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A DOSE-RESPONSE STUDY OF ORAL PREGABALIN PREMEDICATION FOR ATTENTUATION OF HAEMODYNAMIC PRESSOR RESPONSE OF AIRWAY INSTRUMENTATION DURING GENERAL ANAESTHESIA.

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Abstract:

Background: Laryngoscopy and endotracheal intubation have been the mainstay in providing adequate airway management and anesthesia delivery. Hemodynamic response to laryngoscopy and endotracheal intubation is a sympathetic response,[1] which may be the result of an increase in catecholamine activity. Attempts were made by various investigators to reduce the sympathetic response to laryngoscopy and intubation. **Methodology-** The study was conducted in the Anesthesiology department, at the tertiary care hospital for a period of 18 months. 90 patients aged between 18 years to 60 years of ASA Class 1 and 2, posted for elective surgeries under general anaesthesia. 90 normotensive adult patients, after informed consent divided randomly into 3 groups of 30 patients. Group C patients were given the 2 placebo capsules orally one hour prior to induction. Group P75 patients were given 75mg pregabalin capsule and one placebo capsule orally one hour prior to induction. Group P150 patients were given two 75mg pregabalin capsules orally one hour prior to induction. Randomisation of the group was done using shuffled sealed opaque envelope method. Heart rate, Systolic Blood pressure, Diastolic Blood Pressure and Mean Arterial Pressure recordings were done along with sedation scoring (using Ramsay's Sedation Score). **Results:** There was a significant increase in heart rate in the control group as compared to the P75 and P150 group. In the P75 Group, there was a statistically significant increase in heart rate as compared to the P150 group at first minute after laryngoscopy. In the P150 Group there was a statistically significant fall in SBP, DBP and MAP as compared to the other two groups at various time intervals which was statistically significant. Also there was a statistically significant decrease in Propofol and Vecuronium dose requirement in both P75 and P150 group as compared to the control group. **Conclusion:** Pregabalin 150mg is more effective than Pregabalin 75mg in suppressing the haemodynamic response. The requirement of Propofol for induction and requirement of Vecuronium for muscle relaxation, are decreased by oral premedication of Pregabalin. There is no effect of Pregabalin when given as a premedicant on the recovery status and level of sedation after general anaesthesia.

Keywords- Pregabalin, pressor response, laryngoscopy, general anaesthesia.

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Introduction: Patients who have been anesthetised are unable to maintain adequate airway on their own, and artificial airway maintenance devices are used.[1] Intubation has many advantages including the provision of a reliable airway, delivery of anesthetic gases. But endotracheal intubation also has complications. These complications can be seen during insertion, after insertion and during extubation of endotracheal tube and they include airway trauma, physiological reflexes like tachycardia and hypertension, malposition, laryngospasm, increased airway resistance

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as well as pulmonary edema.[1,2] In 1940 Reid and Brace discovered the hemodynamic response to laryngoscopy and endotracheal intubation. The principle mechanism is the sympathetic response,[3] which may be the result of an increase in catecholamine activity.[4] The hemodynamic response is usually transitory, variable and unpredictable. Transitory hypertension and tachycardia are well tolerated in a healthy individual, but they may be hazardous to those with hypertension, coronary artery disease or cerebrovascular diseases.[5] These transient hemodynamic changes can cause potentially deleterious effects like pulmonary oedema, myocardial insufficiency.[6] Attempts were made by various investigators to reduce the sympathetic response to laryngoscopy and intubation. Use of intravenous anesthetic induction agents[7] did not adequately suppress the hemodynamic responses produced by endotracheal intubation. Before laryngoscopy, use of volatile anesthetics,[7] topical and intravenous lidocaine,[8] opioids,[9] Calcium channel blockers[10] ,β-blockers[11], Alpha-2 agonists like Clonidine, Dexmedetomidine[12,13] have been tried by various investigators. All these drugs showed varying results and have not been effective in completely obtunding the sympathetic response to intubation. Nowadays antiepileptic drugs like Gabapentin and Pregabalin, are also being used for the attenuation of intubation response. Both have been found to suppress the hemodynamic response to laryngoscopy. [14,15,16] Gabapentin is 3-4 times less potent as compared to Pregabalin.[31] Onset of action of oral Pregabalin is one hour and Cmax occurs in two hours whereas onset is two hours and Cmax is three hours for Gabapentin.[17] Hence the pharmacokinetic and pharmacodynamic features suggest that Pregabalin is a better drug for suppression of intubation response compared to Gabapentin. Less number of studies have tried to find out the optimal dose of Pregabalin that can be used for suppression of intubation response. Pregabalin is an analogue of the neurotransmitter gamma-aminobutyric acid (GABA). However, pregabalin does not mediate its effects specifically through an effect upon GABA-ergic transmission.[15]

Aim: To find out the effective dose of pregabalin for suppression of hemodynamic response to laryngoscopy and intubation.

