Original Research Article

Oral pregabalin vs placebo for attenuation of hemodynamic response following direct laryngoscopy and endotracheal intubation

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Abstract

Direct laryngoscopy and endotracheal intubation can be detrimental due to the associated hemodynamic response especially in patients with low cardiac reserve. This study aims at comparing the efficacy of oral pregabalin (150 mg) vs placebo in attenuating such a hemodynamic response. This study was designed as a prospective, double blind, randomized control trial set in the operating theatre of a tertiary care teaching hospital. Sixty patients of ASA PS - Ⅰ, Ⅱ, aged 18-60 years, both sex undergoing elective surgeries under general anaesthesia of 1-2 hours duration were divided into two groups. Group Ⅰ-oral placebo, Group Ⅱ-oral Pregabalin(150mg) sixty minutes before receiving general anaesthesia using standard technique. Results were analysed using paired and independent t test, ANOVA. P value < 0.05 was considered statistically significant. Oral pregabalin has a greater attenuating effect on blood pressure than heart rate and effectively attenuates hemodynamic response associated with direct laryngoscopy and endotracheal intubation as compared to placebo.

Key Word: Oral Pregabalin; Placebo; hemodynamic response; intubation; laryngoscopy.

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INTRODUCTION

Direct laryngoscopy and endotracheal intubation form the mainstay of general anaesthesia. This causes intense sympathetic discharge[1,2,3] leading to transient, variable, unpredictable hemodynamic changes[4] manifesting as tachycardia, hypertension, dysrhythmias. In susceptible individuals this manifests as myocardial insufficiency, pulmonary edema, left ventricular failure, cerebrovascular accidents[5,6,7].These changes are at its peak 30-45 seconds following the procedure. Many methods have been developed to attenuate or prevent this hemodynamic response like deepening the plane of anaesthesia[9], using lidocaine [8], using topical anesthesia[10], omitting atropine as a premedicant[11], premedicating with Nitroglycerin[12], Betablockers[13], calcium channel blockers[14] and opioids[15]. The latest entrants to this group are gabapentin [16] and pregabalin[17,18,19,20,21,22,23].Pregabalin is an anticonvulsant[17] which is effective in neuropathic pain, incisional, inflammatory, formalin induced injury, anxiety and sleep modulation. It binds to alpha-2-delta [17] subunit of the presynaptic voltage gated calcium channels, reduces depolarization associated calcium influx and reduces the release of several neurotransmitters like glutamate, noradrenaline, serotonin, dopamine and substance P. It is rapidly absorbed orally with peak blood concentration being attained in 1 hour and 98% of absorbed drug excreted unchanged in urine. Due to this pharmacological profile, pregabalin can be a drug to attenuate

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hemodynamic response. The present study was undertaken to know the efficacy of oral pregabalin, 150mg[18] in attenuating hemodynamic response to laryngoscopy and intubation by comparing it with a placebo in a double blind, prospective, randomized controlled study.

MATERIAL AND METHOD

After obtaining approval from institutional ethical committee and written informed consent from the patients, 60 ASA I and II patients of both sex in the age group of 18-60 years undergoing elective surgeries of 1-2hours duration under general anaesthesia were selected. By using simple random sampling, patients were allocated to two groups of 30 each. Group I received oral placebo capsules and Group II received oral pregabalin [150mg] capsules with sips of water 60 minutes before receiving standard general anaesthesia with endotracheal intubation.

EXCLUSION CRITERIA

- ASA-Physical status III and IV
- Emergency Surgeries
- Anticipated Difficult airway and morbid obesity
- Pre existing cardiac disease, hypertension, asthma, severe renal or hepatic dysfunction.
- History of antidepressant, anxiolytics,antipsychotic medications.
- Pregnancy.
- Elective surgeries of duration more than 2 hours.

Patients were premedicated with tab.Ranitidine 150mg, 12 hours and 90 minutes before and tab. Ondansetron 4mg, 90 minutes before shifting to Operating theatre. The basal heart rate and blood pressure were recorded before administering study drug 60 minutes before proposed procedure.In the OT, monitors – pulse oximeter, ECG, NIBP were connected, i. v access secured and crystalloid infusion started at 6-8ml/kg/hr. Patients received i.v glycopyrrolate 0.2mg and i. v midazolam 1mg. Preoxygenation done with 100% oxygen for three minutes. Inj Fentanyl 2mcg/kg i. v was given followed by Inj. Propofol 2mg/kg i.v, Inj Rocuronium 0.6mg/kg i.v . Mask ventilation done with 67% nitrous oxide, 33% oxygen for 90 seconds. Direct laryngoscopy done with no 3 or 4 Mcintosh blades and intubation with cuffed endotracheal tubes of 7.5 size in females and 8.5 size in males. Time taken for laryngoscopy and intubation was noted. The heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure were noted at 1,3,5,10,15 minutes after intubation and corresponding rate pressure product (mean heart rate x mean systolic blood pressure) calculated. Both groups were maintained with 67% nitrous oxide, 33 % oxygen, Rocuronium 0.1mg/kg i. v boluses and isoflurane 0.4-0.8% with ventilator parameters on closed circuit adjusted to have end tidal carbon dioxide between 30-35mmHg. All patients were reversed with Inj. Neostigmine 0.05mg/kg i. v and Inj. Glycopyrrolate 0.01mg/kg i. v and extubated after complete recovery from neuromuscular blockade. Data analysis was done using Independent and paired sample t test, ANOVA and a p value < 0.05 was considered statistically significant.

