ORIGINAL RESEARCH PAPER

Volume-8 | Issue-6 | June-2019 | PRINT ISSN No. 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A COMPARATIVE STUDY OF ORAL CLONIDINE VERSUS ORAL GABAPENTIN PREMEDICATION IN ATTENUATION OF PRESSOR RESPONSE DURING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

Anaesthesiology

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ABSTRACT

Introduction : Laryngoscopy and endotracheal intubation are essential in maintaining the airway in elective surgeries , emergency surgeries and for mechanical ventilation in intensive care unit. Laryngoscopy and endotracheal intubation are powerful stimuli, which can increase a transient but marked sympathetic and sympatho-adrenal activity leading to tachycardia, hypertension and dysrhythmias. The aim of the present study is to compare the efficacy between oral clonidine and oral gabapentin pre-medication in attenuation of pressor response during Laryngoscopy and Endotracheal intubation.

Methods : A total of 80 patients aged between 20-50 years of both sexes belonging to American Society of anesthesiologists (ASA) physical status I and II scheduled for general anesthesia were randomized into two groups.

Group – G – Received Tab. Gabapentin 800mg, 90 minutes prior to surgery.

Group – C- Received Tab.Clonidine 0.3mg, 90 minutes prior to surgery.

Baseline heart rate [HR], systolic blood pressure [SBP], diastolic blood pressure [DBP] and rate pressure product [RPP] were recorded as 0 minute value just before induction. Thereafter heart rate, systolic blood pressure, diastolic blood pressure , mean arterial pressure and rate pressure product were recorded at 1, 3, 5 and 10 minutes after endotracheal intubation.

Result: At the Base Line and Induction the mean Heart rate in patients with clonidine group is higher when compared to the Gabapentin group which is statistically significant, after that from intubation onwards there is gradual decrease in Heart rate in the both groups and maintained a similar heart rate till 10 min. P value >0.05 in all the times after intubation. There is no significant difference in the mean SBP and MAP between groups at the Base Line and at Induction, P value is>0.5, and later at all time intervals SBP and MAP are lower in Clonidine group when compared to Gabapentin group. P value is <0.05. There is no significant difference in the mean DBP and RPP between groups at all time.

Conclusion:. Oral premedication with clonidine 0.3mg 90 minutes prior to induction of anesthesia is safe and effective compared to oral gabapentin 800mg to attenuate the pressor response during laryngoscopy and endotracheal intubation.

KEYWORDS

Laryngoscopy,Endotracheal intubation,Premedication,Pressor response.

INTRODUCTION:

Laryngoscopy and endotracheal intubation are essential in maintaining the airway in elective surgeries , emergency surgeries and for mechanical ventilation in intensive care unit. Laryngoscopy and endotracheal intubation are powerful stimuli, which can increase a transient but marked sympathetic and sympatho-adrenal activity leading to tachycardia, hypertension and dysrhythmias.(1,2,3,4,5,6,7) In patients with systemic hypertension, coronary artery disease, cerebrovascular diseases and intracranial aneurysms this pressor response leads to deleterious effects like left ventricular failure, pulmonary edema, myocardial ischemia,(8,9,10,11,12,) ventricular dysrhythmias and cerebral hemorrhage. .

Various anesthetic methods and drugs like volatile anesthetic agents, topical and intravenous lidocaine,(13,23) opoids(14) ,sodium nitroprusside(15) ,calcium channel blockers(17), nitroglycerine, beta blockers and dexmedatomidine(16) were used to avoid pressor response during laryngoscopy and intubation.

The aim of the present study is to compare the efficacy between oral clonidine and oral gabapentin pre-medication in attenuation of pressor response during Laryngoscopy and Endotracheal intubation.

MATERIAL AND METHODS : This study was conducted at King George Hospital, Visakhapatnam with approval from institutional scientific and ethics committee and written informed consent from all patients aged between 20-50 years of both sexes belonging to American Society of anesthesiologists (ASA) physical status I and II scheduled for general anesthesia.they are divided into two groups:

Group – G – Received Tab. Gabapentin 800mg, 90 minutes prior to surgery.

Group – C- Received Tab.Clonidine 0.3mg, 90 minutes prior to surgery

All patients who are undergoing planned elective surgery were assessed as per routine pre–operative protocol and all routine investigations were carried out and kept nil by mouth for 8 hours before surgery. Pre-medicated with tab.alprazolam 0.5mg orally on the day before surgery.

Inclusion Criteria:

(1) Age 20-50 years.
(2) American Society of Anesthesiologist status 1 and 2

Exclusion Criteria:

(1) Difficult airway
(2) Allergy to drugs

Patients were randomly allocated to one of two groups by allocation sequences generated by computer generated random number table. Group allocation was done by an anesthesiologist who was not the part of the study.