Primary Objectives:

1. Study the changes in Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure and Mean Arterial Pressure associated with laryngoscopy and intubation.
2. To find out the effective dose of pregabalin to suppress the laryngoscopy and intubation response.

Secondary Objectives:

1. To study any adverse drug effects associated with Pregabalin administration such as increased sedation, dizziness, blurred vision and delayed recovery.
2. To study the dose of propofol required for induction, with different doses of pregabalin.

Methodology: The study was done in government general hospital over a period of 18 months. The study was undertaken after obtaining ethical committee clearance and informed consent from all patients. Source of data: 90 patients posted for surgeries under general anaesthesia belonging to ASA class I and II.

Inclusion criteria: Adult patients of either sex aged between 18-60 years weighing between 40-80 kgs posted for elective surgeries under general anaesthesia belonging to ASA Class I and II. **Exclusion criteria:**Patients with severe systemic disorders like- uncontrolled hypertension, cardiac, renal, hepatic and cerebral diseases. Patients with difficult airway and obese patients. Patients with severe endocrinal diseases like uncontrolled hyperthyroidism, hypothyroidism and diabetes mellitus. Patients posted for emergency surgeries, pregnant and breast feeding women were excluded.

A routine pre-anesthetic examination was conducted. Randomization of the group was done using shuffled sealed opaque envelope method. The double-blind design of the study was assured by the fact that an anesthesiologist not involved in the study was opening the sealed envelopes and issuing the capsules to the patients one hour before the surgery. Patients in Group P150- two 75mg capsules of pregabalin, Group P75-75mg capsule of pregabalin and one placebo capsule Group C patients –2 Placebo capsules,were given orally one hour before induction. Hemodynamic recordings were done. Side effects like dizziness and blurring of vision were also noted. Patients were premedicated with

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1mg of midazolam and 1 microgram/kg bodyweight of fentanyl, 3 minutes before induction. Pain on injection of Propofol was prevented by using intravenous injection of 1.5 mg/kg body weight of preservative-free 2% lidocaine given 90 seconds before Propofol. The patients were preoxygenated for 3 minutes via a face mask while administering premedicants. Patient was induced with propofol 2mg/kg slowly. The dose of propofol required for induction was noted. Suxamethonium 1.5 mg/kg was used for intubation in all the patients. Anesthesia was maintained with Oxygen, Nitrous Oxide, Vecuronium 0.06mg/kg body weight and 1% Sevoflurane . Further Vecuronium 0.01mg/kg body weight was administered as and when required and the total dose required for each patient was noted. After the procedure patients of all the groups were reversed with neostigmine 0.05mg/kg and glycopyrrolate 0.008mg/kg, given intravenously. Sedation scoring and time for recovery were also noted postoperatively after extubation.

Statistcs: The results obtained in the study are analysed using Microsoft Excel and SPSS 20 software.The present study results between the three groups was compared statistically using Analysis Of Variance(ANOVA) and Student 't' test (independent samples 't' test).

Results:

Table 1: Showing the age distribution:

Age group (years)	Group C	Group P75	Group P150	Total
	No.of patients	No.of patients	No.of patients	
18-30	9 (30)	11 (36.6)	12 (40)	32 (35.5)
31-40	5 (16.7)	9 (30)	7 (23.3)	21 (23.4)
41-50	8 (26.65)	5 (16.7)	6 (20)	19(21.1)
51-60	8 (26.65)	5 (16.7)	5 (16.7)	18 (20)
Total	30 (100)	30 (100)	30 (100)	90 (100)
Mean age in years± SD	40.37±12.24	36.73±11.18	38.33±11.23	38.486±11.53
p-value	**0.1 (NS)**			

