



**“COMPARATIVE STUDY OF CLONIDINE VERSUS PREGABALIN AS A
PREMEDICATION FOR PREOPERATIVE SEDATION, ANXIOLYSIS AND TO ATTAIN
OLIGEMIC FIELD IN EAR NOSE AND THROAT SURGERIES: A PROSPECTIVE
RANDOMIZED DOUBLE-BLIND STUDY”**

Anaesthesiology

Dr. Kirankumar M Yalavatti*	3rd year post graduate resident, Department of Anaesthesiology, Government Medical college and SSG hospitals, Vadodara. *Corresponding Author
Dr. Swati A Bhatt	Professor (MD Anaesthesiology), Department of Anaesthesiology, Government Medical college and SSG hospitals, Vadodara.
Dr. Aravind K	3rd year post graduate resident, Department of Anaesthesiology, Government Medical college and SSG hospitals, Vadodara.
Dr. Mayurkumar Trivedi	3rd year post graduate resident, Department of Anaesthesiology, Government Medical college and SSG hospitals, Vadodara.

ABSTRACT

Background and Aims- Preoperative anxiety has been reported in 1 out of 6 adults undergoing surgery, there are different medication on trial to alleviate the anxiety, to provide preoperative sedation and to achieve Intraoperative Hemodynamic stability. This study aims to compare the efficacy of Pregabalin and Clonidine in providing preoperative sedation, anxiolysis and intraoperative Haemodynamic stability to achieve Oligemic surgical field. **Materials and Methods-** After approval from institutional ethics committee, 100 adult patients of either gender, ASA grade I and II scheduled for elective surgery under general anaesthesia were enrolled in a prospective randomised double-blind study. Patients were divided into 2 groups: Group C and Group P. Basal Haemodynamic parameters with Anxiety score and Sedation score were noted before starting the study. Then the patients were given T. Clonidine 200 microgram (Group C) or T. Pregabalin 150 milligram (Group P), he/she was reassessed for Sedation score and Anxiety score 90 minutes after giving the study drug and then taken for surgery. All the Hemodynamic parameters were noted every 15mins and also ISOFE (Intraoperative surgical Field Evaluation Score) score for assessing bloodless field for surgery was noted every half hourly throughout surgery. **Results-** All the demographic parameters were comparable in both the groups. Both anxiety score and Sedation scores were also comparable in both groups ($P>0.05$) before administering study drugs. Preinduction Anxiety score and Sedation score were statistically significant ($P<0.05$) from baseline in group C and both the scores were statistically insignificant ($P>0.05$) from baseline in group P. And ISOFE score was statistically significant ($P<0.05$) in group C compared to group P. **Conclusion-** From this study we conclude that Oral Clonidine 200microgram is better premedication as anxiolytic and sedative than oral Pregabalin 150 mg and it provided good hemodynamic stability with oligemic field intraoperatively in Ear, Nose and Throat surgeries with minimal side effects.

KEYWORDS

Clonidine, Pregabalin, Anxiety, sedation, oligemic field.

1.INTRODUCTION

Preoperative anxiety has been reported to affect up to one out of six adults due to undergo surgery, high anxiety level makes it difficult to control intraoperative hemodynamic stability and postoperative pain. It has been widely selected as model to test the acute anxiolytic effect of various drugs.

High preoperative anxiety levels make control of intraoperative haemodynamics difficult, that can cause an uncontrollable bleeding intraoperatively, which makes operating surgeons' task difficult.

So, control of preoperative anxiety will be beneficial in terms of providing stable intraoperative haemodynamics. There are many studies which tried and tested various drugs for control of preoperative anxiety.

Benzodiazepines have classically been prescribed for preoperative anxiolysis but are associated with adverse effects (e.g., dizziness, somnolence, respiratory depression). Most commonly used among them is midazolam which has drawbacks like: short duration of action, Intravenous route is the preferred route of administration(1)

There is considerable research interest in the development of alternative drugs to treat anxiety, including clonidine and gabapentinoids (One member of this class of drugs, Pregabalin).

