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Original Research Paper

Anaesthesiology

THE EFFECT OF PREOPERATIVE PREGABALIN ON ATTENUATION OF HEMODYNAMIC RESPONSES TO LARYNGOSCOPY & ENDOTRACHEAL INTUBATION

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ABSTRACT

Introduction: This study was designed to evaluate the effect of preoperative pregabalin premedication on attenuation of hemodynamic responses to laryngoscopy and endotracheal intubation.

Material and methods: Eighty patients of either sex , belonging to American Society of Anesthesiologists grade 1 and 2 , undergoing elective surgeries under general anesthesia with endotracheal intubation , were randomly assigned to one of the two groups of forty patients each , in a double blinded manner. Group P received pregabalin 150 mg and Group C received placebo orally, one hour prior to induction . The preoperative level of sedation was assessed by the Ramsay sedation scale in the operating room , before induction . Heart rate , systolic blood pressure (SBP) , diastolic blood pressure (DBP) and mean arterial blood pressure (MAP) were monitored and recorded as - before and after induction ,immediately after intubation and 1, 3 , 5 minutes after intubation ; thereafter at every 5 minute intervals till end of surgery and also every 15 minutes for 4 hours postoperatively .

Results: Patients in Group P had lower heart rate , SBP, DBP and MAP at all time points suggesting greater hemodynamic stability and better attenuation of the hemodynamic response , when compared with Group C.

KEYWORDS : Pregabalin, laryngoscopy, Intubation

INTRODUCTION

Hemodynamic pressor response to airway instrumentation is a hazardous complication of general anaesthesia.[1]

Laryngoscopy and intubation are associated with several adverse hemodynamic responses such as hypertension, tachycardia, arrhythmias and increased circulating catecholamines.[2]

Hypertension and tachycardia are two dynamic predictors of perioperative cardiac morbidity , so prevention of these responses to laryngoscopy and intubation remains an important clinical goal particularly for patients with cardiac or cerebral disease.[3]

Many pharmacological techniques have been evaluated with the aim of attenuating these adverse hemodynamic responses to airway instrumentation. These include deepening the level of anesthesia, pre treatment with vasodilators, adrenoceptor blockers, calcium channel blockers , opioids like fentanyl, remifentanil , α-2 agonists like dexmedetomedine and clonidine and oropharyngeal lidocaine instillation , with variable results .[4,5,6,7,14,15,16]

Gabapentin is another drug, which has been investigated recently and found to have some favourable effect on hemodynamic changes during laryngoscopy and intubation.[2,9,10]

Pregabalin, like gabapentin is a novel drug that has analgesic, anticonvulsant and anxiolytic effects but with a superior pharmacokinetic profile.[8]

It is mainly used for the treatment of neuropathic pain , postherpetic neuralgia and as adjunctive therapy in patients with partial onset seizures.[24]

The efficacy of oral pregabalin on postoperative analgesia and reduction of parenteral analgesics has been demonstrated in several studies .[11,12,13,17]

Only few studies have been carried out to evaluate the role of pregabalin in attenuation of hemodynamic pressor responses of airway instrumentation.[3,21,22,23]

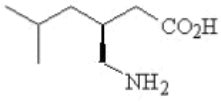
Our enthusiastic desire to further study the above mentioned effects of pregabalin , is based on these studies.

Our study is designed as a prospective , double blind , randomized controlled study to evaluate safety & efficacy of oral pregabalin premedication for attenuation of hemodynamic pressor response of airway instrumentation with pre operative sedation & peri-operative hemodynamic stability.

MATERIALS & METHODS

PREGABALIN:

It is an anticonvulsant drug used for neuropathic pain . It is described chemically as (S)-3-(aminomethyl)-5-methylhexanoic acid. The molecular formula is C8H17NO2 and the molecular weight is 159.23. The chemical structure of pregabalin is:



Pregabalin is a white to off-white, crystalline solid with a pKa 1 of 4.2 and a pKa 2 of 10.6. It is freely soluble in water and both basic and acidic aqueous solutions.

COMMERCIAL PREPARATION:

LYRICA™ (pregabalin) Capsules available in 25mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, and 300 mg.
We have used 150 mg capsules for our study.
Manufactured by Pfizer Limited.

PLACE OF STUDY AND TIME FRAME

The study was carried out in Department of Anaesthesiology of Jaipur Golden Hospital, Rohini, New Delhi-85 after approval by ethical committee and written informed consent from all patients before being included in the study.

STUDY DESIGN

The study was done in a manner of a randomized, double blind, controlled clinical trial.

STUDY POPULATION

The prospective study was carried out in 80 patients of both sexes, aged 25-50 years and posted for elective surgery under general anaesthesia.

INCLUSION CRITERIA

ASA Grade I and II Patients , aged 25-50 years.

EXCLUSION CRITERIA

1. Anticipated difficult intubation

2. Patients with earlier known allergy to study drug
3. Patients taking sedatives or antidepressants
4. Patients on antihypertensive medication esp. clonidine, methyldopa,betablockers
5. Patients with hepatic or renal insufficiency
6. Obesity
7. Patients with COPD
8. Pregnancy, lactating and nursing mothers

SAMPLE SIZE

The study was conducted on 80 patients divided randomly into 2 groups of 40 patients each.

