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COMPARATIVE STUDY OF RISKS AND BENEFITS OF ORAL CLONIDINE AND ORAL GABAPENTIN PREMEDICATION IN ATTENUATING THE HEMODYNAMIC RESPONSE FOLLOWING LARYNGOSCOPY AND TRACHEAL INTUBATION

Anaesthesiology

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ABSTRACT

To evaluate & compare the benefits and risks of clonidine and gabapentin.this randomized double blind study was conducted in dept of anaesthesiaSafdarjung Hospital, New Delhi. 99 ASA-1 Adults patients (18-45 years) of either sex scheduled for elective orthopaedic and general surgical procedures were enrolled into the study. Sample of 99 patients was required assuming effect size as 30%, level of significance 5%, power of study 75% using independent t-test on software G-power-3.1. Patients with (BMI) Body mass index more than 30,hiatal hernia, gastroesophageal reflux, history of allergy to study drugs history of cardiovascular (HT, MI), neurologic, cerebrovascular, respiratory, hepatic and renal disease and patients having difficult intubation (prolonged laryngoscopic time more than 30 seconds) or requiring urgent surgery were excluded from the study. Patients were randomly divided into 3 equal groups of 33 each according to a computerised random table. All patients received premedication drugs 120 minutes before admission to the operating room. GROUP-1. Patients received 0.25mg alprazolam HS night before surgery & 0.3mg clonidine tablets 2 hours before surgery. GROUP-2. Patients received 0.25mg alprazolam HS night before surgery & 600 mg gabapentintablets 2 hours before surgery. GROUP-1.Patients received only 0.25mg alprazolam HS night before surgery. All patients underwent pre-medication with tablet alprazolam 0.25 mg and rantac 150 mg night before the surgery.They received the designated study drug on the morning 2 hour prior to the planned surgery by a person not actively involved in the study. In the operation theatre intravenous cannula, ECG, NIBP, Pulse Oximeter applied.Inside the O.T. after commencing standard monitoring for ECG, NIBP, SPO2, three baseline readings for heart rate and blood pressure were taken at interval of 1 minute, the mean of three readings was taken as baseline parameter. Patients received 2 mcg/kg fentanyl and 0.03mg/kg midazolam intravenously 5 minutes before induction of anaesthesia. All patients will be preoxygenated for 3 min with 100% oxygen and anaesthesia was induced with 5mg/kg thiopental sodium. The patient was intubated with appropriate size ETT &macintosh blade 3 minutes after neuromuscular blockade with 0.1mg/kg vecuronium bromide.Anaesthesia was maintained with 50% N2O in oxygen with 0.8% Isoflurance. Heart rate, systolic, diastolic and mean arterial blood pressure was recorded before induction of anaesthesia, before laryngoscopy and at 1, 3, 5 & 10 minutes after intubation. In our study, Hypertension was defined as SBP > 25% of baseline or 150 mm Hg which ever was higher. Hypotension was defined SBP < 25% of baseline value or 90 mm Hg which ever was lower. Tachycardia was defined as HR > 25% of baseline. Bradycardia was defined as HR < 50 beats/min or decrease in more than 25% of baseline. Arrhythmia was defined as ventricular or supra ventricular premature beat or any rhythm other than sinus. Incidence of all these parameter were recorded in all three groups. If hypertension occurred within 7 minutes, isoflurane was increased. If there was hypotension in above period, then fluid challenge was given. If there was tachycardia associated with hypotension then fluid challenge was given or if associated with hypertension then isoflurane was increased + narcotic was added. If there was bradycardia then that was treated with injection atropine.**Conclusion:** The pressure response to intubation is a detrimental factor in patients. Hence we compared clonidine and gabapentin in fixed doses to know their effectiveness in reducing the haemodynamic responses to intubation.

KEYWORDS

Clonidine, Gabapentin, Tracheal intubation ,Laryngoscopy

INTRODUCTION

Laryngoscopy and tracheal intubation is gold standard for patients undergoing operation under general Anaesthesia but it is associated with hemodynamic and responses consisting of increased circulating catecholamines, heart rate(HR), blood pressure(BP), myocardial oxygen demand and dysrhythmias due to reflex increase in sympathoadrenal activity(2,23).This rise in heart rate & blood pressure are usually well tolerated by healthy individual but it may be fatal in patients with hypertension and Coronary artery disease.