A study in patients with generalised anxiety disorders found that chronic use of Pregabalin and gabapentin was significantly more effective than Benzodiazepines in improving somatic anxiety symptoms, *but its role in acute anxiety needs to be yet evaluated*(2).

Ear, Nose and throat surgeries are delicate surgeries and they are time, consuming because they involve small surgical field with high vascularity. Particularly the middle ear surgeries being done successfully with the help of operative microscope which magnifies surgical field but also magnifies blood droplets(3). Strict control of haemodynamics to maintain oligemic or bloodless surgical field is one

of the important concerns of anaesthetist in such surgeries. To achieve this, many physical techniques are being used like avoidance of venous obstruction and mild elevation of head 15-30 percent. But these techniques may be associated with risk of embolism. This can also be achieved by controlled hypotension with various agents such as inhalational anaesthetics, beta blockers, magnesium, total intravenous anaesthetic agent such as propofol, vasodilators such as nitrate and sodium nitroprusside and alpha 2 agonists such as clonidine and dexmedetomidine, Gabapentanoids (Gabapentine and Pregabalin) with each technique having its own drawbacks (4).

2.MATERIALS AND METHODS:

This study was conducted in Department of Anaesthesiology, Government Medical college and SSG Hospital, Vadodara, after taking permission from Institutional Ethical Committee for Human research.

It was a **prospective randomised double-blind study** in which study population was selected randomly using sealed envelope method involving 100 patients, divided into 2 groups with 50 patients in each group.

Inclusion Criteria:

1. Patients undergoing elective ear, nose and throat surgery under general anaesthesia.
2. Patients belonging to age group 18 - 50 years.
3. Patients conformed to American Society of Anaesthesiologists (ASA) physical Status I and II.
4. Patient belonging to Mallampatti grading I-II on airway assessment.

Exclusion Criteria:

1. Refusal to follow the study protocol or patients who are not willing to participate in the study
2. Patients with history Diabetes mellitus, Hypertension, Arrhythmias, liver and Kidney disorders, cerebral disease, epilepsy, coagulation disorders.

3. Patients with BMI> 30kg/m²
4. Patients on sedatives/hypnotics And Patients allergic to Pregabalin or Clonidine.

Pre-operative Preparation

Detailed pre-anaesthetic check-up was done for all patients undergoing this study. The patient's age, gender, weight, ASA status, duration, and type of surgery were recorded. All systems were examined including airway examination. Basic laboratory investigations were conducted including Complete hemogram, Urine analysis, Blood sugar, Kidney function test, chest x-ray and ECG if indicated

A Day before surgery, the procedure was explained in their own vernacular language to the patients including aims, benefits and complications of our study and study drugs involved. And written informed consent was taken for Anaesthesia and Surgery.

Patients were kept nil by mouth for minimum 8 hours prior to surgery. Tab. Ranitidine 150 mg given orally at bedtime a day before surgery.

Cylinders and circuits were checked, airway equipment, monitor, defibrillator, EtCO₂ and drugs were kept ready before induction.

18G peripheral IV line was secured and Multipara monitor attached to the patient and baseline vital parameters before giving study drug were noted which includes Heart rate (HR), Mean arterial Pressure (MAP), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Peripheral oxygen saturation.

Working central and cylinder Oxygen supply, emergency drugs, intubation cart was ensured before administering study drug to the patient.

Patient was assessed for preoperative sedation and anxiolysis before and 90 minutes after administering drug in preoperative room using following scoring systems.

Anxiety Score.

Score	Definition
0	Patient is quiet and comfortable.
1	Patient is uneasy.
2	Patient is worried and anxious.
3	Patient is very worried and very anxious.
4	Patient is frightened or terrified.

Ramsay Sedation score (RSS) to assess sedation.

Score	Definition
1	Patient is anxious and agitated or restless or both.
2	Patient is co-operative, oriented and tranquil.
3	Patient responds to commands.
4	Patient exhibits brisk response to light glabellar tap or loud auditory stimulus.
5	Patient exhibits sluggish response to light glabellar tap or loud auditory stimulus.
6	Patient exhibits no response to light glabellar tap or loud auditory stimulus.

