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Original Research Paper

Anaesthesiology

ATTENUATION OF HEMODYNAMIC RESPONSES DURING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION: A COMPARATIVE STUDY BETWEEN ORAL GABAPENTIN AND ORAL CLONIDINE.

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ABSTRACT

Background and Aims: Various methods have been used to supress pressor response and tachycardia during laryngoscopy and endotracheal intubation. We compared oral gabapentin and oral clonidine for surgeries under general anaesthesia. **Methods:** After clearance from IEC, sixty patients receiving general anaesthesia were divided into two groups, GROUP C and GROUP G. Group C received tablet Clonidine 200 μg. Group G received capsule Gabapentin 700 mg. Data was analysed using Student-t test for normal distribution and Mann-Whitney U test when not normally distributed. Qualitative data (n%) was compared using Chi-square test. **Result:** Hemodynamic parameters rise on laryngoscopy and 1 minute after endotracheal intubation in both the groups. Further hemodynamic parameters dropped below baseline in both groups subsequently. But as compared to Group C, Group G has less rise in hemodynamic variables. **Conclusion:** Gabapentin was more effective and better than clonidine in attenuating hemodynamic response to laryngoscopy and endotracheal intubation overall.

KEYWORDS : Clonidine, gabapentin, pressor response attenuation.

INTRODUCTION:

Laryngoscopy assisted endotracheal intubation is an integral and essential component of general anaesthesia. It results in sympathetic stimulation and release of catecholamine mainly nor-epinephrine leading to haemodynamic variations in blood pressure and heart rate. The major cause of sympathoadrenal response is believed to arise from stimulation of supraglottic region by laryngoscope blade, tracheal tube placement and cuff inflation contributing little to additional stimulation[1,2].

Clonidine an alpha-adrenoceptor agonist introduced into clinical practice as an antihypertensive agent; has untoward side effects like sedation, drowsiness, dizziness, bradycardia and profound hypotension. However these properties are beneficial when it is used as an adjunct to anaesthesia. It is effective for preoperative sedation, analgesia and perioperative hemodynamic stability. Many workers through their studies have found that clonidine prevents cardiovascular stress response to laryngoscopy and intubation[4,5,6].

Gabapentin is an analogue of gamma amino butyric acid and is used as an anticonvulsant drug. In addition it has been shown to be effective in controlling neuropathic pain. In recent times gabapentin has been used in several randomized controlled trials for attenuation of hemodynamic response[7,8] to laryngoscopy and intubation.

MATERIAL AND METHODS:

After approval from Institutional Ethics Committee, the study was done on 60 patients of ASA grade 1 and 2 in age group of 20-50 years admitted for elective surgery under general anaesthesia. Informed written consent was taken from all the patients.

All patients undergone pre-anaesthetic check-up prior to surgery and routine investigations were done such as CBC (complete blood count), urine examination, coagulation studies, blood sugar, blood urea and serum creatinine, serum electrolytes, liver function tests and ECG (if age more than 40 years). All the patients were divided into two groups of 30 patients each (Group G and Group C). On the morning of surgery, the study drug (gabapentin 700 mg in group G and clonidine 200 mcg in group C) was given orally with a sip of water two hours prior to surgery.

In preoperative waiting area, patients were assessed and wheeled in the operation theatre. Baseline heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure were recorded. Wide bore intravenous line was secured and all patients were started on Lactated Ringer solution 5 ml/kg. Premedication was done with i.v Glycopyrrolate 0.004 mg, i.v Ondansetron 0.1 mg, i.v. Fentanyl 2μg/kg and pre oxygenated with 100% oxygen for 3 minutes. Thereafter, patients were induced with i.v Propofol 2 mg/kg followed by i.v Vecuronium 0.1 mg/kg to facilitate muscle relaxation.

After 3 minutes of assisted ventilation, laryngoscopy was performed and patients were intubated with a single use, high volume, low pressure, cuffed pvc endotracheal tube of appropriate internal diameter.

Care was taken for laryngoscopy to be less than 20 seconds in all the patients. Continuous ECG and $EtCO_2$ monitoring was done to look for any events of cardiac arrhythmias and desaturation respectively. At the end of 10 minutes after intubation, volatile anaesthetic agent was started and surgery was allowed to commence. Anaesthesia was maintained with 50% Nitrous Oxide + 50% Oxygen + volatile anaesthetic agent and i.v Vecuronium for muscle relaxation.

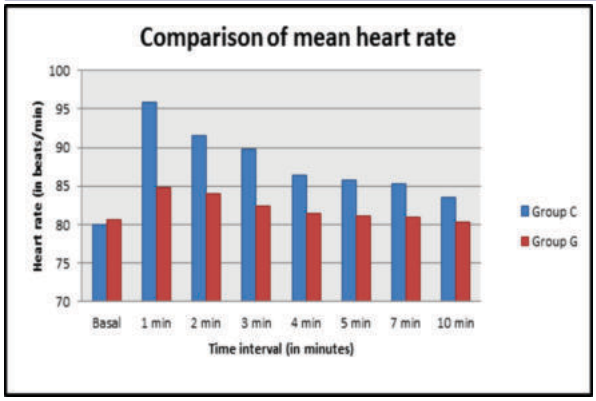
Heart rate, systolic blood pressure, diastolic blood pressure & mean arterial pressure were recorded at 1, 2, 3, 4, 5, 7 and 10 minutes after endotracheal intubation. All the patients were observed for haemodynamic changes and side effects.