Several techniques have been proposed to prevent or attenuate the heamodynamic responses following laryngoscopy and tracheal intubation such as deepening of plane of anaesthesia(3), using alternative methods of intubation (Macoylaryngos copicblade, intubating LMA), limiting duration of laryngoscopy for <15 seconds, several drugs such as vasodilators (NTG) (9,26,28), beta blockers (esmolol) (18,19,26,27), calcium channel blockers(nicardipin, verapamil,diltiazem) (15,20,24,25) and opiods (fentanyl, sufentenil, alfentanil, ramifentanil) (12,16,18,21,32,33), lignocaine (3,5,6,16,17,18,21), magnesium(21,41) etc.. but these agents are known to produce undesirable side effects like hypotension, severe bradycardia and may delay arousal. The method or drug of choice depends on many factors, including the urgency and length of surgery, choice of anesthetic technique, route of administration, medical condition of the patient, and individual preference.

Alpha 2-adrenoceptor agonists like clonidine were initially introduced as antihypertensive and are the most commonly used alpha 2 agonist by anaesthesiologists (13,29,34,40). It not only decreases sympathetic tone and attenuates the stress responses to anesthesia and surgery; but also causes sedation and analgesia so it may be helpful in reducing the hemodynamic response to laryngoscopy and intubation.

Gabapentin, a structural analogue of gamma-amino butyric acid is primarily an antiepileptic and it has been shown to be effective in neuropathic pain, diabetic neuropathy, post herpetic neuralgia and reflex sympathetic dystrophy. Furthermore, a growing body of evidence suggests that perioperative administration is efficacious for preoperative anxiolysis, postoperative analgesia, postoperative nausea and vomiting and delirium. Recently gabapentin has been effectively used to attenuate hemodynamic response to laryngoscopy and trachcal intubation (42,43,44,45).

Several studies have been conducted for studying clonidine & Gabapentin alone and their effect when given in different doses on attenuation of hemodynamic response such as BP, PR. But very limited literature is available till date to compare both of them and their effects on hemodynamic response.

The present study is designed as double blinded randamized controlled trial to compare the effect of preoperative oral clonidine 0.3mg and oral gabapentin 600mg on the changes in the systolic, diastolic, mean blood pressure and heart rate measured following laryngoscopy and tracheal intubation.

MATERIALS & METHODS

DATA SOURCE

After institutional board approval this randomized double blind study was conducted in dept of anaesthesiaSafdarjung Hospital, New Delhi. 99 ASA-1 Adults patients (18-45 years) of either sex scheduled for elective orthopaedic and general surgical procedures were enrolled into the study. Sample of 99 patients was required assuming effect size as 30%, level of significance 5%, power of study 75% using independent t-test on software G-power-3.1. Patients with (BMI) Body mass index more than 30,hiatal hernia, gastroesophageal reflux,

history of allergy to study drugs history of cardiovascular (HT, MI), neurologic, cerebrovascular, respiratory, hepatic and renal disease and patients having difficult intubation (prolonged laryngoscopic time more than 30 seconds) or requiring urgent surgery were excluded from the study.

RANDOMIZATION & DRUGS

Patients were randomly divided into 3 equal groups of 33 each according to a computerised random table. All patients received premedication drugs 120 minutes before admission to the operating room.

GROUP-1. Patients received 0.25mg alprazolam HS night before surgery & 0.3mg clonidine tablets 2 hours before surgery.

GROUP-2. Patients received 0.25mg alprazolam HS night before surgery & 600 mg gabapentintablets 2 hours before surgery.

GROUP-3. Patients received only 0.25mg alprazolam HS night before surgery.

TECHNIQUE OF ANAESTHESIA

All patients underwent pre-medication with tablet alprazolam 0.25 mg and rantac 150 mg night before the surgery.They received the designated study drug on the morning 2 hour prior to the planned surgery by a person not actively involved in the study. In the operation theatre intravenous cannula, ECG, NIBP, Pulse Oximeter applied.Inside the O.T. after commencing standard monitoring for ECG, NIBP, SPO2, three baseline readings for heart rate and blood pressure were taken at interval of 1 minute, the mean of three readings was taken as baseline parameter.

Patients received 2 mcg/kg fentanyl and 0.03mg/kg midazolam intravenously 5 minutes before induction of anaesthesia. All patients will be preoxygenated for 3 min with 100% oxygen and anaesthesia was induced with 5mg/kg thiopental sodium. The patient was intubated with appropriate size ETT &macintosh blade 3 minutes after neuromuscular blockade with 0.1mg/kg vecuronium bromide. Anaesthesia was maintained with 50% N2O in oxygen with 0.8% Isoflurance. Heart rate, systolic, diastolic and mean arterial blood pressure was recorded before induction of anaesthesia, before laryngoscopy and at 1, 3, 5 & 10 minutes after intubation.

In our study

Hypertension was defined as SBP > 25% of baseline or 150 mm Hg which ever was higher.

Hypotension was defined SBP < 25% of baseline value or 90 mm Hg which ever was lower.

Tachycardia was defined as HR > 25% of baseline.