Patient shifted to operating room 90 minutes after oral Clonidine hydrochloride or Pregabalin premedication.

In operating room, Preinduction vital parameters were noted which includes Heart rate (HR), Mean arterial Pressure (MAP), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Peripheral oxygen saturation (SPO₂).

Patient preparation inside operation theatre:

Multipara monitor was attached to the patient and baseline vital parameters were noted which includes Heart rate (HR), Mean arterial Pressure (MAP), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Peripheral oxygen saturation (SPO₂).

Inj. Glycopyrrolate 5mcg/kg IV (5 mins before induction)

Inj. Ondansetron 0.1mg/kg IV (5 mins before induction).

Inj. Paracetamol 1 gram IV (5 mins before induction).

No other sedatives other than drugs involved in our study were given to the patient as we are going to compare these drugs for anxiolysis and sedation.

Induction of anaesthesia

Patients was pre-oxygenated with **100% oxygen for 3 minutes** using tight fitting mask. Induction with Inj. Propofol 2 mg/kg IV, followed by Vecuronium bromide 0.1mg/kg IV. Patient's lungs were manually ventilated with 100% oxygen before orotracheal intubation. Direct laryngoscopy was performed after 3mins by appropriately sized Macintosh blade and tracheal intubation was performed within 15 seconds using appropriately sized endotracheal tube.

Intraoperative

Patients' lungs were mechanically ventilated with volume control mode with Tidal volume 6-8 ml/kg and respiratory rate 12/min to maintain end tidal PCO₂ 30-35 mmHg. Anaesthesia was maintained with Oxygen 33%, Nitrous oxide 66% and sevoflurane on controlled ventilation. Muscle relaxant was given as intermittent doses of vecuronium Bromide IV. (1/3rd of loading dose as a maintenance). All the vital parameters were monitored intraoperatively and noted on every 15 mins which includes Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean Arterial Pressure (MAP), Heart rate (HR), Peripheral oxygen saturation (SPO₂) and EtCO₂ (End tidal carbon dioxide).

Intraoperatively surgeons were asked about oligemic field during surgery every 30 minutes and Response is noted under following grades.

Intraoperative Surgical Field Evaluation score (ISOFE Score).(4)

Grade	Definition
0	No bleeding.
1	Bleeding, in which no suctioning required.
2	Slight bleeding; occasional suctioning required; surgical field not threatened.
3	Minimal bleeding; frequent suctioning required; bleeding threatened surgical field a few seconds after suction was removed.
4	Moderate bleeding; frequent suctioning required; bleeding threatened surgical field immediately after suction was removed.
5	Severe bleeding, constant suction required Bleeding presents faster than could be removed by suction, surgical field severely threatened and surgery not possible.

Post operative

Patient was given reversal using Inj. Neostigmine 50 microgram/kg & Inj. Glycopyrrolate 10 microgram/kg IV,

Extubation was done when the patient was completely awake and shifted to recovery room. Patients were closely monitored for 4hrs after surgery for any post operative complications and every 2nd hourly for next 24 hours.

Perioperative observation:

patient is followed up for 24 hours in postoperative period for any side effects of our study drugs.

3.RESULTS

Both these groups were compared and statistically analyzed using **unpaired t Test and Fischer test for quantitative data** (Demographic data), **Chi-square test for qualitative data** (Anxiety score, Sedation score and ISOFE score); Significance was evaluated by P value. P value <0.05 was considered as significant. P value >0.05 was considered as nonsignificant. P value <0.01 was considered as highly significant

Table 1: Demographic Data

GROUP	GROUP C	GROUP P	P VALUE	SIGNIFICANCE
Age in years (Mean± SD)	36.14± 8.420117	33.82± 9.62074	P VALUE >0.05 (0.2025)	Not Significant
Gender (M: F)	27:23	24:26	P VALUE >0.05	Not Significant
BMI (kg/m ²)	23.63±2.64	23.62±2.56	P VALUE >0.05	Not Significant
ASA grade (I: II)	33:17	38:12	P VALUE >0.05	Not Significant

Table 1 shows that both Groups were comparable with respect all demographic data i.e age, gender, BMI and ASA classification and the differences between both groups was Statistically **Non significant** with respect to the above parameters (**P value > 0.05**)

Table 2: Preoperative baseline haemodynamic parameters before giving study drug.