Figures in the parentheses indicate the percentage, NS – Not significant

Table 2: Showing the sex distribution between three groups

Sex	Group C	Group P75	Group P150	Total
	No. of patients	No. of patients	No. of patients	
Male	15 (50)	7 (23)	9 (30)	31 (34)
Female	15 (50)	23 (77)	21 (70)	59 (66)
Total	30 (100)	30 (100)	30 (100)	90 (100)
p-value	**0.078 (NS)**			

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Table 3: Showing the intergroup comparison of mean heart rate (bpm) changes inresponse to laryngoscopy and intubation between all the groups

	Group C	Group P75	Group P150	p-value
Basal	87.97±11.59	88.03±13.47	85.97±10.51	0.505(NS)
AD-30th min	88.03±10.09	84.90±11.93	81.67±10.79	0.017(S)
AD-60th min	86.80±10.84	84.77±12.81	81.37±12.04	0.47(NS)
After induction before Succinylcholine	85.23±10.76	82.27±13.21	79.40±10.28	0.332(NS)
AI- 1st min	122.10±13.86	96.23±13.32	87.50±11.38	0.00(HS)
AI- 3rd min	115.77±13.60	89.57±12.66	86.60±12.55	0.00(HS)
AI- 5th min	108.80±12.59	86.43±12.37	81.77±11.32	0.001(HS)
AI- 10th min	100.43±11.83	84.43±12.14	79.90±10.22	0.001(HS)
AI- 15th min	99.33±10.73	84.17±12.57	80.57±10.68	0.045(S)

($p<0.01$) – Highly significant (HS); ($p<0.05$) – Significant (S);($p>0.05$) – Not significant(NS); AD- After study drug administration; AI- After intubation.

The increase is 34 bpm in control group, 8 bpm in P75 group and 2 bpm in P150 group. Compared to the 3 groups at 1st minute, it is statistically highly significant. By 5th minute after laryngoscopy and intubation, the heart rate in Group P75 and P150 have reached the basal values, whereas with the control group, even at 15th minute the heart rate has not reached the baseline value, but still on the higher side which is statistically highly significant.

Table 4: Showing the intergroup comparison of Systolic Blood Pressure (mmHg) changes in response to laryngoscopy and intubation between all three groups

	Group C	Group P75	Group P150	p-value
Basal	127.57±6.15	124.27±13.73	121.17±11.84	0.087(NS)
AD-30th min	128.57±7.81	121.53±13.25	119.10±14.75	0.011(S)
AD-60th min	129.53±7.78	122.07±13.39	113.57±13.83	0.00(HS)
After induction before Succinylcholine	131.10±6.69	113.50±12.59	108.67±11.53	0.00(HS)
AI- 1st min	154.87±6.69	128.33±14.67	115.67±13.12	0.00(HS)
AI- 3rd min	141.27±12.49	115.47±18.41	110.10±13.04	0.00(HS)
AI- 5th min	131.30±14.15	110.90±14.38	108.60±12.50	0.00(HS)
AI- 10th min	127.63±10.12	114.57±12.51	109.47±11.21	0.00(HS)
AI- 15th min	123.23±9.25	115.57±13.08	110.53±12.31	0.00(HS)

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There is a statistically highly significant difference between the three groups at 60th minute after study drug administration, after induction and after laryngoscopy and intubation at 1, 3, 5,10 and 15 minutes. There is a fall in SBP after drug administration at 60th minute and after induction in Group P75 and Group P150 and this is highly significant. The fall in SBP after 30min of drug administration is significant compared to control group.

Table 5: Showing the intergroup comparison of Diastolic Blood Pressure(mmHg) changes in response to laryngoscopy and intubation between all three groups

	Group C	Group P75	Group P150	p-value
Basal	76.40±6.04	80.47±10.81	76.97±8.63	0.153 (NS)
AD-30th min	77.00±7.06	76.73±9.61	75.87±7.23	0.850 (NS)
AD-60th min	77.13±7.31	77.80±11.30	71.90±9.22	0.033 (S)
After induction before Succinylcholine	78.07±7.73	75.63±11.2	71.13±10.69	0.028 (S)
AI- 1st min	99.47±6.28	86.50±12.13	76.93±9.46	0.000 (HS)
AI- 3rd min	87.57±8.84	77.03±16.32	72.03±11.06	0.000 (HS)
AI- 5th min	85.80±8.91	74.13±10.95	73.93±10.18	0.000 (HS)
AI- 10th min	81.50±9.46	74.97±11.85	72.93±8.58	0.004 (HS)
AI- 15th min	80.83±8.7	76.90±10.30	74.30±8.23	0.024 (S)

There is a statistically significant difference among the three groups in DBP after induction. There is a fall of DBP in Group P75 and Group P150, and this is significant as compared to the control group after induction.