Bradycardia was defined as HR < 50 beats/min or decrease in more than 25% of baseline.

Arrhythmia was defined as ventricular or supra ventricular premature beat or any rhythm other than sinus.

Incidence of all these parameter were recorded in all three groups.

If hypertension occurred within 7 minutes, isoflurane was increased. If there was hypotension in above period, then fluid challenge was given. If there was tachycardia associated with hypotension then fluid challenge was given or if associated with hypertension then isoflurane was increased + narcotic was added. If there was bradycardia then that was treated with injection atropine.

OBSERVATIONS AND RESULTS

Table 1-Age distribution

Group	Clonidine	Gabapentin	Control	
	Mean + SD	Mean + SD	Mean + SD	Significance
Age (years)	35.45 + 9.118	33.18+9.986	34.18+10.318	0.643

The mean age (yrs.) was comparable between the groups. Statistically the difference was not significant(P>0.05) between various groups.

Table-2 Sex Distribution

Sex	Clonidine	Gabapentin	Control	Total
Male	16	16	19	51
Female	17	17	14	48
Total	33	33	33	99

The mean sex distribution (M:F) were comparable between the groups and statistically the difference was insignificant.

Table-3 Weight Distribution

Groups	Clonidine	Gabapentin	Control	
	Mean + SD	Mean + SD	Mean + SD	Significance
Weight (kg)	55.58+9.401	52.39+10.642	56.94+10.727	0.188

The mean weight (Kg) was comparable between the groups. Statistically the difference was insignificant between the groups(P>0.05)

Table-4 BMI Distribution (BMI = Wt./Ht^2)

Groups	Clonidine	Gabapentin	Control	
	Mean + SD	Mean + SD	Mean + SD	Significance
BMI	23.09 + 3.339	21.45 + 3.251	22.48 + 3.261	0.129

The Mean BMI was comparable in between the groups and statistically the difference was in significant(P>0.05).

Table-5 Duration of laryngoscopy and tracheal intubation

Groups	Clonidine	Gabapentin	Control	
	Mean + SD	Mean + SD	Mean + SD	Significance
Duration (seconds)	17.36 + 2.289	17.52+ 2.884	17.79 + 2.484	0.793

The mean duration of laryngoscopy (seconds) was comparable between the groups and statistically the difference between the groups was insignificant(P>0.05).

Table-6 Heart rate before, at and after tracheal intubation in various groups

	Clonidine	Gabapentin	Control
	Mean	Mean	Mean
HR 0	86.18	91.82	92.18
HR 1	82.00	80.52	82.15
HR2	89.73	95.88	98.67
HR 3	88.76	94.61	98.39
HR 4	85.64	88.94	93.45
HR 5	79.33	82.58	89.94

HR 0 – baseline heart rate before induction

HR 1 – heart rate 3 minutes after induction and just before laryngoscopy
HR 2 - heart rate 1 min after intubation
HR 3 - heart rate 3 min after intubation
HR 4 – heart rate 5 min after intubation
HR 5 – heart rate 10 min after intubation

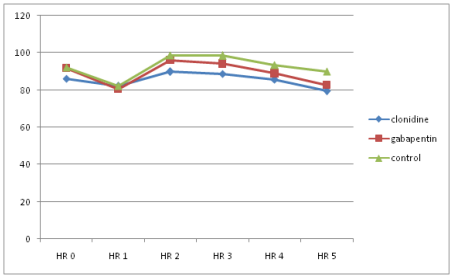

Figure-6 Heart rate before, at and after tracheal intubation in various groups

HR 0 – baseline heart rate before induction

HR 1 – heart rate 3 minutes after induction and just before laryngoscopy
HR 2 - heart rate 1 min after intubation
HR 3 - heart rate 3 min after intubation
HR 4 – heart rate 5 min after intubation
HR 5 – heart rate 10 min after intubation

Table-7 Systolic Blood Pressure before, at and after tracheal intubation in various groups

	Clonidine	Gabapentin	Control
	Mean	Mean	Mean
SBP 0	119.12	126.36	126.15
SBP 1	104.21	105	112.36
SBP 2	115.15	126.06	139.06
SBP 3	110.18	124.06	131.42
SBP 4	104.12	116.91	117.45
SBP 5	101.06	105.91	114.79

SBP 0 – baseline systolic blood pressure before induction

SBP 1 – systolic blood pressure 3 minutes after induction and just before laryngoscopy
SBP 2 – systolic blood pressure 1 min after intubation
SBP 3 - systolic blood pressure 3 min after intubation
SBP 4 – systolic blood pressure 5 min after intubation
SBP 5 – systolic blood pressure 10 min after intubation

SBP before induction of anesthesia in the clonidine group was119.12 mmgh (mean), as comparison to 126.36 mmhg and 126.15mmhg in gabapentine and control group respectively. Patients in clonidine group had more fall in SBP before induction as compared to patients in control group and gabapentine group. This fall in MBP was statistically significant. P value was (.045) for the clonidine and control group, and .038 for the clonidine and gabapentine group. The fall in MBP in control and gabapentine group was not significant. (P value - 0.997).

