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Clinical Investigation

A Comparative Study of Oral Pregabalin and Clonidine for Attenuation of Hemodynamic Responses to Laryngoscopy and Tracheal Intubation

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Abstract

Background: Airway instrumentation by direct laryngoscopy and tracheal manipulation are powerful noxious stimuli causing adverse hemodynamic responses. This study evaluates and compares oral clonidine and pregabalin premedication on the hemodynamic responses following laryngoscopy and tracheal intubation and to assess the adverse events associated with these drugs. **Materials & Methods:** Sixty patients of ASA Grade I or II and aged between 18-60 years, of either sex, who were posted for elective surgeries under general anaesthesia were selected. The patients were randomly divided into 2 groups of 30 each where Group C received 200µg Clonidine and group P 150mg Pregabalin 90 mins before surgery. After three mins of pre-oxygenation with 100% oxygen, pre-medication given was 5µg/kg of IV glycopyrolate and 2.5µg/kg IV Fentanyl was given for analgesia. Patients were induced with IV Thiopentone 5mg/kg followed by IV Suxamethonium 2mg/kg for intubation. Anaesthesia was maintained with Nitrous Oxide, Oxygen and Isoflurane. Muscle relaxation was achieved with IV Vecuronium 0.1mg/kg (loading dose) and 0.02mg/kg for maintenance dose. During laryngoscopy and endotracheal intubation the heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure were recorded at 0,1,3,5 and 10 mins. Statistical difference between the two groups were analyzed using student's 't' test. **Results:** Attenuation of increase in BP was better in group P whereas tachycardia response was better attenuated in group C and sedation was more commonly obtained in Group P which were statistically significant. **Conclusions:** Both Pregabalin and Clonidine successfully attenuated the hemodynamic response to laryngoscopy and tracheal intubation. Pregabalin better attenuates pressor response and clonidine better attenuates tachycardia response.

Keywords: laryngoscopy, endotracheal intubation, hemodynamic response, pregabalin, clonidine

Introduction

Direct laryngoscopy and tracheal intubation are noxious stimuli that can provoke undesirable responses in the cardiovascular, respiratory and other physiologic systems.[1] Significant tachycardia, hypertension and dysrhythmias can arise due to these manipulations. The magnitude of the response is greater with increasing force and time of laryngoscopy.[2] The pressor response of laryngoscopy or endotracheal intubation does not present a problem for most patients. However, in patients with cardiovascular and cerebral diseases these transient responses can result in morbidity and mortality from tachycardia and hypertension. An array of anaesthetic techniques and drugs are available to control the hemodynamic responses to laryngoscopy and intubation like administration of topical anaesthesia, reducing the duration of laryngoscopy and intubation to less than 15 seconds, increasing the depth of anaesthesia, and administration of drugs like topical and intravenous lidocaine, vasodilators, opiods, beta blockers, calcium channel blockers and α_2 adrenergic agonists. [1],[3-13] Yet no single agent has been established as apt for this purpose.

Clonidine is a α_2 adrenergic agonist which was originally introduced as an antihypertensive. There are few studies to show clonidine to be useful in attenuating pressor response to laryngoscopy and intubation. Pregabalin a gabapentinoid is emerging as an effective and safe drug as it leads to sedation, analgesia and haemodynamic stability perioperatively. A single, oral dose of 150 mg of

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pregabalin premedication seems to be effective in attenuating the haemodynamic response to tracheal intubation after the first attempt, an effect which may be useful in patients suffering from coronary insufficiency.[14] The aim of this study is to assess the efficacy and compare Pregabalin and Clonidine used orally for premedication to attenuate the hemodynamic responses following laryngoscopy and tracheal intubation and to assess the adverse events.

Materials and Methods

This comparative study was done on 60 patients posted for elective surgeries under general anaesthesia at a rural medical college hospital at Kolar in Karnataka state. Patients of ASA Grade 1 and 2 in the age group of 18 to 60 years, of either sex who were posted for elective surgeries under general anaesthesia were selected for the study. The exclusion criteria were patients physically dependent on narcotics, history of drug allergy to clonidine or pregabalin, cerebrovascular, neurologic, respiratory and Ischemic heart disease, renal and hepatic dysfunction, head injuries, hypertension, pheochromocytoma, diabetes mellitus and patients on beta blockers, antidepressants, anti-anxiety drugs, anticonvulsants or anti-psychotics.