Table 6: Showing the intergroup comparison of Mean Arterial Pressure(mmHg) changes in response to laryngoscopy and intubation between all three groups

	Group C	Group P75	Group P150	p-value
Basal	93.13±6.62	95.27±12.24	90.93±7.94	0.199(NS)
AD-30th min	93.50±7.99	91.00±10.03	89.80±7.52	0.240(NS)
AD-60th min	93.47±8.95	92.23±12.02	85.20±9.80	0.005(HS)
After induction before Succinylcholine	93.47±5.56	87.07±10.41	83.00±10.50	0.000(HS)
AI- 1st min	117.97±5.72	100.40±12.74	88.93±10.27	0.000(HS)
AI- 3rd min	106.53±11.10	91.27±17.39	85.43±11.22	0.000(HS)
AI- 5th min	103.77±8.77	88.23±12.59	85.10±9.93	0.000(HS)
AI- 10th min	98.30±9.17	88.57±12.36	85.43±7.44	0.000(HS)
AI- 15th min	94.83±9.01	90.27±11.78	87.10±8.31	0.011(HS)

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There is a statistically highly significant difference among the three groups in MAP at 60th minute after study drug administration and after induction. There is a fall of MAP in Group P75 and Group P150, and this is highly significant as compared to thecontrol group. At 1st minute after laryngoscopy and intubation, there has been an increase in the MAP in control group, which has not reached basal value even at the 15th minute. Whereas in the P75 group, there is an increase in MAP by 5mmHg at 1st minute as compared to the basal, whereas there is a decrease by 2mmHg in Group P150 at 1st minute. Compared to the MAP at different time intervals from 1st to 15th minute, there is statistically highly significant difference among the three groups.

Table7: Showing the intragroup comparison of Mean Arterial Pressure changesin response to laryngoscopy and intubation in Group C

	Group C		p-value
Basal - AD-30 min	93.13±6.62	93.50±7.99	0.647 (NS)
Basal- AD-60min	93.13±6.62	93.47±8.95	0.719 (NS)
Basal- After induction	93.13±6.62	93.47±5.56	0.719 (NS)
Basal - 1 min AI	93.13±6.62	117.97±5.72	0.000 (HS)
Basal- 3min AI	93.13±6.62	106.53±11.10	0.000 (HS)
Basal- 5min AI	93.13±6.62	103.77±8.77	0.000 (HS)

Compared with the basal mean arterial blood pressure, there is a statistically highly significant increase at 1st, 3rd and 5th minute after laryngoscopy and intubation.

Table 8: Showing the intragroup comparison of Mean Arterial Pressure changesin response to laryngoscopy and intubation in Group P75

	Group P75		p-value
Basal - AD-30 min	95.27±12.24	91.00±10.03	0.010 (S)
Basal- AD-60min	95.27±12.24	92.23±12.02	0.223 (NS)
Basal- After induction	95.27±12.24	87.07±10.41	0.001 (HS)
Basal - 1 min AI	95.27±12.24	100.40±12.74	0.055 (NS)
Basal- 3min AI	95.27±12.24	91.27±17.39	0.237 (NS)
Basal- 5min AI	95.27±12.24	88.23±12.59	0.007 (HS)

Compared with the basal mean arterial pressure, there is a statistically significant decrease at 30th minute after drug administration and highly significant decrease after induction and 5 minutes after intubation.