The SBP taken three minutes after the induction of anesthesia and just before laryngoscopy was 104.21mmhg (mean) in clonidine group, 105mmhg in gabapentine group and 112.36 mmhg in control group. There was more fall in SBP in clonidine group in comparison to patients in control group.(p value -.036) which is statistically significant. However, the fall in SBP in other groups were comparable The SBP taken one minute after laryngoscopy and intubation in patients who received clonidine was 115.15 mmhg (mean, as comparison to 126.06 mmhg in gabapentine group and 139.06 mmhg in control group. Patients in control group had more increased in SBP as comparison to clonidine and gabapentine group. This increase in SBP was more significant while comparing control and clonidine group. The p value was 0.000 for control and clonidine group , which is statistically significant.The p value for clonidine and gabapentine group was .053 and for control and gabapentine group was .016, both of which are also statistically significant. This concludes that the patient in clonidine group had less increase in SBP in comparision to gabapentine and control group,alsogabapentine group patients had less increase in SBP than control group The SBP taken three minute after laryngoscopy and intubation in patients who received clonidine group was 110.18 mm hg (mean) , as comparison to 124.06 mmhg in gabapentine group and 131.42 mm hg in control group. Patients in control group had more increased in SBP as comparison to clonidine and gabapentine group. The p value was 0.000 for control and clonidine group and for clonidine and gabapentine group was .003,both of which are statistically significant .However the p value result between the group control and gabapentine were comparable, P value being .176 which is statistically non significant. Hence, the clonidine group patient had less increased in SBP as compared to both the groups.

Similarly , the SBP taken five minutes after laryngoscopy in clonidine group was 104.12 mm hg (mean) , as comparison to 116.91mmhg in gabapentine group and 117.45mmhg in control group. The fall in SBP(mean) was more in clonidine group as compared to control and gabapentine group. The p value was 0.000 for control and clonidine group , and .000 for clonidine and gabapentine group, both of which are statistically significant. However, the p value for control and gabapentine group was .984, which is statistically non significant. Hence, the patients in clonidine group had more fall in SBP even after five minutes of laryngoscopy as compared to both the groups.

The SBP(mean) taken ten minutes after laryngoscopy in clonidine group was 101.16 mmhg (mean), as comparison to 105.91 mmhg in gabapentine group and 114.79 mmhg in control group. The fall in SBP(mean) was more in clonidine group as compared to control group. The p value was 0.000 for control and clonidine group, which is statistically significant. However, the p value for clonidine and gabapentine group was .227, which is comparable. There was more fall in SBP in gabatentine group in comparison to control group. The p value was .009 for control and gabapentine group, which is statistically significant. Hence, the patients in both clonidine and gabapentine group had more fall in SBP than the patients in control group, after ten minutes of laryngoscopy .

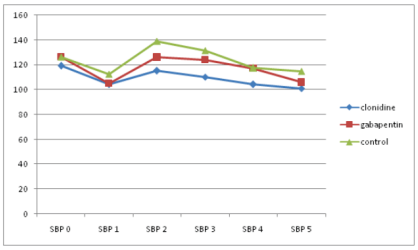

Figure-7 Systolic Blood Pressure before, at and after tracheal intubation in various groups

SBP 0 – baseline systolic blood pressure before induction

SBP 1 – systolic blood pressure 3 minutes after induction and just before laryngoscopy
SBP 2 – systolic blood pressure 1 min after intubation
SBP 3 - systolic blood pressure 3 min after intubation
SBP 4 – systolic blood pressure 5 min after intubation
SBP 5 – systolic blood pressure 10 min after intubation

Table-8 Diastolic blood pressure before, at and after tracheal Intubation in various groups

	Clonidine	Gabapentin	Control
	Mean	Mean	Mean
DBP 0	75.64	78.76	79.85
DBP 1	68.33	69.79	65.15
DBP 2	74.85	86.67	90.45
DBP 3	69.73	81.24	85.75
DBP 4	66.21	71.48	75.33
DBP 5	62.15	66.52	75.33

DBP 0 – baseline diastolic blood pressure before induction

DBP 1 – diastolic blood pressure 3 minutes after induction and just before laryngoscopy
DBP 2 – diastolic blood pressure 1 min after intubation
DBP 3 - diastolic blood pressure 3 min after intubation
DBP 4 – diastolic blood pressure 5 min after intubation
DBP 5 – diastolic blood pressure 10 min after intubation

DBP before induction of anesthesia in the clonidine group was75.64 mmgh (mean), as comparison to 78.76 mmhg and 79.85mmhg in gabapentine and control group respectively. Patients in clonidine group had more fall in DBP before induction as compared to patients in control group and gabapentine group. This fall in DBP in all the groups were compareable.