- Group 1 : Control group (Group C)
- Group 2 : Pregabalin 150 mg group (Group P)

The sample size was decided in consultation with the statistician, and was based on initial pilot observations, indicating that approximately 35–37 patients should be included in each group in order to ensure a power of 0.80 for detecting clinically meaningful reduction by 10–20% in heart rate and mean arterial blood pressure. Assuming a 5% dropout rate, the final sample size was set at 80 patients, which would permit a type I error of alfa=0.05, with a type II error of beta=0.5 and power of 0.8.

METHODOLOGY

(A)Pre anaesthetic check-up : Details pertaining to clinical history, h/o any previous operation , any drug intake , drug allergy, general and systemic examination , routine investigations comprising of hemogram, urine analysis, liver and kidney function test ,chest x-ray & ECG was done and noted.

(B)Preoperative orders :
Nil orally 8 hrs prior to surgery
Pre anaesthetic written informed consent

(C)Anesthetic technique :

- ASA Grade 1 & 2 patients selected for elective surgery under general anaesthesia were divided randomly into 2 groups of 40 patients each: Group C & P.
- Baseline heart rate ,systolic ,diastolic & mean arterial blood pressure was recorded
- Patients received either 150 mg of pregabalin or placebo in a double blinded manner . Placebo capsules were prepared after meticulous emptyingof the pregabalin capsules and filled with thin sugar. All doses of pregabalin or placebo were given per oral 1 hr prior to induction of generalanaesthesia with a sip of water .
- The preoperative level of sedation was assessed by the Ramsay sedation scale29 in the operating room before induction .

Table 1 – Ramsay scale[4]

1	Patient anxious and agitated or restless, or both
2	Patient co-operative, orientated, and tranquil
3	Patient responds to commands only
4	Brisk response to a light glabellar tap or auditory stimulus
5	Sluggish response to a light glabellar tap or auditory stimulus
6	No response to the stimuli mentioned in items 4 and 5

- Routine monitoring in the form of NIBP, pulse oximetry and ECG was instituted on arrival in operation theatre & heart rate , systolic, diastolic and mean arterial blood pressure was recorded .
- A crystalloid i.v. infusion of 6-8 ml/kg was started .
- Preoxygenation was done for 3 minutes.
- All patients were given fentanyl 2 mcg/kg i.v. prior to induction .
- Induction : Sleep dose of propofol .Direct laryngoscopy and intubation was facilitated by succinyl choline 2 mg/kg and was performed 60 seconds after its administration.
- Maintainence: Isoflurane (MAC 1 - 1.2) with nitrous oxide 60% in oxygen by gas monitoring & vecuronium 0.1 mg/kg The patients were mechanically ventilated to maintain normocapnia(30-40 mm hg). Ondansetron 4 mg (in infusion) was given intravenously, to every patient intraoperatively. Clinically insufficient analgesia was controlled with supplementary doses of i.v. fentanyl 0.5 mcg/kg .
- Intraoperatively heart rate , systolic blood pressure , diastolic blood pressure ,mean arterial blood pressure were monitored and recorded as :
- before(T 0) and after induction(T 1) ,
- Immediately after intubation(T 2) and ,
- 1(T3) ,3(T 4),5(T 5)minutes after intubation ;
- thereafter at every 5 minute interval till end of surgery.
- Electrocardiography, pulse oximetry and EtCO2 monitors were continuosly used throughout the surgery.
- Hypertension was defined as rise in MAP>20% from the baseline & tachycardia > 20% from the baseline heart rate, and was treated by NTG infusion & β-blocker respectively.
- Hypotension was defined as fall in mean arterial blood pressure by more than 20% from the baseline and treated by increasing the i.v. infusion and additionally with vasoactive drugs. Bradycardia was defined as heart rate < 60 beats/min and was treated with iv. atropine 0.01 mg/kg if required.
- After completion of surgery , neuromuscular block was antagonized with neostigmine 0.05mg/kg and glycopyrrolate 0.01mg/kg , and extubation was performed when respiration was spontaneous & adequate .
- The patients were transferred to the post anesthesia care unit and monitored with recording of Systolic, diastolic & mean arterial pressure, Spo2, Heart rate & Respiratory rate every 15 min. for 4 hours after surgery and watched for any postoperative complications like dizziness , somnolence, nausea & vomiting.
- Any episode of nausea & vomiting in the postoperative period was treated by i.v. ondansetron 4mg as a rescue antiemetic.

RESULTS

A total of 80 patients were enrolled for the study after taking informed consent. Patients were randomly allocated to either of the 2 study groups comprising 40 patients each. Randomization was done using closed envelope method. Procedures as per study design were completed in all the enrolled patients and data collected.

AGE DISTRIBUTION

The mean age in group P was 38.32 years while in group C it was 37.85 years, thus the mean age in two groups were comparable (P value > 0.05)

TABLE 1

	Group P (n=40)	Group C (n=40)	P Value		
	Mean ± SD	Min - max	Mean ± SD	Min - max	
Age (YRS)	38.32 ± 9.46	25 - 50	37.85 ± 9.22	23 - 50	0.821

WEIGHT DISTRIBUTION

The mean weight in group P was 63.18 kgs while in group C it was 62.88 kgs, thus the mean weight in two groups were comparable (P value > 0.05)

TABLE 2

	Group P (n=40)	Group C (n=40)	P Value		
	Mean ± SD	Min - max	Mean ± SD	Min - max	
Weight (Kg)	63.18 ± 9.35	40 - 82	62.88 ± 9.35	40 - 80	0.885

P<0.05 was considered statistically significant.