Vital parameters	Group C	Group P	P value	Significance
Heart rate (Per minute) (Mean $\pm$ SD)	82.28 $\pm$ 9.68	81.44 $\pm$ 7.004	P value >0.05 (P value = 0.6202)	Not Significant
SBP (mmHg) (Mean $\pm$ SD)	120.28 $\pm$ 11.23	117.84 $\pm$ 9.586	P value >0.05 (P value = 0.3035)	Not Significant
DBP (mmHg) (Mean $\pm$ SD)	76.6 $\pm$ 8.41	75.08 $\pm$ 6.79	P value >0.05 (P value = 0.7578)	Not Significant
MAP (mmHg) (Mean $\pm$ SD)	91.06 $\pm$ 5.95	89.3 $\pm$ 5.92	P value >0.05 (P value = 0.3472)	Not Significant
Spo2(%)	99 $\pm$ 1	99 $\pm$ 1	P value >0.05 (P value = 0.7678)	Not Significant

Mean and SD was calculated for each haemodynamic parameter (Heart rate, SBP, DBP, MAP, SPO2) and the p value was calculated, it shows there was **no statistically Significant (P value > 0.05)** difference exists between hemodynamic parameters. i.e., **both the groups were hemodynamically comparable before giving study drug.**

Table 3: Changes in Anxiety score After administering study drug in Group C (Clonidine group) and Group P (Pregabalin).

ANXIETY SCORE	GROUP 'C'		GROUP 'P'	
	BEFORE PREMEDICATION (Nor of patients)	AFTER PREMEDICATION (Nor of patients)	BEFORE PREMEDICATION (Nor of patients)	AFTER PREMEDICATION (Nor of patients)
0	4	21	5	15
1	16	27	13	12
2	15	2	25	19
3	13	0	5	4
4	2	0	2	0
P value	<0.05	Statistically Significant	>0.05	Not Significant

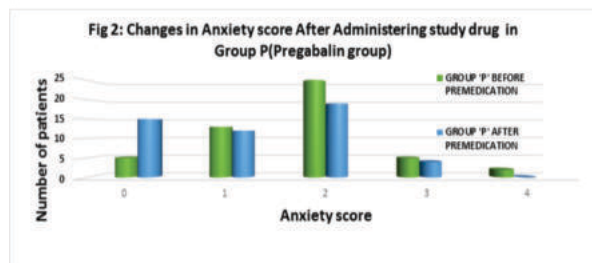
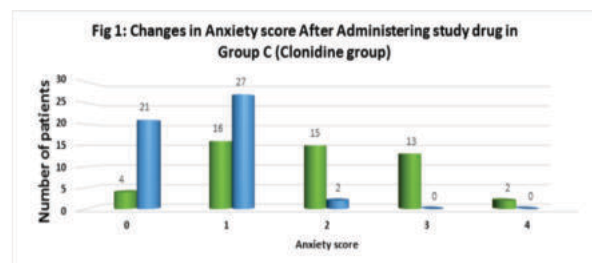


Table 3, Fig 1 & 2 shows Changes in anxiety score after administering study drugs. It shows that data was statistically significant (**p value < 0.05**) i.e., there was a **significant change in anxiety score in Group C after giving study drug**. And it was statistically not significant (**p value > 0.05**) i.e., there was **no significant change in anxiety score in Group P after giving study drug**.