The DBP taken three minutes after the induction of anesthesia and just before laryngoscopy was 68.33mmhg (mean) in clonidine group, 69.79mmhg in gabapentine group and 65.15 mmhg in control group. The fall in DBP at this point of time in all the groups were comparable.

The DBP taken one minute after laryngoscopy and intubation in patients who received clonidine was 74.85 mmhg (mean), as comparison to 86.67 mmhg in gabapentine group and 90.45 mmhg in control group. Patients in control group had more increased in DBP in comparison to clonidine and gabapentine group. The p value was 0.000 for control and clonidine group ,and .007 for clonidine and gabapentinegroup,both of which are statistically significant. However ,the p value for control and gabapentine group was .583 which is comparable. This concludes that the clonidine group patients had less increase in DBP in comparision to gabapentine and control group.

The DBP taken three minute after laryngoscopy and intubation in clonidine group was 69.73 mm hg (mean) , as comparison to 81.24 mmhg in gabapentine group and 85.75 mm hg in control group. There was more fall in DBP in clonidine group patients in comparison to gabapentine and control group. The p value was 0.000 for control and

clonidine group and for clonidine and gabapentine group was .000,both of which are statistically significant .However the p value result between the group control and gabapentine were comparable, P value being .188 which is statistically non significant. Hence, the clonidine group patient had more fall in DBP as compared to both the other groups.

Similarly , the DBP taken five minutes after laryngoscopy in clonidine group was 66.21mm hg (mean) , as comparison to 71.48mmhg in gabapentine group and 75.33mmhg in control group. The fall in DBP(mean) was more in clonidine group as compared to control group. The p value was 0.004 for control and clonidine group , which is statistically significant. However, the p value for clonidine and gabapentinegroup(.147) and, control and gabapentine group (.355), was comparable. Hence, the patients in clonidine group had more fall in DBP even after five minutes of laryngoscopy as compared to both the groups.

The DBP(mean) taken ten minutes after laryngoscopy in clonidine group was 62.15mmhg (mean) , as comparison to66.52 mmhg in gabapentine group and 75.33 mmhg in control group. The fall in DBP(mean) was more in clonidine group as compared to control group. The p value was 0.000 for control and clonidine group, which is statistically significant. However, the p value for clonidine and gabapentine group was .252, which is comparable. There was more fall in SBP in gabatentine group in comparison to control group. The p value was .005 for control and gabapentine group, which is statistically significant. Hence, the patients in both clonidine and gabapentine group had more fall in DBP than the patients in control group, after ten minutes of laryngoscopy .

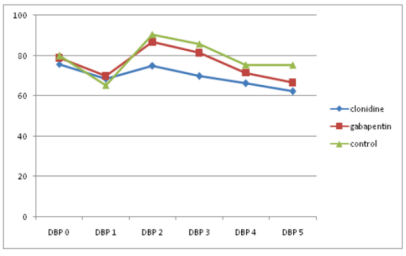

Figure-8 Diastolic blood pressure before, at and after tracheal Intubation in various groups

DBP 0 – baseline diastolic blood pressure before induction

DBP 1 – diastolic blood pressure 3 minutes after induction and just before laryngoscopy
DBP 2 – diastolic blood pressure 1 min after intubation
DBP 3 - diastolic blood pressure 3 min after intubation
DBP 4 – diastolic blood pressure 5 min after intubation
DBP 5 – diastolic blood pressure 10 min after intubation

Table--9Mean arterial pressure before, at and after tracheal intubation in various groups

	Control	Gabapentin	Control
	Mean + SD	Mean + SD	Mean + SD
MBP 0	88.88	94.64	95.06
MBP 1	80.48	81.36	81.18
MBP 2	89.30	96.76	105.09
MBP 3	83.45	96.15	100.09
MBP 4	77.55	87.09	89.36
MBP 5	75.82	80.24	88.61

MBP 0 – baseline mean blood pressure before induction

MBP 1 – mean blood pressure 3 minutes after induction and just before laryngoscopy
MBP 2 – mean blood pressure 1 min after intubation
MBP 3 - mean blood pressure 3 min after intubation
MBP 4 – mean blood pressure 5 min after intubation
MBP 5 – mean blood pressure 10 min after intubation

MBP before induction of anesthesia in the clonidine group was 88.88mmgh (mean), as comparison to 94.64mmhg and 95.06 mmhg in gabapentine and control group respectively. Patients in clonidine group had more fall in MBP before induction as compared to patients in control group and gabapentine group. This fall in MBP was statistically significant. P value was (.010) for the clonidine and control group, and .017 for the clonidine and gabapentine group. The fall in MBP in control and gabapentine group was not significant. (P value - 0.977).