HEIGHT DISTRIBUTION

The mean height in group P was 1.60 meters while in group C it was 1.63 meters, thus the mean height in the two groups were comparable (P value > 0.05)

TABLE 3

Group	Group P (n=40)	Group C (n=40)	P Value		
	Mean ± SD	Min - max	Mean ± SD	Min - max	
HEIGHT (meters)	1.60 ± 0.141	1.45 - 1.87	1.63 ± 0.103	1.46 - 1.89	0.320

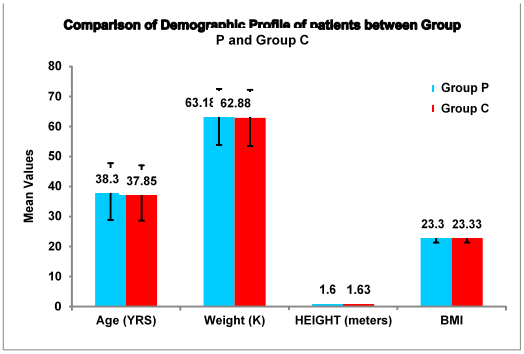
P<0.05 was considered statistically significant.

BMI DISTRIBUTION

The mean BMI in group P was 23.36 kg/m2 while in group C it was 23.33 kg/m2, thus the mean BMI in the two groups were comparable (P value > 0.05)

Group	Group P (n=40)	Group C (n=40)	P Value		
	Mean ± SD	Min - max	Mean ± SD	Min - max	
BMI(kg/m2	23.36±2.04	19.0 - 27.3	23.33± 2.01	19.0 – 27.3	0.956

P<0.05 was considered statistically significant.



SEX DISTRIBUTION

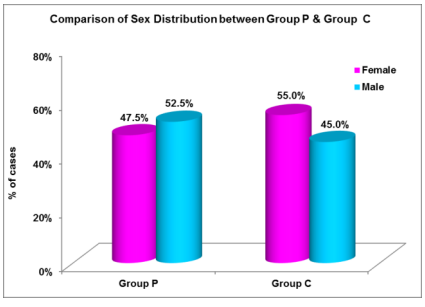
Female patients formed 55% of Group C and 47.5% of Group P.The male patients constituted 45% of Group C and 52.5% of Group P. The sex distribution in the two groups were comparable (P value > 0.05)

TABLE 5

Sex	Group P	Group C	P Value		
	Frequency	%	Frequency	%	
F	19	47.5%	22	55.0%	0.502
M	21	52.5%	18	45.0%	
Total	40	100%	40	100%	

P<0.05 was considered statistically significant.

FIGURE 2



ASA PHYSICAL STATUS DISTRIBUTION

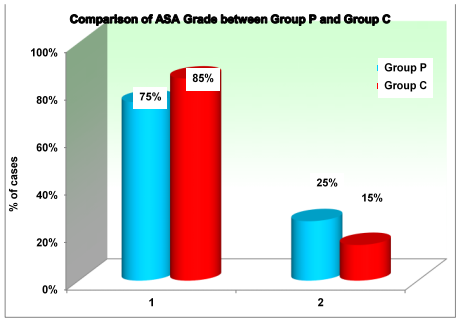
The patients included in both the groups were ASA physical status 1 / 2. Out of 40 , 75% of patients in group P belonged to ASA grade 1 and 25% were of ASA grade 2. In group C , 85% of patients belonged to ASA grade 1 and 15% were of ASA grade 2.The ratio of patients belonging to grade 1 and 2 between both the groups was comparable and the difference was not statistically significant (P value > 0.05)

TABLE 6

ASA Grade	Group P	Group C	P Value		
	Frequency	%	Frequency	%	
1	30	75%	34	85%	0.264
2	10	25%	6	15%	
Total	40	100%	40	100%	

P<0.05 was considered statistically significant.

FIGURE 3



PREOPERATIVE LEVEL OF SEDATION

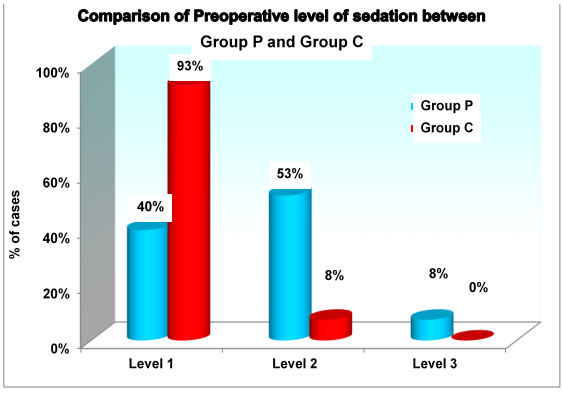
The level of sedation was assessed by the Ramsay sedation scale. 53% of patients in group P achieved Level 2 as compared to 8 % in group C which is statistically significant (P value < 0.001). Also, Level 3 sedation was seen in 8% of patients in group P when compared to 0% in group C which is statistically significant (P value < 0.001). Levels of sedation 4, 5 and 6 were not seen in any patient in the 2 groups.

TABLE 7

Preoperative level of sedation	Group P	Group C	P Value		
	Frequency	%	Frequency	%	
Level 1	16	40%	37	93%	<0.001*
Level 2	21	53%	3	8%	
Level 3	3	8%	0	0%	
Total	40	100%	40	100%	

P<0.05 was considered statistically significant.