Table 4: Changes in Sedation score After administering study drug in Group C (Clonidine group) and Group P (pregabalin)

SEDATION SCORE	GROUP 'C'		GROUP 'P'	
	BEFORE PREMEDICATION (Nor of patients)	AFTER PREMEDICATION (Nor of patients)	BEFORE PREMEDICATION (Nor of patients)	AFTER PREMEDICATION (Nor of patients)
1	39	9	28	26
2	11	34	22	24
3	0	7	0	0
4	0	0	0	0
5	0	0	0	0
6	0	0	0	0
P value	<0.05	Statistically Significant	>0.05	Not Significant

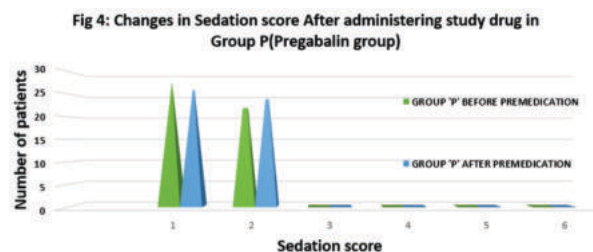
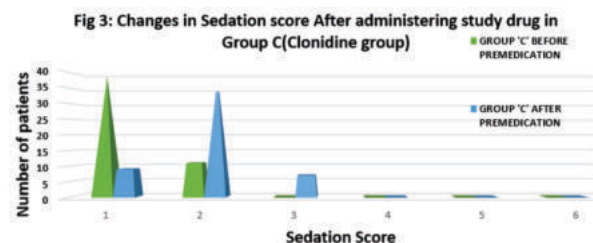


Table 4, Fig 3 & 4 shows that, Data was statistically **significant (p value < 0.05)** i.e., there was a **significant change in Sedation score in Group C after giving study drug**. And it was statistically **not significant (p value > 0.05)** i.e., there was **no significant change in Sedation score in Group P after giving study drug**

Table 5: Comparison of Intraoperative ISOFE score in Group C (Clonidine group) and Group P (Pregabalin group)

ISOFE SCORE	GRO UP 'C' 30 mins	GRO UP 'P' 30 mins	GRO UP 'C' 1 hr	GRO UP 'P' 1 hr	GRO UP 'C' 1hr 30 mins	GRO UP 'P' 1hr 30 mins	GRO UP 'C' 2hrs	GRO UP 'P' 2hrs
0	0	0	0	0	0	0	0	0
1	25	15	25	9	17	5	20	5
2	21	24	20	29	28	24	28	38
3	3	11	5	10	5	21	2	7
4	1	0	0	2	0	0	0	0
5	0	0	0	0	0	0	0	0
P value	<0.05 (0.0407)		<0.05 (0.005)		<0.05 (0.0003)		<0.05 (0.0013)	

ISOFE score in this study helps us to analyse the oligemic field (bloodless surgical field) provided by each drug and above results were such comparison between our study drugs at different time period during surgery.

Table 5 represents **Inter group comparison** of ISOFE Score between two study groups and the results were **statistically significant (P < 0.05)**, indicating there was a statistically significant difference in two groups with respect to ISOFE score during the study.

Hence, we can conclude that, Group C (Clonidine group) had better hemodynamic control compared group P (Pregabalin group) throughout surgery.

4. DISCUSSION

Preoperative anxiety is one of the important factors affecting preoperative and intraoperative haemodynamics. A well-controlled haemodynamics in patients gives bloodless surgical field for surgery.

Ear, Nose and throat surgeries are delicate surgeries, involving small surgical field with high vascularity which makes the surgeries difficult and time consuming.

If we are able to provide good haemodynamic control in such surgeries, it makes operating surgeons task easy, reduces the total time duration for surgery and in turn it lessens the patient's exposure to anaesthetic drug, early recovery and mobilisation due to reduced adjuvants use as a part of anaesthesia and pain control.

As we know Preoperative anxiety being one of the factors affecting intraoperative haemodynamics of the patient, control over preoperative anxiety will help us to control and maintain favourable intraoperative haemodynamics.

Clonidine and Pregabalin are two such drugs which are tried and tested for control of preoperative anxiety and intraoperative haemodynamics of patients.