The MBP taken three minutes after the induction of anesthesia and just before laryngoscopy was 80.48mmhg (mean) in clonidine group, 81.36mmhg in gabapentine group and 81.18 mmhg in control group. There is no statistically significant fall in MBP in any of the three groups. All the three groups have near similar MBP(mean) values a t this point of time , hence the P value result between different groups were comparable.

The MBP taken one minute after laryngoscopy and intubation in patients who received clonidine was 89.30 mmhg (mean), as comparison to 96.76mmhg in gabapentine group and 105.09 mmhg in control group. Patients in control group had more increased in MBP as comparison to clonidine and gabapentine group. This increase in MBP was more significant while comparing control and clonidine group. The p value was 0.002 for control and clonidine group , which is statistically significant. The p value for control and gabapentine group was .151 and for clonidine and gabapentinegroup was .218, both of which are non significant. Hence, the clonidine group patient had less increased in MBP as compared to both the groups.

The MBP taken three minute after laryngoscopy and intubation in patients who received clonidine group was 89.30 mmhg (mean) , as comparison to 96.76mmhg in gabapentine group and 105.09 mmhg in control group. Patients in control group had more increased in MBP as comparison to clonidine and gabapentine group. This increase in MBP was more significant while comparing control and clonidine group. The p value was 0.002 for control and clonidine group , which is statistically significant. The p value for control and gabapentine group was .151 and for clonidine and gabapentinegroup was .218, both of which are non significant. Hence, the clonidine group patient had less increased in MBP as compared to both the groups.

The MBP taken three minute after laryngoscopy and intubation in clonidine group was 83.45 mmhg (mean), as comparison to 96.15mmhg in gabapentine group and 100.09 mmhg in control group. Patients in clonidine group had less increased in MBP in comparison to control and gabapentine group. This small increase in MBP in clonidine group was significant when compared with patients in control and gabapentine group. The p value was 0.000 for control and clonidine group , and .000 for clonidine and gabapentine group, both of which are statistically significant. However, the p value for control and gabapentine group was .372 which is statistically non significant. Hence, the patients in clonidine group had less increased in MBP even after three minutes of laryngoscopy as compared to both the groups.

Similarly, the MBP taken five minutes after laryngoscopy in clonidine group was 77.55 mmhg (mean), as comparison to 87.09 mmhg in gabapentine group and 89.36 mmhg in control group. The fall in MBP(mean) was more in clonidine group as compared to control and gabapentine group. The p value was 0.000 for control and clonidine group , and .001 for clonidine and gabapentine group, both of which are statistically significant. However, the p value for control and gabapentine group was .669, which is statistically non significant. Hence, the patients in clonidine group had more fall in MBP even after five minutes of laryngoscopy as compared to both the groups.

The MBP(mean) taken ten minutes after laryngoscopy in clonidine group was 75.82 mmhg (mean), as comparison to 80.24 mmhg in gabapentine group and 88.61 mmhg in control group. The fall in MBP(mean) was more in clonidine group as compared to control and gabapentine group. The p value was 0.000 for control and clonidine group, which is rsstatistically significant. However, the p value for clonidine and gabapentine group was .174, which is comparable. There was more fall in MBP in gabatentine group in comparison to control group. The p value was .003 for control and gabapentine group, which is statistically significant. Hence, the patients in both clonidine and gabapentine group had more fall in MBP than the patients in control group, after ten minutes of laryngoscopy .

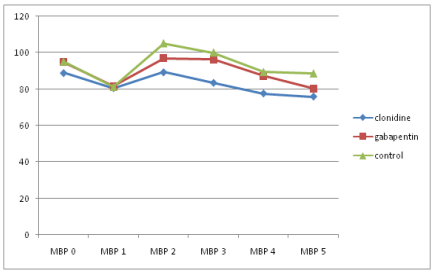

Figure-9 Mean arterial pressure before, at and after tracheal intubation in various groups

MBP 0 – baseline mean blood pressure before induction

MBP 1 – mean blood pressure 3 minutes after induction and just before laryngoscopy
MBP 2 – mean blood pressure 1 min after intubation
MBP 3 - mean blood pressure 3 min after intubation
MBP 4 – mean blood pressure 5 min after intubation
MBP 5 – mean blood pressure 10 min after intubation