FIGURE 4



NUMBER OF ATTEMPTS FOR INTUBATION

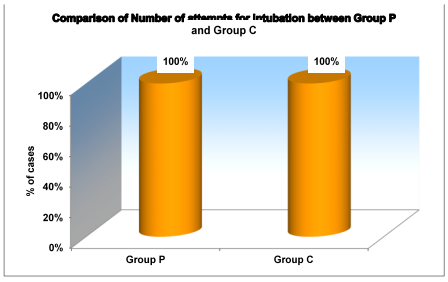
No second attempt for intubation was required in any of the groups P or C .The results were statistically insignificant (P > 0.05).

TABLE 8

Number of attempts for intubation	Group P	Group C	P Value		
	Frequency	%	Frequency	%	
1	40	100%	40	100%	
Total	40	100%	40	100%	

P<0.05 was considered statistically significant.

FIGURE 5



DURATION OF LARYNGOSCOPY

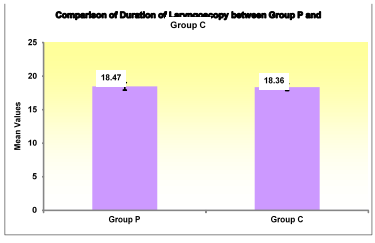
The mean duration of laryngoscopy was 18.47 seconds in group P as compared to 18.36 seconds in group C which was statistically insignificant (P > 0.05)

TABLE 9

	Group P (n=40)	Group C (n=40)	P Value		
	Mean ± SD	Min - max	Mean ± SD	Min - max	
DURATION OF LARYNGOSCOPY(Seconds)	18.47 ± 0.554	17.60 - 19.30	18.36 ± 0.512	17.60 - 19.10	0.393

P<0.05 was considered statistically significant.

FIGURE 6



BASELINE HEMODYNAMIC DATA

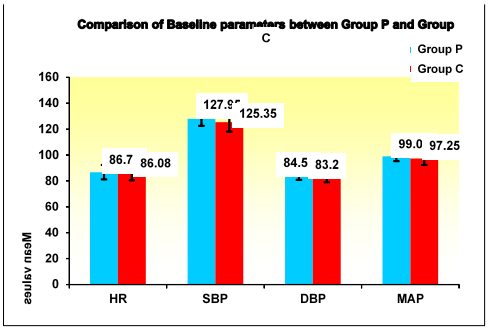
TABLE 10

BASELINE	Group P (n=40)	Group C (n=40)	P Value		
	Mean ± SD	Min - max	Mean ± SD	Min - max	
Heart Rate(bpm)	86.72 ± 5.57	72 - 96	86.08 ± 5.63	72 - 95	0.593
SBP(mmHg)	127.95 ± 5.40	117 - 136	125.35 ± 7.32	112 - 135	0.074
DBP(mmHg)	84.55 ± 3.76	77 - 91	83.20 ± 4.22	74 - 90	0.135
MAP(mmHg)	99.04 ± 3.73	92 - 104	97.25 ± 4.94	87 - 105	0.075

P<0.05 was considered statistically significant.

The mean values of baseline hemodynamic parameters like Heart Rate , SBP, DBP and MAP of the 2 groups are comparable and do not show a statistically significant difference. (P > 0.05)

FIGURE 7



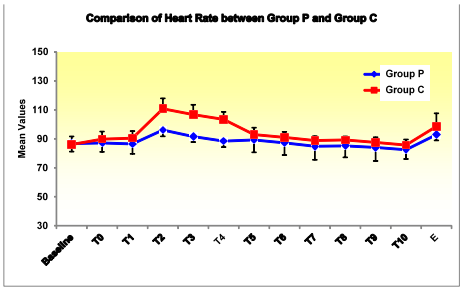
HEART RATE

TABLE 11

Heart Rate(bpm)	Group P (n=40)	Group C (n=40)	P Value		
	Mean ± SD	Min - max	Mean ± SD	Min – max	
Baseline	86.72 ± 5.57	72 - 96	86.08 ± 5.63	72 - 95	0.593
T0	87.15 ± 6.14	68 - 98	89.83 ± 5.20	78 - 98	0.039*
T1	86.55 ± 6.87	68 - 98	90.48 ± 4.89	78 - 99	0.004*
T2	96.12 ± 4.39	86 - 102	110.80 ± 7.21	98 - 123	<0.001*
T3	91.60 ± 3.77	85 - 100	106.75 ± 6.83	96 - 119	<0.001*
T4	88.45 ± 4.13	73 - 96	103.45 ± 5.20	95 - 115	<0.001*
T5	89.28 ± 8.61	68 - 116	92.95 ± 4.76	83 - 103	0.021*
T6	87.28 ± 8.44	73 - 112	91.07 ± 3.79	83 - 99	0.012*
T7	84.92 ± 9.34	68 - 108	88.85 ± 2.97	83 - 94	0.015*
T8	85.12 ± 7.92	68 - 102	89.25 ± 2.47	84 - 94	0.003*
T9	84.12 ± 9.42	68 - 116	87.60 ± 3.51	81 - 95	0.034*
T10	82.52 ± 6.38	70 - 96	85.68 ± 3.91	80 - 93	0.009*
E	92.87 ± 3.90	84 - 100	98.62 ± 9.06	87 - 116	<0.001*

P<0.05 was considered statistically significant.