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Table9: Showing the intragroup comparison of Mean Arterial Pressure changesin response to laryngoscopy and intubation in Group P150

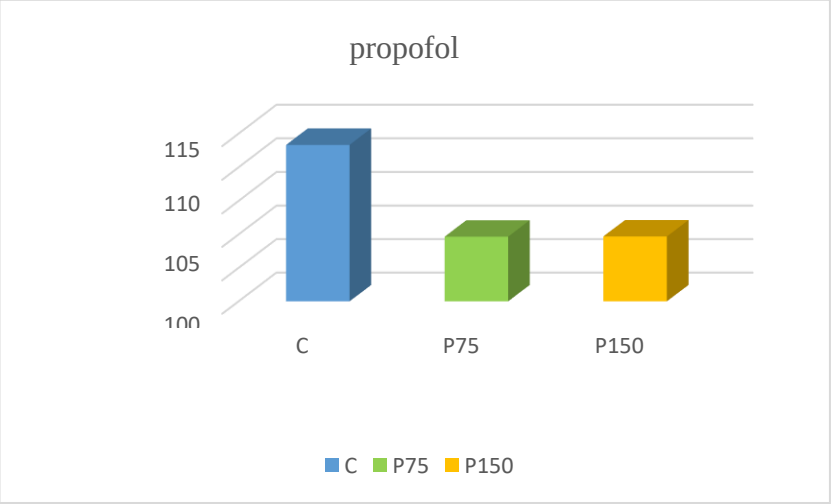
	Group P150		p-value
Basal - AD-30 min	90.93±7.94	89.80±7.52	0.182 (NS)
Basal- AD-60min	90.93±7.94	85.20±9.80	0.002 (HS)
Basal- After induction	90.93±7.94	83.00±10.50	0.000 (HS)
Basal - 1 min AI	90.93±7.94	88.93±10.27	0.237 (NS)
Basal- 3min AI	90.93±7.94	85.43±11.22	0.005 (HS)
Basal- 5min AI	90.93±7.94	85.10±9.93	0.003 (HS)

There was statistically highly significant decrease at 60th minute after studydrug, after induction, 3rd minute and 5th minute after laryngoscopy and intubation.

Table10: Showing the Mean total amount of Propofol used between three groups (in mgs):

Group C	Group P75	Group P150	P value
113.33±11.55	99.67±16.71	99.67±13.77	0.000(HS)

Figure1: Showing the Mean total amount of Propofol used between three groups(in mgs):



In Group P75 and Group P150, there is a statistically highly significant decreasein the total dose of Propofol used for induction (14mg in both the groups) as comparedto the control group.

Table 11: Showing the Mean total dose of Vecuronium used between three groups (mgs)

Group C	Group P75	Group P150	P value
4.72±0.85	3.62±0.90	3.42±0.47	0.000 (HS)

In Group P75 and Group P150, there is a statistically highly significant decreasein the total dose of Vecuronium used (1.1mg and 1.3mg respectively) as compared to the control group.

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Table12: Showing the Mean Duration of Laryngoscopy between three groups:

Group C	Group P75	Group P150
12.93±2.16	13.53±2.76	13.00±2.21

Table13: Showing the Mean Ramsay Sedation Score between three groups:

	After study drug 30th minute(mean)	After study drug 60th minute(mean)	Post-op (mean)
Control	2	2	2
Group P75	2	2	2
Group P150	2.03	2.03	2.03

There is no statistically significant difference in the sedation scoring among the three groups.

Discussion:

Heart Rate Response: The HR response is statistically significant after induction and highly significant at 1st, 3rd, 5th, 10th and 15th minutes after laryngoscopy and intubation in comparison between the control and P150 groups. Between Pregabalin 75mg and Pregabalin 150mg Groups, pregabalin 150mg was found to be better, as there was no increase in the HR at various time intervals after intubation. With Pregabalin 75mg, there was a significant increase in the HR only at 1st minute compared to Pregabalin 150mg. But this was only 8 bpm increase as compared to 34 beats increase with the control group. In Group C, compared with basal heart rate, there is a sustained increase in heart rate after laryngoscopy and intubation from 1st to 5th minute which is statistically highly significant. The decrease in HR after induction is statistically significant in Group P75, compared with basal heart rate, there is a statistically significant decrease in heart rate after induction. Statistically highly significant increase at 1st minute after laryngoscopy and intubation. In Group P150, compared with the basal heart rate, there is a statistically highly significant decrease in heart rate at 30th after study drug administration and after induction and statistically significant decrease in heart rate 60 minutes after study drug administration and 5minutes after intubation. Then the heart rate has remained almost same as the basal values. In 2012, Ayya Syama Sundar et al[15] conducted a randomized, double-blind study to evaluate and compare single perioperative dose of pregabalin 150mg to a placebo regarding the hemodynamic responses to laryngoscopy and endotracheal intubation, to assess perioperative fentanyl requirement and any side effects in patients undergoing off-pump coronary artery bypass grafting. They have found a significant increase in heart rate in the control group as compared to the Pregabalin 150mg group at 1st minute after intubation, which compares with present study. There was no statistically significant difference in the heart rate at 3rd minute and 5th minute in their study, which does not compare with present study. In 2012, Rastogi Bhawna et al[14] conducted a prospective, double-blind, randomized controlled study to evaluate the effects of pregabalin 75mg and 150mg orally on hemodynamic pressor response of airway instrumentation during general anesthesia. They found a statistically significant difference regarding the Heart rate after induction and at 1st and 5th minute after intubation, compared to the control group, which also compares with present study. In their study, there is an increase in the Heart rate in the Pregabalin 75 and Pregabalin 150 Groups after intubation, which did not reach the basal value even after 15 minutes, which does not compare with present study. In the above study, the authors concluded that Pregabalin 150mg is more effective than 75mg, which compares with present study. In 2012 Ebru Salman et al.,[18] did not find a statistically significant difference in heart rate, between the Control