It was concluded from our study that Oral Clonidine 200 microgram given 90 minutes before surgery in patients undergoing elective ear, Nose and Throat surgeries under General anaesthesia will provide better control over Preoperative anxiety, provides good sedation and better hemodynamic control compared to Oral Pregabalin 150mg. Thus, it provides better surgical field during surgery.

Similar findings were reported by **MS Hossain et al (2018)** who compared Oral Clonidine and Gabapentin as Premedication for Anxiolysis, Sedation and Attenuation of Pressor Response to Laryngoscopy and Tracheal Intubation. They found that **Oral clonidine provided good attenuation of hemodynamic response to laryngoscopy and intubation as compared with oral gabapentin. Also, clonidine is better agent as anxiolytic and sedative than gabapentin (5).**

Chandrakant Waikar et al (2017) compared oral Pregabalin, gabapentin and Oral clonidine for anxiolysis, sedation, and attenuation of pressor response to endotracheal intubation, and they found that oral Pregabalin and gabapentin attenuated blood pressure response fairly well and **heart rate significantly attenuated by clonidine. All three drugs are very effective for relieving anxiety and improving sedation. (7)**

In this study their main focus was attenuation of pressor response to intubation unlike our study in which we compared these drugs for overall control of haemodynamics intraoperatively so they found gabapentanoids perform better over clonidine for pressor response to intubation.

Mansi Jain et al Compared Hemodynamic Effects between Clonidine and Pregabalin in Laparoscopic Cholecystectomy with placebo group as a control.

They found that There was a significant increase in the heart rate (HR) & systolic, diastolic, and mean blood pressure during laryngoscopy and pneumoperitoneum in the control group as compared to both Pregabalin and clonidine. HR was significantly lower in clonidine group after extubation & in postoperative period than both control group & Pregabalin group. There was **no major difference in the incidence of side effects(8).**

And they concluded that both **Pregabalin (150 mg) and clonidine (200 ug)** were effective in controlling the hemodynamic parameters, with **clonidine providing better hemodynamic stability than Pregabalin.(8).**

Irukulla Avanthi et al compared efficacy of oral clonidine and oral Pregabalin before induction on rate pressure product.

And they concluded that **Clonidine was found to be more effective than Pregabalin in lowering of blood pressure and heart rate changes associated with laryngoscopy and endotracheal intubation. (9)**

Taruna Murari et al Compared Oral Clonidine with Oral Pregabalin Premedication for the Attenuation of Pressor Response to Direct Laryngoscopy and Tracheal Intubation in Elective Surgery.

And they concluded that oral premedication with either clonidine or Pregabalin attenuates hemodynamic response to laryngoscopy and tracheal intubation, but **Clonidine is superior to Pregabalin. (10)**

Kumkum Gupta et al compared Oral premedication with Pregabalin and clonidine for hemodynamic stability during laryngoscopy and laparoscopic cholecystectomy

They found that **Clonidine was superior to Pregabalin for attenuation of the hemodynamic responses to laryngoscopy and laparoscopy.** No significant differences in the parameters of recovery were observed in patients receiving both the drugs and **None of the premedicated patient had suffered from any postoperative side effects.**

They concluded that Oral premedication with **Pregabalin 150 mg or clonidine 200 µg** causes sedation and **anxiolysis with hemodynamic stability** during laryngoscopy and laparoscopic cholecystectomy, without prolongation of recovery time and side effects. (11)

5. CONCLUSION

From our study we conclude that, Giving Premedication to the patients undergoing Ear, Nose and Throat surgeries with either Tablet Clonidine 200 microgram (Alpha-2 agonist) or Tablet Pregabalin 150 mg (Gabapentanoid) 90 minutes prior to surgery showed: **Clonidine to be more effective in Reducing preoperative anxiety, to provide Sedation and Bloodless surgical field compared to Oral Pregabalin.**

6. Financial Support And Sponsorship

None

7. Conflicts Of Interest

None

Clinical Trial Registration Number:

CTRI/2022/03/0412999

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