FIGURE 8



Mean Heart rate in Group P was significantly lower than Group C

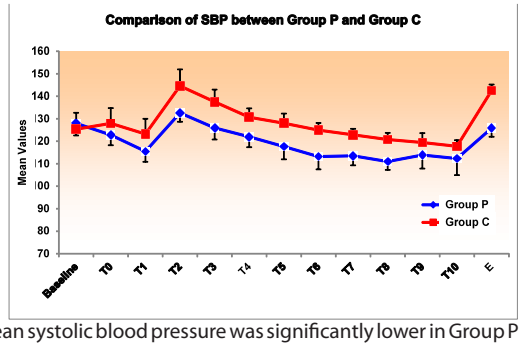
SYSTOLIC BLOOD PRESSURE

TABLE 12

SBP(mmHg)	Group P (n=40)	Group C (n=40)	P Value		
	Mean ± SD	Min - max	Mean ± SD	Min - max	
Baseline	127.95 ± 5.40	117 - 136	125.35 ± 7.32	112 - 135	0.074
T0	122.82 ± 4.58	116 - 130	127.98 ± 6.77	116 - 136	<0.001*
T1	115.50 ± 4.66	110 - 120	123.20 ± 6.80	112 - 132	<0.001*
T2	132.58 ± 3.90	124 - 136	144.60 ± 7.38	136 - 160	<0.001*
T3	125.95 ± 5.20	120 - 133	137.55 ± 5.43	130 - 150	<0.001*
T4	122.00 ± 4.67	117 - 132	130.67 ± 3.98	122 - 136	<0.001*
T5	117.62 ± 5.67	110 - 127	128.05 ± 4.24	120 - 132	<0.001*
T6	113.18 ± 5.65	110 - 124	124.95 ± 3.17	120 - 130	<0.001*
T7	113.52 ± 4.24	106 - 124	122.85 ± 2.70	116 - 126	<0.001*
T8	110.97 ± 3.68	106 - 117	120.75 ± 2.99	116 - 126	<0.001*
T9	113.90 ± 6.03	106 - 130	119.45 ± 4.18	114 - 126	<0.001*
T10	112.33 ± 7.40	100 - 136	117.75 ± 2.73	114 - 120	<0.001*
E	125.85 ± 3.87	120 - 136	142.52 ± 2.73	130 - 150	<0.001*

P<0.05 was considered statistically significant.

FIGURE 9



Mean systolic blood pressure was significantly lower in Group P than Group C

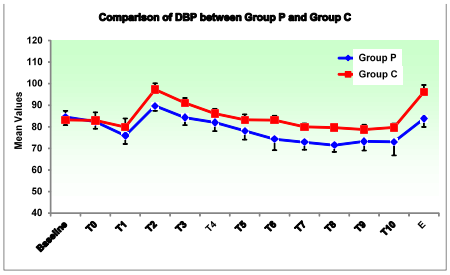
DIASTOLIC BLOOD PRESSURE

TABLE 13

DBP(mmHg)	Group P (n=40)	Group C (n=40)	P Value		
	Mean ± SD	Min - max	Mean ± SD	Min - max	
Baseline	84.55 ± 3.76	77 - 91	83.20 ± 4.22	74 - 90	0.135
T0	82.40 ± 3.30	76 - 88	83.00 ± 3.73	76 - 88	0.448
T1	75.90 ± 3.82	70 - 84	79.90 ± 4.00	72 - 86	<0.001*
T2	89.70 ± 2.29	86 - 97	97.30 ± 2.88	92 - 102	<0.001*
T3	84.25 ± 3.45	80 - 90	91.10 ± 2.22	88 - 96	<0.001*
T4	82.05 ± 4.06	76 - 90	86.15 ± 2.19	84 - 90	<0.001*
T5	78.15 ± 4.11	70 - 88	83.25 ± 2.55	80 - 86	<0.001*
T6	74.25 ± 5.07	70 - 86	83.10 ± 2.07	80 - 86	<0.001*
T7	72.85 ± 3.48	70 - 80	80.00 ± 1.57	76 - 82	<0.001*
T8	71.50 ± 3.10	70 - 82	79.65 ± 1.69	76 - 82	<0.001*
T9	73.30 ± 4.26	70 - 80	78.75 ± 2.25	76 - 82	<0.001*
T10	73.05 ± 6.29	62 - 90	79.75 ± 1.77	76 - 82	<0.001*
E	83.78 ± 3.83	77 - 90	96.20 ± 3.16	92 - 100	<0.001*

P<0.05 was considered statistically significant.