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Group and the Pregabalin150mg Group, after intubation at various time intervals, which does not compare with present study.

Systolic blood pressure: There is a maximum increase in SBP of 27mmHg in control group compared with basal at 1st minute after laryngoscopy and intubation, and it has reached the baseline values at only 10th minute. With P75 group, there is an increase of 4mmHg after laryngoscopy and intubation as compared to the basal values, and has reached basal values by 3rd minute only. The SBP response is statistically significant at 30th and 60th minute after drug administration, highly significant after induction and 1st, 3rd, 5th, 10th and 15th minute after laryngoscopy and intubation in comparison between the control and P75 Groups. There was no increase in the SBP with 150mg of pregabalin at any of the time intervals after laryngoscopy and intubation. Whereas the SBP increased significantly with the control group after 1st minute and did not return to the basal level even after 15 minutes. The SBP response is statistically significant at 30th and 60th minute after drug administration, highly significant after induction and 1st, 3rd, 5th, 10th and 15th minute after laryngoscopy and intubation in comparison between the control and P75 Groups. The SBP response is statistically highly significant at 30th and 60th minute after drug administration, after induction and 1st, 3rd, 5th, 10th and 15th minute after laryngoscopy and intubation in comparison between the control and P150 Groups. Present study is similar to that of Ayya Syam Sundar et al[15] and Ebru et al[18] study findings wherein there is a decrease in SBP at various time intervals after intubation in the Pregabalin 150mg Group and significant rise of SBP with control groupafter laryngoscopy and intubation at 1st, 3rd and 5th minute.

Diastolic Blood Pressure :There is a maximum increase in DBP of 23mmHg in control group compared with basal at 1st minute after laryngoscopy and intubation, and it has not reached the basal values even at 15th minute. With P75 group, there is an increase of 6mmHg after laryngoscopy and intubation as compared to the basal values, and has reached basal values at 3rd minute only. The DBP response is statistically highly significant at 1st, 3rd and 5th minute and significant in 10th minute after laryngoscopy and intubation in comparison between the control and P75 Groups. The DBP response is statistically highly significant at 1st, 3rd and 5th minute and significant in 10th minute after laryngoscopy and intubation in comparison between the control and P75 Groups. The DBP response is statistically significant at 60th minute after drug administration and highly significant after induction and 1st, 3rd, 5th, 10th and 15th minute after laryngoscopy and intubation in comparison between the control and P150 Groups. There is a statistically significant decrease in DBP after 60minutes of drug administration in the P150 group compared to P75 group. In group C, compared with the basal diastolic blood pressure, there is a statistically highly significant increase at 1st, 3rd and 5th minute after laryngoscopy and intubation in the P150 group. In group P75, compared with the basal Diastolic Blood Pressure there is a statistically significant decrease at 30th minute after study drug, at induction and highly statistically significant decrease in diastolic blood pressure at 5minutes after intubation.There was a statistically significant increase at 1st minute after laryngoscopy and intubation. In group P150, compared with the basal diastolic blood pressure, there was statistically highly significant decrease after induction and significant decrease in DBP 60 minutes after drug administration and 3rd minute after laryngoscopy. There was a statistically significant decrease in the DBP in 75mg Pregabalin and 150mg Pregabalin groups after 60 minutes of test drug administration, induction and 1, 5, 10, 15 minutes after intubation as compared to the control. Also, there was a statistically significant difference in the Pregabalin 150mg Group as compared to the Pregabalin 75mg group at 1 minute after intubation, where with 75mg Group the DBP increased by 6mmHg and in P150 Group there was a decrease by 1mmHg. This concurs with the findings of Ayya Syama Sundar et al.,[15] where there was statistically significant decrease in the DBP with Pregabalin 150 group at various intervals after laryngoscopy.