RESULTS:

Table 1- Mean heart rate:

Time	Heart rate (Beats per min)		P value
	Group Clonidine	Group Gabapentin	
Basal	80.03±7.69	80.97±5.17	0.69
1 min	95.8±9.94	84.77±4.61	<0.0001
2 min	91.6±9.59	83.93±3.83	<0.0001
3 min	89.73±9.04	82.37±3.50	<0.0001
4 min	86.43±7.98	81.47±3.52	0.003
5 min	85.83±7.66	81.13±3.77	0.005
7 min	85.33±7.48	80.93±3.68	0.007
10 min	83.5±5.46	80.37±3.17	0.03

Comparison of mean heart rate:
P-value <0.05 was considered significant.



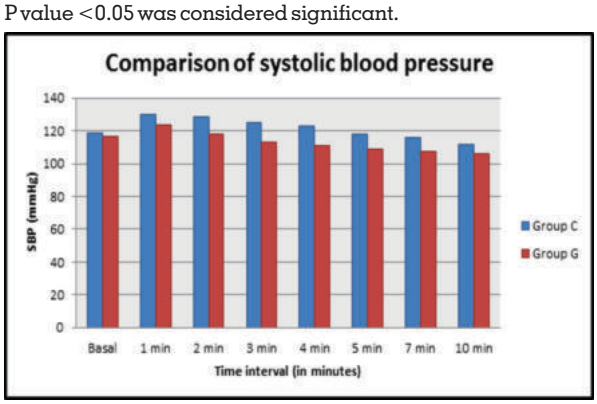
Graph 1- Mean heart rate:

Basal mean HR in both groups were comparable initially, but thereafter attenuation of HR in the Gabapentin group was clinically much better than Clonidine group and statistically highly significant ($p<0.0001$) at 1, 2, 3 minutes and significant (<0.05) at 4, 5 and 7 minutes.

Table 2- Systolic Blood Pressure:

Time	SBP (mmHg)		P value
	Group Clonidine	Group Gabapentin	
basal	118.73±7.39	116.6±4.8	0.19
1 min	130.03±6.96	123.83±4.08	<0.0001
2 min	128.6±7.12	117.8±3.54	<0.0001
3 min	125.17±7.08	112.83±3.9	<0.0001
4 min	122.6±6.43	110.9±3.77	<0.0001
5 min	118.23±6.06	108.8±3.79	<0.0001
7 min	115.93±5.51	107.23±3.9	<0.0001
10 min	111.57±6.34	105.77±3.83	<0.0001

Comparison of systolic blood pressure:
P value <0.05 was considered significant.



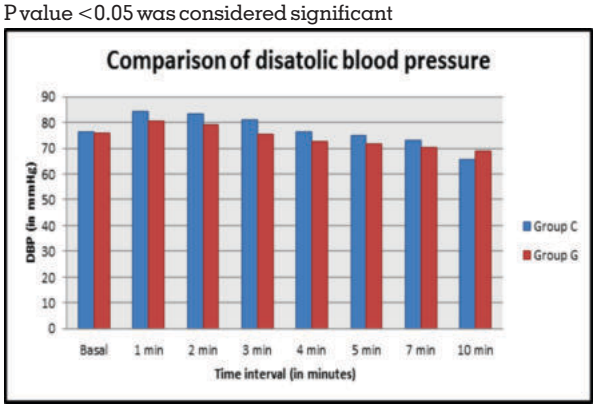
Graph 2- Systolic Blood Pressure:

The mean SBP fell below base line at 3rd min in Gabapentin and at 5th min in Clonidine group indicating that Gabapentin attenuates SBP response to laryngoscopy and intubation better than Clonidine.

Table 3: Diastolic Blood Pressure:

Time	DBP (mmHg)		P value
	Group Clonidine	Group Gabapentin	
Baseline	76.43±8.03	75.63±6.45	0.67
1 min	84.17±6.79	80.87±6.04	0.049
2 min	83.17±6.07	79.2±5.65	0.015
3 min	80.83±5.98	75.3±5.97	0.001
4 min	76.27±6.76	72.8±5.34	0.04
5 min	74.7±6.06	71.7±5.36	0.03
7 min	73.27±6.18	70.37±5.12	0.048
10 min	65.43±3.67	68.97±4.8	0.007