FIGURE10



Mean diastolic blood pressure was significantly lower in Group P than Group C

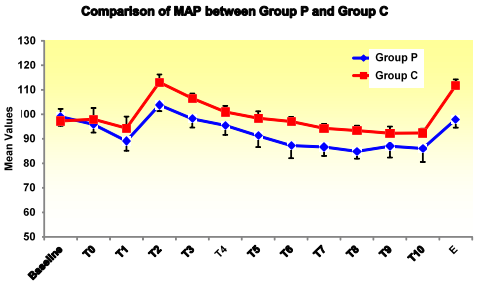
MEAN ARTERIAL PRESSURE

TABLE14

MAP(mmHg)	Group P (n=40)	Group C (n=40)	P Value		
	Mean ± SD	Min - max	Mean ± SD	Min - max	
Baseline	99.04 ± 3.73	92 - 104	97.25 ± 4.94	87 - 105	0.075
T0	95.87 ± 3.31	90 - 101	97.99 ± 4.58	89 - 104	0.020*
T1	89.10 ± 3.96	84 - 96	94.33 ± 4.73	85 - 101	<0.001*
T2	103.82 ± 2.52	99 - 106	113.06 ± 3.18	107 - 118	<0.001*
T3	98.15 ± 3.55	93 - 104	106.51 ± 1.97	103 - 110	<0.001*
T4	95.49 ± 3.86	90 - 104	100.98 ± 2.44	96.66 - 104	<0.001*
T5	91.21 ± 4.60	84- 101	98.43 ± 2.80	93 - 105	<0.001*
T6	87.22 ± 5.14	82 - 98.66	97.08 ± 1.85	93.33 - 99.33	<0.001*
T7	86.68 ± 3.65	82 - 94.66	94.27 ± 1.81	89.33 - 96.66	<0.001*
T8	84.86 ± 2.98	82 - 94	93.35 ± 2.04	89 - 97	<0.001*
T9	86.96 ± 4.63	82 - 97	92.31 ± 2.70	89 - 97	<0.001*
T10	86.05 ± 5.51	74.66 - 93.66	92.41 ± 1.74	89.33 - 94.66	<0.001*
E	97.96 ± 3.43	92 - 105	111.80 ± 2.46	107 - 116	<0.001*

P<0.05 was considered statistically significant.

FIGURE11



Mean arterial pressures were significantly lower in Group P than Group C

POSTOPERATIVE SIDE EFFECTS

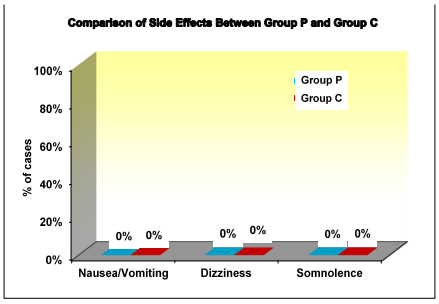
TABLE 15

Postoperative Side Effects	Group P (n=40)	Group C (n=40)			P Value
	Frequency	%	Frequency	%	
Nausea/Vomiting	0	0%	0	0%	-
Dizziness	0	0%	0	0%	-
Somnolence	0	0%	0	0%	-

P<0.05 was considered statistically significant.

None of the patients in both the groups had side effects like nausea and vomiting, dizziness or somnolence in the postoperative period .

FIGURE 12



DISTRIBUTION OF SURGICAL PROCEDURES

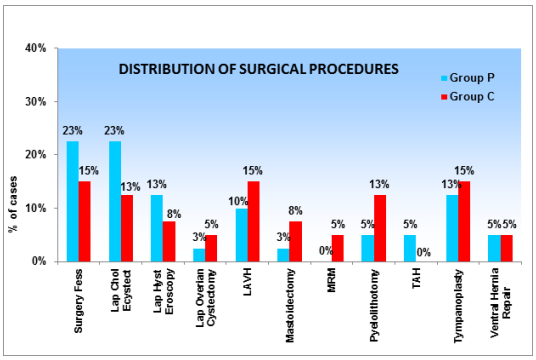
TABLE 16

	Group P	Group C			P Value
	Frequency	%	Frequency	%	
FESS	9	23%	6	15%	0.499
Lap Cholecystectomy	9	23%	5	13%	
Lap Hysteroscopy	5	13%	3	8%	
Lap Ovarian Cystectomy	1	3%	2	5%	
LAVH	4	10%	6	15%	
Mastoidectomy	1	3%	3	8%	
MRM	0	0%	2	5%	
Pyelolithotomy	2	5%	5	13%	
TAH	2	5%	0	0%	
Tympanoplasty	5	13%	6	15%	
Ventral Hernia Repair	2	5%	2	5%	
Total	40	100%	40	100%	

P<0.05 was considered statistically significant.

Data from the above table shows that there is no statistically significant difference between the type of surgeries done in the 2 groups.(P value > 0.05)

FIGURE 13



DISCUSSION

Laryngoscopy and endotracheal intubation form an integral part of balanced anesthesia wherein the airway is secured with an endotracheal tube , and controlled ventilation is administered to the patient.. The cardiovascular responses to laryngoscopy and tracheal intubation such as hypertension, tachycardia, dysrythmias and even myocardial ischemia25 are well known and associated with increase in circulating catecholamine levels.[18]. Effective attenuation of this response ,therefore ,is an important goal in modern day anesthesiaVarious techniques have been proposed to attenuate such responses.

Incidence of tachycardia and rhythm disturbances as a result of intubation are less if atropine was avoided as premedicant.[26] Topical and systemic lidocaine, alpha or beta adrenergic blockers, opioids, dexmedetomidine have been used with various success .[4,6,14,1] Nitroglycerin administered intranasally attenuated the hypertensive response to laryngoscopy and intubation but tachycardia was observed in both nitroglycerine and control groups.[5]. Calcium channel blockers given intravenously attenuated this hypertensive response , but among them only verapamil blunted the tachycardic response to tracheal intubation.7 Remifentanil 1µg/kg followed by 0.5µg/kg/min. given intravenously attenuated the pressor response to intubation but was associated with bradycardia and and/or hypotension.[14]

Recently, oral gabapentin has been studied as an efficacious premedication for attenuation of pressor response to laryngoscopy and intubation.[2,9,10]Pregabalin ,which is a successor of gabapentin shares the same mechanism of action but has a superior pharmacokinetic profile.[8]

The present study has been conducted on 80 ASA Class 1 and 2 patients to evaluate the effects of oral pregabalin premedication 150 mg on hemodynamic responses to laryngoscopy and intubation , in comparison with the control group. These 80 patients were randomly divided into 2 groups of 40 patients each:

Group P(n = 40) : received pregabalin 150 mg p.o. 1 hour prior to inductionGroup C(n = 40) : received placebo p.o. 1 hour prior to inductionThe parameters studied were preoperative level of sedation, perioperative hemodynamic variables – (heart rate , systolic blood pressure, diastolic blood pressure , mean arterial pressure) and incidence of any untoward side effect , if any , in the postoperative period.