The study medications were given by staff nurse who was not the part of data collection and analysis. Group C received oral clonidine 0.3mg and group 'G' received oral gabapentin of 800mg 90 minutes prior to surgery with sips of water. In the operation theatre, electrocardiogram, non-invasive BP and pulse oximeter were connected and basal parameters recorded. Intravenous (IV) access with 18G cannula was established.Patients were premedicated. Preoxygenated with 100% oxygen for 3 minutes. Anesthesia was induced with inj. Thiopentone sodium 5mg/kg till loss of patients responsiveness to verbal commands and loss of eyelash reflex. Laryngoscopy and endotracheal intubation was facilitated with intravenous succinyl choline 2mg/kg. Anesthesia was maintained with N2O+O2+ Sevoflurane and muscle relaxation was achieved with intravenous vecuronium 0.1mg/kg. Both groups were intubated with same anesthesiologist throughout the study, in a single attempt and duration of laryngoscopy was within 15 seconds.

Baseline heart rate [HR], systolic blood pressure [SBP], diastolic blood pressure [DBP] and rate pressure product [RPP] were recorded as 0 minute value just before induction. Thereafter heart rate, systolic blood pressure, diastolic blood pressure , mean arterial pressure and rate pressure product were recorded at 1, 3, 5 and 10 minutes after endotracheal intubation. Sevoflurane was stopped 5 minutes before

skin closure and nitrous oxide was stopped after completion of surgery. Muscle relaxation was reversed with injection glycopyrrolate10 micrograms /kg and neostigmine 40micrograms /kg. Patients were extubated after all extubation criteria met and after the return of protective airway reflexes .All patients were observed in post anesthesia care unit. The findings of the study were noted.

Clonidine causes dry mouth, sedation, hypotension and marked bradycardia. Gabapentin causes somnolence, dizziness, ataxia, nystagmus, headache, tremors, diplopia and nausea.

Few side effects like sedation and drowsiness was observed in some patients and none of the side effects warranted any active clinical intervention. However single use of these drugs is unlikely to cause above effects.

RESULTS:

HR,SBP,DBP,MAP and RPP were measured at baseline effects. RESULTS**:** HR,SBP,DBP,MAP and RPP were measured at baseline and after 1,3,5,10 minutes after intubation.

The Mean Age of patients who received Gabapentin is 39±18 Years, the Mean Age of patients who received Clonidine is 35±98 Years and this difference is not statistically significant.

The Mean Weight of patients who received Gabapentin is 58±60 Years, the Mean Age of patients who received Clonidine is 56.68 Years and this difference is not statistically significant.

At the Base Line and Induction the mean Heart rate in patients with clonidine group is higher when compared to the Gabapentin group which is statistically significant, after that from intubation onwards there is gradual decrease in Heart rate in the both groups and maintained a similar heart rate till 10 min. P value >0.05 in all the times after intubation.

There is no significant difference in the mean SBP between groups at the Base Line and at Induction, P value is>0.5, and later alltime intervals there is a significant mean differences in SBP between groups and it is lower in Clonidine group when compared to Gabapentin group. P value is <0.05.

There is no significant difference in the MAP between groups at the Base Line and at Induction, later at alltime intervals there is a significant mean differences in MAP between groups and it is lower in Clonidine group when compared to Gabapentin group.

P value at baseline and at induction.>0.05.After intubation at all times at 1min, 3min,5min,10min<0.05

Table 1 : Mean Heart rates at different time intervals

	Group	N	Mean	Std. Deviation	P Value
HR Base Line	Gabapentin	40	82.75	12.209	0.001*(Sig)
	Clonidine	40	94.3	14.774	
HR Induction	Gabapentin	40	87.93	15.234	0.038*(Sig)
	Clonidine	40	96.15	19.393	
HR Intubation	Gabapentin	40	102	14.803	0.348(N.S)
	Clonidine	40	98.63	17.07	
HR 1Min	Gabapentin	40	99.3	11.938	0.872(N.S)
	Clonidine	40	98.78	16.68	
HR 3Min	Gabapentin	40	91.58	13.878	0.343(N.S)
	Clonidine	40	94.6	14.493	
HR 5Min	Gabapentin	40	87.78	11.335	0.858(N.S)
	Clonidine	40	88.28	13.411	
HR 10Min	Gabapentin	40	82.9	11.86	0.978(N.S)
	Clonidine	40	82.83	12.015	

Table 2: Mean Systolic Blood pressure at different time intervals

	Group	N	Mean	Std. Deviation	Sig. (2-tailed)
SBP Base Line	GABAPENTIN	40	120.35	11.226	0.801(N.S)
	CLONIDINE	40	119.7	11.717	
SBP Induction	GABAPENTIN	40	120.85	12.15	0.219(N.S)
	CLONIDINE	40	116.83	16.537	
SBP Intubation	GABAPENTIN	40	150.13	23.213	0.003(Sig)
	CLONIDINE	40	133.33	25.597	
SBP 1Min	GABAPENTIN	40	148.58	19.311	0.001(Sig)
	CLONIDINE	40	134.15	16.285	
SBP 3Min	GABAPENTIN	40	137.25	15.676	0.001(Sig)
	CLONIDINE	40	121.88	11.368	
SBP 5Min	GABAPENTIN	40	123.78	15.741	0.001(Sig)
	CLONIDINE	40	110.95	13.5	
	CLONIDINE	40	107.28	7.211	

No difference in age and weight distribution in both oral clonidine and gabapentin group.