Comparison of diastolic blood pressure:
P value <0.05 was considered significant



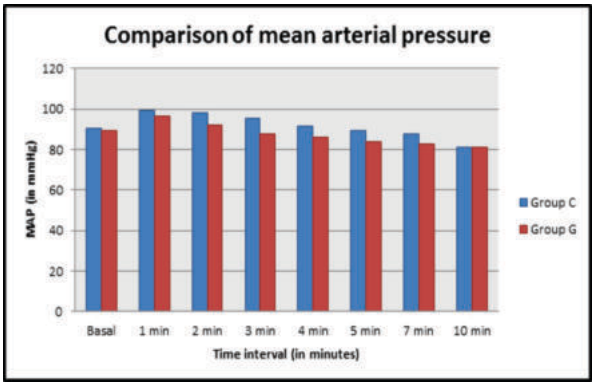
Graph 3: Diastolic Blood Pressure:

The mean DBP fell below base line at 3rd min in Gabapentin group and at 4th min in Clonidine group indicating that Gabapentin attenuates DBP more than Clonidine.

Table 4- Mean Arterial Pressure:

Time	MAP		P value
	Group C	Group G	
Basal	90.53±7.27	89.29±4.3	0.435
1 min	99.46±6.4	95.19±3.95	0.002
2 min	98.31±6.33	92.07±3.59	<0.0001
3 min	95.63±6.12	87.81±3.95	<0.0001
4 min	91.71±5.81	85.94±3.65	<0.0001
5 min	89.26±4.97	84.07±3.69	<0.0001
7 min	87.49±5.08	82.66±3.56	<0.0001
10 min	80.79±4.77	81.23±3.36	0.67

Comparison of mean arterial pressure:
P value <0.05 was considered significant.



Graph 4- Mean Arterial Pressure:
The MAP at all the time intervals was clinically lesser in Gabapentin group than in Clonidine group except at 10 min. MAP fell to baseline at 3rd min in Gabapentin group and at 5th min in clonidine group indicating that Gabapentin showed earlier recovery to baseline values.

DISCUSSION:
As Clonidine has narrow therapeutic index, most of the earlier clinical trials have utilized either 200 mcg i.e. 0.2 mg (Waikar C et al[10], Joshi V et al[14], Raval D and Mehta[3], Marashi SM[17]) or 300 mcg i.e. 0.3 mg (Praveen S et al[12], Sharma S et al[15], Jehangir A et al[9]) oral dose with 300 mcg showing more hypotension and bradycardia, so we decided to take 200 mcg dose for our study. On the other hand, Gabapentin has a wide range of therapeutic dose and has been used in several doses like 400 mg (Memis and Turan[8], Sharma S[15]), 600 mg (Bafna et al[16]), 800 mg (Upendra K[11], Sharma S[15], Kiran and Verma D[18], Memis and Turan[8]), 900 mg (Waikar C[10], Marashi SM[17]) and 1000 mg (Bafna et al[16]). It has been observed that there was significant

rise in HR and BP with doses 400 mg and 600 mg, whereas 800 mg, 900 mg and 1000 mg better attenuated hemodynamic responses, but higher doses were associated with sedation and dizziness in postoperative period. Hence, we decided to take an intermediate dose of 700 mg for our study as no previous trials have used this dose.

Haemodynamic changes:

In our study, we have compared oral clonidine 200 mcg and oral gabapentin 700 mg given as a premedication drug 2 hours prior to surgery to attenuate hemodynamic response to laryngoscopy and endotracheal intubation. We found that there was rise in SBP, DBP, MAP and HR to laryngoscopy and endotracheal intubation at 1 minute after intubation in both the groups. Further the SBP, DBP, MAP and HR dropped below the baseline parameters in both the groups subsequently. But as compared to Group C receiving Clonidine; Group G receiving Gabapentin has less rise in hemodynamic variables in response to laryngoscopy and endotracheal intubation.

Above hemodynamic changes found in our study were in accordance with the studies done by Marashi SM et al[17] in 2009 (clonidine vs gabapentin), Waikar C et al[10] in 2014 (clonidine vs pregabalin vs gabapentin), Upendra Kumar Kapse and Pradnya Milind Bhalerao11 in 2016 and by Sharma S et al15 in 2012.

However, Shreedhara NS et al[13] in 2014, conducted a similar study and concluded that both clonidine and gabapentin attenuate hemodynamic response to laryngoscopy and intubation, but clonidine is better drug compared to gabapentin and tachycardia response was significantly attenuated which does not correlate with our study.

Although the molecular targets of gabapentin remains unknown, the inhibition of Ca^{2+} flux in muscle cells with a consequent inhibition of smooth muscle contraction might explain the effectiveness of gabapentin in attenuation of the pressor response to laryngoscopy. Thus it may act in a manner similar to Ca^{2+} channel blockers.

In our study, none of the patients at any time during the study developed any episode of severe bradycardia (heart rate less than 40 per minute or required inj. atropine) and severe hypotension with systolic blood pressure less than 90mmHg or required intravenous fluid resuscitation and vasopressors support.

CONCLUSION:

We concluded that although 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 (HR, SBP, DBP and MAP) to laryngoscopy and endotracheal intubation overall.

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Conflicts of interest:

No conflicts of interest.

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