The demographic data (mean age, weight , height , BMI) , sex ratio and ASA grades were comparable and did not bear any statistical significance.

The baseline hemodynamic variables and duration of laryngoscopy were comparable in both the groups.

One hour after administration of study drug , level of sedation was significantly higher in the pregabalin 150 mg group as compared to control group .

Infact , 21 patients achieved level 2 sedation and 3 patients achieved level 3 sedation. This observation was in accordance with an earlier study by B.Rastogi et al21 who reported a significantly higher degree of sedation in patients receiving pregabalin 150 mg premedication as compared to pregabalin 75 mg and control groups.

A significant difference in heart rate was observed between group P and group C starting from 1 hour after premedication (T0) until 60 minutes after laryngoscopy and intubation.Values were highly significant immediately ,1 minute and 3 minutes after intubation and also after extubation. Ayya syama sundar et al 23had also reported a significantly higher increase in heart rate 1 min after intubation in the control group in comparison with the pregabalin group in their study.

The reduction in Systolic Blood Pressure was more in group P as compared with group C with highly significant difference at all time points (T0 to E). This observation is similar to the study conducted by Ebru Salman et al 3who found that Systolic blood pressure after anesthesia induction, at intubation and 1 minute post intubation was significantly lower in pregabalin group as compared to placebo The reduction in Diastolic Blood Pressure was more in group P when compared with group C with highly significant difference at all time points from T1 to E .

The attenuation of Mean Arterial Pressure in the pregabalin group was highly significant statistically as compared with the control group.at all time points from T0 to E. B.Rastogi et al21 had found a similar attenuation in MAP in the pregabalin 150 mg group in comparison with placebo in their study.

Our study shows, that oral premedication with pregabalin 150 mg one hour before surgery attenuated the hemodynamic response to laryngoscopy and endotracheal intubation. This might be due to adequate analgesia and sedation. The effect of pregabalin on the hemodynamic response to laryngoscopy and tracheal intubation might be explained by its inhibitory effects on membrane voltage gated calcium channels. Pregabalin, binds potently and selectively to the alpha 2 delta subunit of hyperexcited voltage gated calcium channels. It modulates the release of excitatory neurotransmitters in hyperexcited neurons, restoring them to normal physiologic state, by reducing calcium influx at nerve terminals , thus producing adequate analgesia and sedation.[27]

We did not measure stress mediators such as endogenous plasma catecholamines or cortisone and this is considered as a limitation of our study.

We only included ASA grade 1 and 2 patients in the age group of 25 to 50 years in our study , as elderly patients more often take drugs such as antidepressants, hypnotics and antihypertensives with increased sensitivity to anaesthetic medications and the safety and effectiveness of pregabalin in children and adolescents has not been established.

We chose the dose of pregabalin as 150 mg based on the study of White et al[19] who found that preoperative medication with pregabalin at doses 75 mg was not effective in attenuating acute preoperative anxiety and at the dose of 300 mg produced increased level of sedation before and after ambulatory surgery.

As pregabalin is rapidly absorbed when administered empty stomach, with peak plasma concentration reaching at one hour, we chose to administer it 1 hour prior to induction , in order to attain maximal plasma concentration and hence peak effect at the time of laryngoscopy and intubation.

Since we have used ondansetron 4mg [28] in i.v. infusion intraoperatively for prevention of nausea and vomiting , we did not observe this side effect in any of our patient. Also, dizziness or somnolence was not seen in any patient in the study.

The attenuation of pressor response of airway instrumentation of direct laryngoscopy and intubation with near-stable haemodynamic variables and nopost-operative complication during the present study was an indication of clinically effective and safe analgesia and sedation with oral pregabalin (150 mg)premedication.

Several mechanisms may contribute to the beneficial effects, which includes the modulation of visceral pain and central sensitization.[8,29] It will beappropriate at this juncture to put forward that the favourable pharmacokinetics of pregabalin make it a valuable premedicant for attenuation of haemodynamic
pressor response of airway instrumentation during general anaesthesia[30,31]

The intraoperative haemodynamic stability may be beneficial in obese, hypertensive and cardiac compromised patients. The pregabalin may be used inasthmatic and airway-compromised patients as it does not cause post-operative respiratory depression.

In our study, the 150 mg oral pregabalin has sedated the patients pre-operatively and effectively attenuated the laryngoscopy and intubation-induced haemodynamic pressor response intraoperatively. There was perioperative haemodynamic stability with no post-operative side-effects and respiratory
inadequacy.

