressure in group C was 91 ± 7.294 The mean arterial pressure was 101.2 ± 6.63 , 95.39 ± 6.123 , 91.03 ± 6.784 and 85.9 ± 6.68 at 1 minute, 3 minute, 5 minute and 10 minute time intervals respectively. As compared to the mean value of baseline mean arterial blood pressure, both the groups showed an increase in the mean arterial blood pressure at 1 min and then a gradual fall at subsequent time intervals The mean blood pressure at 1 minute, 3 minute, 5 minute and 10 minute time interval was clinically less in Gabapentin group than in the Clonidine group. At all time intervals, p value was <0.0001 indicate of that this difference was statistically highly significant. The fall to baseline value in the gabapentin group was at 3rd minute and in Clonidine group at 5th minute and statistically it was significant, indicating Gabapentin group showed earlier recovery to baseline values compared to Clonidine group.

Table 4: Post-Operative Period Sedation Score
Ramsay sedation score

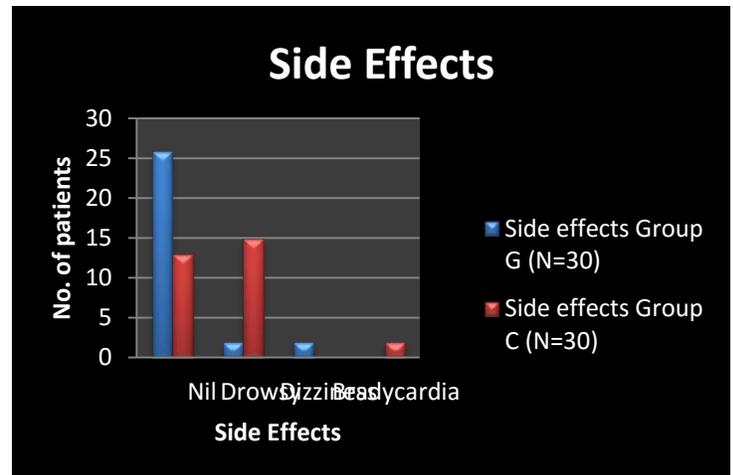
Sedation score	Group G	Group C	p-value
Score 0	-	-	--
Score 1	18	2	
Score 2	10	9	
Score 3	2	19	
Total	30	30	
Mean ± SD	1.46±0.63	2.56±0.64	0.0001

In Gabapentin group, 18 patients had a sedation score of 1 followed by 10 with sedation score of 2 and rest 2 had a score of 3. In Clonidine group 2 patients had a sedation score of 1 followed by 9 with sedation score of 2 and rest 19 had a score of 3. The difference in mean sedation score was highly statistically significant indicating that clonidine provides more sedation as compared to Gabapentin (p value < 0.0001).

Table 5: Side effects

Side effects	Group G (N=30)	Group C (N=30)
Nil	26	13
Drowsy	2	15
Dizziness	2	0
Bradycardia	0	2
Inference	Incidence of side effects was significantly less in Group G with P<0.001	

Graph 2



In Gabapentin group 2 of the patients complained of drowsiness, 2 patients complained of dizziness whereas rest 26 patients did not report any side effects. In Clonidine group 15 of the patients complained of drowsiness whereas 2 patients had an episode of bradycardia which was treated by injection atropine 0.6mg. Rest 13 did not report any side effects. 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. Two patients had an episode of bradycardia in the Clonidine group whereas none of the patients in gabapentin group had bradycardia. Overall the Incidence of side effects was significantly less in Group G with P<0.001.

Discussion

The laryngoscopy and endotracheal intubation lead to a reflex cardiovascular response which attributes to hypertension and tachycardia in adults. Though well tolerated in healthy adult patients, it can has catastrophic consequences in patients with coronary artery disease and cerebrovascular diseases. To achieve this it is important to understand the dynamic interactions between the drugs used, onset of drug effects and the delicate balance between the therapeutic effects of drugs and the effects of the noxious stimuli. One should avoid over treating these

responses which are usually short lived and well tolerated by most patients. Clonidine and Gabapentin are the two drugs which are studied extensively for suppression of hemodynamic response to laryngoscopy and intubation. Earlier several studies have documented the attenuating effect of clonidine on hemodynamic responses to airway manipulation. Ghignone et al, Mikawa et al and Raval and co workers noted that the response to heart rate following laryngoscopy and intubation was less in clonidine premedicated group as compared to diazepam. Carabine et al they studied that on i.v. clonidine 15 min before to intubation also found less increase in heart rate and blood pressure in response to laryngoscopy and intubation, Vyankatesh et al. Deepshikha et al also found similar results in their study with i.v. clonidine. Joshi Vyankatesh S et al also concluded that patients receiving oral clonidine had significantly less haemodynamic response to laryngoscopy and intubation as compared to the control group. Harshvardhana et al also found similar results with i.v clonidine given 15 min before intubation. They also found reduced requirement of thiopentone and vecuronium and arousable sedation after extubation as compared to the control group. Sameena kousar et al compared iv clondine with i.v fentanyl and found that the attenuation of sympathetic response to laryngoscopy and intubation was better with clonidine than fentanyl. Rushikesh et al also noted significant reduction in MAP and HR in patients receiving i.v. clonidine as compared to the control group. Study conducted by Vinay Marulasiddappa et al comparing clonidine and lignocaine for hemodynamic response to laryngoscopy and intubation in neurosurgery cases showed that there was less increase in HR in patients receiving clonidine than lignocaine. They also concluded that there was no rise in SBP after intubation, and the SBP continued to be below baseline parameters after administration and intubation.

In our study we have compared oral clonidine 200 mcg and oral gabapentin 900 mg given as premedication 2 hours prior to surgery to attenuate hemodynamic response to laryngoscopy and orotracheal intubation. We found that there was rise in SBP, DBP, MAP and HR to laryngoscopy and orotracheal intubation at 1 minute in both the groups. Further the SBP, DBP, MAP and HR dropped below the baseline parameters in both the groups after 1 minute of intubation. But as compared to Group C receiving Clonidine, Group G receiving Gabapentin had less hemodynamic response to laryngoscopy and orotracheal intubation.

In our study we have compared clonidine an α_2 adrenergic receptor agonist and an established drug in attenuation of hemodynamic responses to laryngoscopy and intubation with gabapentin which belongs to the class of anticonvulsants and is now being increasingly used not only for neuropathic pain but also for pre and post operative analgesia as well as in control of perioperative stress responses including that of laryngoscopy and intubation.

Clonidine and gabapentin have certain adverse effects inherent to their structure. Clonidine can cause sedation, dry mouth, hypotension and marked bradycardia. The most frequent side effects reported with gabapentin are, dizziness, ataxia, fatigue, unsteadiness, nystagmus, headache, tremors, diplopia, and nausea. In our study, none of the patients at any time during the study had developed any episode of severe bradycardia (heart rate less than 40 per minute or required injection atropine) and severe hypotension with systolic blood pressure less than 90mmHg, or required intravenous fluid resuscitation and vasopressors.

Conclusion

Our study concluded that, though gabapentin and clonidine both were not able to completely attenuate the

rise in heart rate ,but gabapentin was more effective and better than clonidine in attenuating hemodynamic response to laryngoscopy and intubation.

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Ethical approval: The study was approved by the Institutional Ethics Committee GMC Bhopal

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