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Mean arterial pressure: There is a maximum increase in MAP at 1st minute after laryngoscopy and intubation by 5 mmHg as compared to the basal value in Group P75, whereas there is a decrease in MAP by 2mmHg as compared to the basal value in Group P150 at 1st minute, which is statistically highly significant. There is a statistically significant decrease in MAP at 60minutes after drug administration with P150 group compared to P75 group. The MAP response is statistically highly significant after induction and at 1st, 3rd, 5th and 10th minute after laryngoscopy and intubation in comparison between the control and P75 Groups. The MAP response is statistically highly significant at 60th minute after drug administration. There is a statistically significant decrease in MAP at 60minutes after drug administration with P150 group compared to P75 group. In present study, there was a significant increase in MAP after laryngoscopy and intubation at various time intervals in the control group compared to P75 and P150 groups, which compares with the studies done by Rastogi Bhawna et al[14], Ayya Syama Sundar et al[15] and Ebru et al[18]. MAP was significantly reduced in Pregabalin 75mg and pregabalin 150mg groups after intubation at 3,5,10 and 15 minutes. This concurs with study of Rastogi Bhawna at al[14] and Ayya Syam Sundar et al.[15] Moreover, the decrease in Mean arterial pressure was statistically more significant in 150mg Pregabalin Group as compared to 75mg Pregabalin Group, similar to as stated in the study by Rastogi Bhawna et al[28]. In the Pregabalin 75 group, there was 5mmHg increase in MAP compared to the control at 1st minute after laryngoscopy and intubation, which compares with the study done by Rastogi Bhawna et al[14].

A decreased amount of Propofol was required with Pregabalin 75mg (99.67±16.71mg) and with Pregabalin 150mg (99.67±13.77mg) compared to the control group (113.33±11.54mg) for achieving loss of vocal response. This compares to the studies by Bhawna R[14]et al. and Gupta K et al.[19] A decreased amount of vecuronium was required with Pregabalin 75 (3.62±0.90mg) and with Pregabalin 150 (3.42±0.47mg) as compared to the control (4.72±0.85mg), which is statistically highly significant. The reason for Pregabalin premedication decreasing the requirement of propofol and Vecuronium is probably its effect in reducing the amount of excitatory neurotransmitters, as it partially reduces neurotransmitter release in several in vitro systems at concentrations near 10μM (1.6 ng/mL). The sedation score was insignificant, with only one patient in Pregabalin150mg group showing level 3 sedation preoperatively and postoperatively, which compares with the studies conducted by Ayya Syama Sundar et al.[15]and Kukum Gupta et al.[19] Adverse effects were also statistically insignificant with only three patients in the Pregabalin 150mg developing dizziness preoperatively.

Summary: In present study, both 75mg and 150mg of oral Pregabalin administered one- hour prior to induction and laryngoscopy are found to be effective in obtunding the hemodynamic response of HR, SBP, DBP and MAP to laryngoscopy and intubation when compared to control group. The hemodynamic variability was much less in Pregabalin 150mg Group as compared to the Pregabalin 75mg Group. There is a statistically significant reduction of the dose of propofol required for induction and vecuronium for muscle relaxation with Pregabalin 75mg, and 150mg is significant than control. There is no effect of Pregabalin when given as a premedicant on the recovery status and level of sedation after general anesthesia. Oral Pregabalin in the dose of 75mg and 150mg produces minimal side effects.

Conclusion: There is a statistically significant reduction of dose of propofol required for induction and vecuronium for muscle relaxation with Pregabalin 75mg, and 150mg is significant than control. Both 75mg and 150mg of oral Pregabalin, administered one hour prior to induction and laryngoscopy are effective in obtunding the hemodynamic response when compared to control group. Pregabalin 150mg is more effective than Pregabalin 75mg in suppressing the hemodynamic response to laryngoscopy and intubation.

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