DISCUSSION

The cardiovascular changes to laryngoscopy and tracheal itubation are well known and extensively studied. These are associated with increase in the arterial pressures along with a increase in serum catecholamine levels. The pressor response to intubation is a considerable factor in patients and more so in those with comorbid conditions. Thus the hemodynamic variations need to be controlled which if not done can be detrimental.Several techniques have been proposed to prevent or attenuate the heamodynamic responses following laryngoscopy and tracheal intubation such as deepening of plane of anaesthesia(3), using alternative methods of intubation (Macoylaryngoscopicblade,intubating LMA), limiting duration of laryngoscopy for <15 seconds, several drugs such as vasodilators (NTG) (9, 26, 28), beta blockers (esmolol) (18, 19, 26, 27), calcium channel blockers (nicardipin, verapamil, diltiazem) (15, 20, 24, 25) , clonidine, opiods (fentanyl, sufentenil, alfentanil, ramifentanil) (12,16,18,21,32,33), lignocaine (3, 5, 6, 16, 17, 18, 21), magnesium (21,41) and recently gabapentin But there was no literature available till date to compare among the newer gabapentin and well known clonidine and find a better option among the 2 for attenuation of heamodynamic stress response.

In search of an answer to the above question, we planned a double blind randomised control study in our hospital. A total of 99 patients, 33in clonidine group (Group I), 33 in gabapentin group (Group II) and 33 in control group were selected for the completion of our study in the stipulated time period.

Patients with (BMI) Body mass index more than 30,hiatal hernia, gastroesophageal reflux, history of allergy to study drugs history of cardiovascular (HT, MI), neurologic, cerebrovascular, respiratory, hepatic and renal disease and patients having difficult intubation (prolonged laryngoscopic time more than 30 seconds) or requiring urgent surgery were excluded from the study because in these patients, an unusual pressor response may occur which may be deleterious and may confound the results of this study.

The demographic data thus collected, after the completion of our study, was comparable. This was also comparable in the previous studies.

Gabapentin, 1-(aminomethyl) cyclohexane acetis acid, is a structural analogue of the neurotransmitter -aminobutyric acid (GABA). The absorption of gabapentin is dose dependent due to a saturable L-amino acid transport mechanism in the intestine. Thus the oral bioavailability varies inversely with dose. After a single dose of 300 or 600 mg, bioavailability was approximately 60% and 40% respectively.

A study was conducted by D. Memis et al in 2006 to compare the effects of two doses of gabapentin 400mg and 800mg with controls. Ninety ASA-1 patients undergoing elective surgeries were divided into three groups of 30 each receiving placebo(group-1), gabapentin 400mg (group-2), gabapentin 800mg (group-3) 1 hour before undergoing laryngoscopy and intubation. Heart rate and MAP were recorded as baseline, which is the mean of three resting measurements in the operating room before any instrumentation, 1, 3, 5, 10 and 15 minutes after intubation no premedication was done and anesthesia was induced with propofol and atracurium. Maintainance was done with 2% sevoflurane with a fresh gas flow of 2 L /min (50% N20 in O2). They concluded that given 1 hour prior operation gabapentin 800mg blunted the arterial pressure and heart rate increase in the first 10 minutes due to endotracheal intubation.

However in this study no premedication was done contrary to our study where we premedicated the patients with midazolam and fentanyl. Also they induced the patients with propofol contrary to our thiopentone induction. Propofol causes more hypotension in comparison to thiopentonesodium,alsopropofol blunts the baroreceptor reflex to hypotension. These fectors can act as confounding factors while measuring the heamodynamic stress response to laryangoscopy and intubation. Than in the above mentioned study they didn't mention the duration of laryngoscopy which is a major factor which affects the amount of heamodynamic changes after laryngoscopy and intubation. In our study the heamodynamic responses in gabapentin group were less than the control group but these were statistically not significant and gabapentin 600mg offered no specific advantage over the control group which might be due to the inadequate dose of gabapentin.

Another study by A.Fassoulaki et al in 2006 done on 46 patients undergoing abdominal hysterectomy showed that 1600 mg of this drug in four divided doses attenuated the pressor response significantly when compared to placebo group, but the effect on heart rate was not of significance. However in their study also, no premedication was done and propofol was used as induction agents as was used in the previous study. Although they tried to limit the duration of laryngoscopy theydidnot record the duration of each intubation. Again this 1600 mg dose was more than what we had used in our study. Furthermore the study design was of multiple dosing as compared to our single dosing study design. So multiple dosing in divided doses might have more benefit than single dosing of gabapentin for attenuating heamodynamic stress response to laryngoscopy and tracheal intubation.