OBSERVATIONS AND RESULTS

On comparison, the two groups were similar in demographic profile and time taken for intubation , the predominant surgery in both groups were gynaecological procedures and pregabalin had a greater attenuation of blood pressure [p value < 0.01] at 1,3,5 minutes than placebo as compared to heart rate [p value= 0.4] at 1,3 minutes as shown in table 3

Table 1: showing demographic profile and duration of intubation

	Group I (Placebo)	Group II (Pregabalin)
Mean age [years]	43.5± 7.23	45.2±5.84
Sex ratio [M:F]	10:20	10:20
Mean body weight [kg]	61.56 ± 11.27	59.13 ± 10.19
Mean Duration of intubation[seconds]	16.23 ± 2.215	16 ± 2.302

Table 2: showing type of surgeries

Type of surgery	Group I (placebo) Number of patients	Group II (pregabalin) Number of patients
General surgeries	8	9
Gynecological surgeries	17	18
Orthopedic surgeries	2	1
Ear Nose Throat surgeries	3	2

Table 3: showing hemodynamic variables

VARIABLE	GROUP	BASAL	PRE INDUCTION	1 MIN	3 MIN	5 MIN	10 MIN	15 MIN
Mean Heart rate	Placebo	80.76±15.89	87.26±16.19	94.96±18.41	94.5±16.75	93.93±15.74	89.23±14.9	87.4±12.18
	Pregabalin	84.13±10.15	85.3±10.33	92.13±8.3	91.6±11.24	87.8±10.02	81.76±9.9	80.56±7.64
	P value	0.34	0.58	0.4	0.42	0.08	0.02	0.01
Mean Systolic Blood Pressure	Placebo	131.76±16.78	132.53±21.04	124.83±26.5	116.93±23.7	110.23±15.63	108.93±14	112.1±17.1
	Pregabalin	132.16±10.96	131.43±14.39	109.09±15.0	101.8±8.17	99.86±11.47	94.6±14	102.5±12.1
	P value	0.91	0.81	0.00	0.00	0.00	0.01	0.02
Mean Diastolic Blood Pressure	Placebo	85.5±10.09	81.23±14.24	82.96±21.64	77.26±17.52	72.4±13.71	72.5±9.41	75.06±10.1
	Pregabalin	83.26±8.41	80.63±9.3	71.23±9.67	64.53±9.11	65.33±10.06	62.93±9.71	67.06±7.98
	P value	0.36	0.83	0.01	0.00	0.02	0.00	0.00
Mean Mean Arterial Pressure	Placebo	102.46±11.72	98.9±13.7	96.4±22.68	90.83±18.59	85.1±13.68	84.3±10.61	87.46±12.1
	Pregabalin	99.5±8.51	97.86±8.51	84.03±11.08	77.43±8.38	77.1±10.29	75.66±11.3	79.56±8.89
	P value	0.27	0.77	0.01	0.00	0.01	0.00	0.00
Mean Rate Pressure Product	Placebo	10584±2163	11283±2112	11726±2879	10910±2295	10247±1840	9648±1627	9789±2002
	Pregabalin	11006±1666	11183±1716	10072±1776	9370±1596	8828±1830	8213±1888	8315±1626
	P value	0.36	0.84	0.01	0.00	0.00	0.00	0.00

DISCUSSION

Direct laryngoscopy and endotracheal intubation leads to 10-20% rise in heart rate and 20-30% rise in blood pressure which can be detrimental in patients with hypertension, heart disease and cerebrovascular disease. Using a method to control heart rate and blood pressure can be life saving in such patients. Sundar AS et al[20] showed that pregabalin more effectively attenuated the rise in blood pressure than heart rate in patients undergoing off pump CABG, much like our study. However, Gupta K et al[18] compared oral pregabalin [150mg] and oral clonidine[200mcg] in elective laparoscopic cholecystectomy and found that both attenuated hemodynamic response with clonidine having increased incidence of intraoperative and postoperative bradycardia. Rastogi B et al[22] compared two doses of pregabalin-75mg vs 150mg and found that 150mg attenuated hemodynamic response better.

Heart rate changes: Sundar AS et al[20] had a lower rise in heart rate compared to this study probably due to use of preoperative beta blockers and higher doses of fentanyl [5mcg/kg], midazolam [50mcg/kg], Thiopentone [4mg/kg] compared to present study.

Systolic Blood pressure changes: The trend and magnitude of fall in systolic blood pressure was higher with pregabalin than placebo group.

Diastolic blood pressure changes: There is a greater fall in diastolic blood pressure in our study than Sundar AS et al [20].

Mean arterial pressure changes: Mean arterial pressure fell by 15-24 mmHg similar to study done by Sundar AS etal[20]. However, Gupta K[21] showed a rise in mean arterial pressure at1,3,5 minutes. Rastogi B et al[22] showed a fall lesser than this study probably due to use of butorphanol as premedicant against fentanyl.

Rate pressure product changes: This is the product of systolic blood pressure and heart rate which correlates with myocardial oxygen consumption. Product of more than 20,000 is associated with myocardial ischemia. The increase in rate pressure product was higher in control group than pregabalin [p value <0.01].The other studies did not give information on rate pressure product. There were no side effects like nausea, vomiting in both groups. Three patients in pregabalin group had dizziness lasting 3-4 hours postoperatively which subsided by itself. Plasma catecholamines, the mediators of hemodynamic response were not measured and dose response effect of pregabalin was not studied. Drug interactions of pregabalin were not studied. The effect of pregabalin in patients with hypertension, diabetes mellitus needs to be studied as they are most susceptible for hemodynamic response.

CONCLUSION

Oral pregabalin (150 mg) given sixty minutes preoperatively successfully attenuates the hemodynamic response associated with direct laryngoscopy and endotracheal intubation. This effect is more prominent with the blood pressure component of the hemodynamic response than the heart rate component. However, the rise in heart rate is lower with pregabalin than placebo and the trend of the heart rate response is better and predictable with pregabalin.

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