Both drugs are equally effective in controlling HEART-RATE and DBP.

Clonidine is superior to gabapentin in controlling SBP and MAP. It is statically significant.

Clonidine is superior in controlling RPP compared to gabapentin but it is statically in-significant.

Table 3 : Mean RPP values in two groups

	Group	N	Mean	Std. Deviation	P value
RPP	GABAPENTIN	40	18981.80	13774.168	0.3 Not Significant
	CLONIDINE	40	14831.78	3025.474	

Table 4 : Mean Diastolic Blood Pressure at different intervals
Table 5: Mean arterial pressure at different time intervals

	Group	N	Mean	Std. Deviation	Sig. (2-tailed)
DBP Base Line	GABAPENTI	40	79	8.212	0.064(N.S)
	CLONIDINE	40	82.93	10.351	
DBP Induction	GABAPENTI	40	77.75	10.923	0.686(N.S)
	CLONIDINE	40	76.75	11.133	
DBP Intubation	GABAPENTI	40	93.55	11.616	0.316(N.S)
	CLONIDINE	40	90.78	12.962	
DBP 1Min	GABAPENTI	40	90.45	9.674	0.126(N.S)
	CLONIDINE	40	86.58	12.537	
DBP 3Min	GABAPENTI	40	84.05	9.873	0.153(N.S)
	CLONIDINE	40	80.88	9.801	
DBP 5Min	GABAPENTI	40	80.13	6.595	0.001(N.S)
	CLONIDINE	40	74.43	10.114	
DBP 10Min	GABAPENTI	40	77.45	7.096	0.335(N.S)
	CLONIDINE	39	72.36	1246.996	

DISCUSSION :

Gabapentin readily crosses blood-brain-barrier and its concentration in brain is nearly similar to that present in blood. So gabapentin at its higher concentration in plasma and brain tissue prevent peripheral and central sensitization by decreasing hyper-algesia and allodynia associated with surgical manipulation by inhibiting membrane bound voltage gated Ca^{++} channels .Gabapentin attenuates the pressor response by inhibiting membrane bound Ca^{++} channels and subsequent release of excitatory neurotransmitters in pain pathways by binding to α_2- subunit of presynaptic voltage- gated Ca^{++} channels. (18,19,20,)

Clonidine is mostly used as an antihypertensive drug and it also has an analgesic, sedative and anxiolytic properties. By its central sympatholytic action, it attenuates the pressor response to any surgical stimulus and improves peri-anesthetic CVS stability by central $_2$-agonist activity. The study population between 20 years to 50 years of age is selected because elderly patients more than 60 years often are on drugs such as oral hypoglycemic drugs, anticoagulants, antidepressants, hypnotics and anti-hypertensive drugs which interfere with study drugs and elderly patients also exhibit increased sensitivity to drugs which causes increased adverse effects.They also have other co-existing illness like coronary artery diseases, COPD, myocardial ischemia and other diseases.

It is known that response to laryngoscopy is great with increasing force and duration of laryngoscopy, the elevation in arterial pressure typically starts within 5 seconds of laryngoscopy and increased to peak between 1 minute to 2 minutes and returns to baseline value within 5 minutes. In this study, the mean duration of laryngoscopy and intubation didn't exceed 11 seconds.

Gabapentin and clonidine were choosen for this study because both the drugs have less side effects compared to other iv drugs and have anxiolytic , sedative and analgesic properties. **Singhal and colleagues et al** Studied attenuation of pressor response during laryngoscopy and endotracheal intubation with oral clonidine 0.2mg and oral gabapentin 900mg premedication.(21). **Nagol Shekharappa Shreedhara et al** studied attenuation of pressor response during laryngoscopy and endotracheal intubation with oral gabapentin 900mg and oral clonidine 0.2mg .(22).The present study coincides with both these studies. There is no difference in age and weight distribution in both oral clonidine and gabapentin group.Both drugs are equally effective in controlling Heart rate and DBP.Clonidine is superior to gabapentin in controlling SBP and MAP. It is statically significant.

Clonidine is superior in controlling RPPcompared to gabapentin but it is statically in-significant. Hence,both drugs oral clonidine 0.3mg and oral gabapentin 800mg are equally effective in controlling HR and DBP at 0, 1, 3, 5 and 10 minutes after intubation. Clonidine 0.3mg is effective compared to gabapentin 800mg in controlling the systolic blood pressure, mean arterial pressure and it is statistically significant. Clonidine is superior to gabapentin in controlling RPP but it is statically not-significant**.**

CONCLUSION:

Both oral clonidine and gabapentin attenuate the pressor response during laryngoscopy and endotracheal intubation. The attenuation of pressor response is by far greater with oral clonidine compared to oral gabapentin Hence it is concluded that oral premedication with clonidine 0.3mg 90 minutes prior to induction of anesthesia is safe and effective compared to oral gabapentin 800mg to attenuate the pressor response during laryngoscopy and endotracheal intubation.

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