Clonidine, an imidazole compound, is a selective agonist for alpha2adrenoceptors. It is rapidly and almost completely absorbed after oral administration and reaches peak plasma concentrations within 60-90 minutes by this route. The elimination half life of clonidine is between 9 and 12 hours. It causes sedation and anxiolysis. It potentiates the anaesthetic action of other agents and reduce anaesthetic requirements during surgery. It reduces fentanyl requirements for induction and intubation by 45%. Doses of thiopentone and propofol required for induction are reported to be reduced by preanaesthetic medication with clonidine.

It also acts on the receptors of medulla and presynaptically on peripheral nerve terminals to reduce activity of the sympathetic nervous system. Clonidine is known to reduce noradrenaline and adrenaline concentrations particularly during sympathetic nervous system stimulation the lowering of these could be a factor in the attenuation by clonidine of the pressor response to laryngoscopy and intubation.

Study conducted by R. Orko et al in 1987 on sixty three ASA1-2 patients scheduled for elective surgery under general anaesthesia were divided into three groups randomly receiving clonidine , diazepam and cimetidine. They concluded that the mean maximal increase in heart rate was lowest in the clonidine group but there was no significant differences in mean arterial pressure associated with intubation.

Y.K. Batra in 1988 conducted a study on 40 (ASA 1-2)patients of both sexes aged between 20 to 45 years undergoing routine surgical procedures were divided into 2 groups of 20 each. One group receiving clonidine 5µg/kg 90 minutes before induction of anaesthesia and other group without any pretreatment acting as controls. They concluded that controls showed a significant rise in heart rate and blood pressure compared to clonidine receiving group.

Another study by P.M.C.Wright done in 1990 also confirmed that clonidine premedication is associated with intraoperative and postoperative hypotension they also urged caution in its use as a premedicant due to hypotension.

Another study by S. Roy et al in 1993 done on 30 patients which were divided in two groups receiving clonidine 0.2 mg and diazepam 10 mg ninety minutes before induction of anaesthesia with thiopentone and suxamethonium. The author concluded that clonidine premedication was associated with a significant reduction in the increments of heart rates and MAP at 1 and 5 minutes after laryngoscopy and tracheal intubation in comparison to diazepam group.

Another interesting study was done by J. Pouttu in 1987 assessed the effects of oral clonidine premedication on stress response along with the estimation of serum catecholamines. They compared clonidine with diazepam and concluded that clonidine attenuated the sympathoadrenal response to intubation. They observed that noradrenaline levels were lower throughout and 3 hours after surgery in clonidine group. Adrenaline levels were lower in this group 2 minutes after intubation.

In our study also clonidine has resulted in decrease in the mean blood pressure and heart rate even before induction of anaesthesia as shown in previous studies. Also stress response caused by laryngoscopy and tracheal intubation was more blunted in clonidine group patients as compared to other two groups.

As, there was no single study conducted previously comparing the attenuation of haemodynamic response to laryngoscopy by clonidine and gabapentin premedication, We have attempted to do that. In our study clonidine affords better attenuation of pressor response when compared to gabapentin or placebo. Also we found that,though gabapentin has lesser pressor response than control group but the difference wasstatistically not significant. This could be because of the fact that the dose we have chosen is probably not enough to attenuate the pressor response.

SUMMARY &CONCLUSION

The pressure response to intubation is a detrimental factor in patients. Hence we compared clonidine and gabapentin in fixed doses to know their effectiveness in reducing the haemodynamic responses to intubation.

A total of 99 patients, 33in clonidine group (Group I), 33 in gabapentin group (Group II) and 33 in control group (Group III) were selected.

Patients with (BMI) Body mass index more than 30,hiatal hernia, gastroesophageal reflux, history of allergy to study drugs history of cardiovascular (HT, MI), neurologic, cerebrovascular, respiratory, hepatic and renal disease and patients having difficult intubation (prolonged laryngoscopic time more than 30 seconds) or requiring urgent surgery were excluded from the study.

Endotracheal intubation was performed using clonidine and gabapentin premedication after standardized induction of anaesthesia. Systolic (SBP), diastolic (DBP), mean arterial blood pressure (MAP), heart rate (HR) were recorded before induction, 3 minutes after induction just before laryngoscopy, 1 minute,3 minute, 5 minute & 10 minute after laryngoscopy and intubation.

There was no significant inter group variations among age, sex, weight, height or BMI (table 1). There was no significant difference between the time for intubation between the two groups with intubation after clonidine and gabapentin premedication.We observed that attenuation of haemodynamic response offered by clonidine premedication 300 µg wasbetter than gabapentin 600mg.

Hence we conclude that clonidine is superior to gabapentin in attenuating the stress response induced by laryngoscopy and intubation. We further recommend studies to be done in future with higher doses of gabapentin. Estimation of serum catecholamines could be added in future studies to get better results.

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