REFERENCES:

1. Prys Roberts C, Green LT, Meloche R, Foex P. Studies of Anesthesia in relation to hypertension II,Hemodynamic consequences of induction and endotracheal intubation.Br J Anaesth 1971;43:531-47
2. Fassoulaki A,Melimeni A.,Paraskeva A.,Petropoulos G. Gabapentine attenuates the pressor response to direct laryngoscopy & tracheal intubation.Br J Anesth 2006;96:769-73
3. Salman E, Celik C ,Candan S(2012).Premedication with single dose pregabalin 150 mg attenuates hemodynamic response to laryngoscopy & tracheal intubation.1;297.doi :10.4172/scientific reports 297
4. Kautto UM.Attenuation of the Circulatory Response to Laryngoscopy and Intubation by Fentanyl.Acta Anesthesiol Scand 1982;26(3):217-21
5. Fassoulaki A, Kaniaris P. Intranasal administration of nitroglycerine attenuates the presser response to laryngoscopy and intubation of the trachea. Br J Anaesth1983;55:49-52.
6. Helfman SM, Gold MI, Delisser EA, Herrington CA. Which drug prevents tachycardia and hypertension associated with tracheal intubation: Lidocaine, Fentanyl, or Esmolol? AnesthAnalg 1991;72:482-6.
7. Mikawa K , Nishina K , Maekawa N ,Obora H. Comparison of Nicardipine , diltiazem and Verapamil for controlling cardiovascular response to tracheal intubation. Br J Anaesth 1996;76:221-26
8. Ben-Menachem E. Pregabalin pharmacology and its relevance to clinical practice. Epilepsia 2004;45:13-8.
9. Memis D, Turan A, Karamanlioglu B, Seker S, Ture M. Gabapentin reduces cardiovascular responses to laryngoscopy and tracheal intubation. Eur J Anaesth 2006;23:686-90.
10 Bafna U., Goyal V., Garg A .A camparison of different doses of gabapentin to attenuate hemodynamic responses to laryngoscopy and tracheal intubation in normotensive patients.J Anaesthesiol Clin Pharmacol. 2011 Jan-Mar; 27(1): 43–46.
11. Jokela R, Ahonen J, Tallgren M, Haanpaa M, Korttila K.Premedication with pregabalin 75 or 150 mg with ibuprofen to control pain after day-case gynaecological laparoscopic surgery. Br J Anaesth 2008;100:834-40.
12. Saraswat V , Arora V.Preemptive Gabapentin vs Pregabalin for Acute Postoperative Pain after Surgery under Spinal Anaesthesia. Indian J Anesth 2008; 52 (6):829-834
13. Ghai A., Gupta M, Hooda S,Singla D, Wadhera R. Saudi J Anaesth.2011 Jul-Sep; 5(3): 252–257
14. Thompson JP, Hall AP, Russell J, Cagney B, Rowbotham DJ. Effect of remifentanil on the haemodynamic response to orotracheal intubation. Br J Anaesth 1998; 80: 467–9
15. Sagiroglu A E, Celik M , Orhon Z , Yuzer S , Sen B.Different doses of dexmedetomedine on controlling hemodynamic responses to tracheal intubation.Int J Anesthesiol 2010;27(2)
16. Sameenakousar, Mahesh , Srinivasan K V. Comparison of fentanyl and clonidine for attenuation of the hemodynamic response to laryngoscopy and endotracheal intubation. J Clin Diagn Res. 2013 January; 7(1): 106–111.
17. Bornemann–Cimenti,H ;Lederer. Preoperative pregabalin administration significantly reduces postoperative opioid consumption & mechanical hyperalgesia after transperitoneal nephrectomy.Br J Anesth May 2012, 108;5:845
18. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. Br J Anaesth 1987; 59: 295–9
19. White PF, Tufanogullari B, Taylor J, Klein K (2009)The effect of pregabalin on preoperative anxiety and sedation levels:a dose ranging study.Anesth Analg 108: 1140-1145.
20. Gonano C , Latzke D .The anxiolytic effect of pregabalin in out patients undergoing

minor orthopedic surgery.Journal of psychopharmacology Feb 2011;25(2):249-53
21. Rastogi B , Gupta K , Gupta P , Agarwal S , Jain M , Chauhan H .Oral pregabalin premedication for attenuation of hemodynamic pressor response of airway instrumentation during general anesthesia.Indian J Anesth 2012;56:49-54
22 Gupta K , Sharma D ,Gupta P K.Oral premedication with pregabalin or clonidine for hemodynamic stability during laryngoscopy & lap. Cholecystectomy.Saudi J Anesth 2011Apr-Jun ;5(2):179-184
23. Syama Sundar A, Kodali R, Sulaiman S, Ravullapalli H, Karthekeyan R, Vakamudi M.The effects of preemptive pregabalinon attenuation of stress response to endotracheal intubation and opioid sparing effect in patients undergoing off-pump coronary artery bypass grafting Annals of Cardiac Anaesthesia Jan-Mar-2012;15:1
24. Gajraj NM. Pregabalin: Its pharmacology and use in pain management. Anesth Analg 2007;105:1805-15.
25. Kovac AL. Controlling the hemodynamic response to laryngoscopy and endotracheal intubation. J Clin Anesth 1996; 8: 63–79
26. Fassoulaki A, Kaniaris P. Does atropine premedication affect the cardiovascular response to laryngoscopy and intubation?Br J Anaesth 1982; 54: 1065–8
27. Kavoussi R . Pregabalin : From molecule to medicine. Eur Neuropschycopharmacol 2006;16: 128-133.
28. Claybon L. Single dose intravenous ondansetron for the 24 hour treatment of postoperative nausea and vomiting. Anaesthesia 1994;49(Suppl):24-9.
29. Stawicki SP. Sedation scales: Very useful, very underused. OPUS12 Scientist 2007;1:10-2.
30. Bovill JG, Howie MB. Clinical pharmacology for Anesthetists. Philadelphia: W.B. Saunders; 1999.
31. Davies NJ, Chashman JN. Lee's synopsis of anaesthesia 13th Ed, Oxford: Butterworth-Heineman Elsevier; 2006;3.3:352.