After obtaining informed written consent, patients were randomly divided into two groups of 30 each. Patients of Group P received 150mg Pregabalin and of Group C received 200µg Clonidine. All patients were examined a day before surgery and were kept fasting overnight after 10 pm. Diazepam 10 mg and Ranitidine 150 mg was given orally in tablet form as premedication on the night before surgery. On the morning of surgery the study patients received either oral Pregabalin or Clonidine 90 mins before admission to OT. Pulse rate, systolic and diastolic blood pressure, oxygen saturation and ECG were recorded. Intravenous line was secured and all patients were started on intravenous fluids at 5 ml/kg/hr. The level of sedation was assessed by four point score described by Chernik et al., where Grade 0 - patient wide awake; Grade 1 - patient is sleeping comfortably but responding to verbal commands; Grade 2 - deep sleep but arousable; and Grade 3 - deep sleep, unarousable. After 3 mins of pre-oxygenation with 100% oxygen, pre-medication given was 5µg/kg of i.v glycopyrolate and 2.5µg/kg i.v Fentanyl was given for analgesia. Patient was induced with i.v Thiopentone 5mg/kg followed by i.v Suxamethonium 2mg/kg for intubation. Anaesthesia was maintained with Nitrous Oxide, Oxygen and Isoflurane. Muscle relaxation was achieved with i.v Vecuronium 0.1mg/kg for loading dose and 0.02mg/kg for maintenance dose.

During laryngoscopy and endotracheal intubation, heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure and rate pressure product were recorded at 0,1,3,5 and 10 mins. Student's 't'-test was used to analyses the differences in the parameters between the two groups. $P < 0.05$ was considered as statistically significant.

Results

Table 1 presents the haemodynamic and pressor responses of the patients following laryngoscopy and intubation. The responses were measured basally at 1,3,5 and 10 minutes. The mean heart rate following laryngoscopy and intubation among the groups receiving Clonidine was lesser than among the group receiving Pregabalin and was statistically significant at 1 minute and 3 minutes. Whereas the mean systolic, diastolic and mean blood pressure was significantly less among the patient group receiving Pregabalin following laryngoscopy and tracheal intubation. There was no significant differences in the rate pressure product among the two groups. Sedation amend by sedation scores were more pronounced among the patient groups who had received Pregabalin and was statistically significant (Fig 1)

Table 1. Characteristics of the studied patients

Characteristics	Group P (n=30)	Group C (n=30)
Sex (n (%))		
Male	11 (36.7)	20 (66.7)
Female	19 (63.3)	10 (33.3)
Age (n (%))		
18 - 35 yrs	22 (73.3)	19 (63.3)
15 - 55 yrs	8 (26.7)	11 (36.7)
Weight (mean ± SD)	56.93± 4.1	56.17± 4.5

Fig. 1. Comparison of preoperative sedation scores among the two group following Pregabalin and Clonidine administration

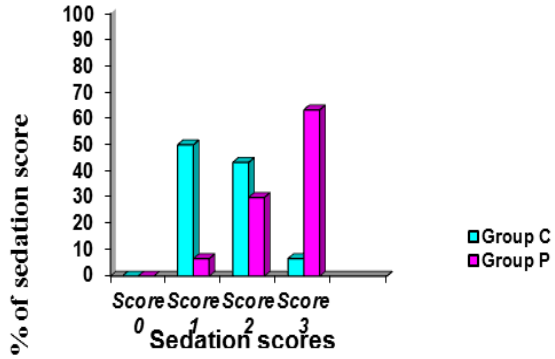

Table 2. Haemodynamic Changes in the two groups receiving Pregabalin and Clonidine following Laryngoscopy and Tracheal Intubation

Haemodynamic Measurement	Baseline (mean ± SD)	1 Minute (mean ± SD)	3 Minute (mean ± SD)	5 Minute (mean ± SD)	10 Minute (mean ± SD)
Heart rate					
Gr P	85±12.36	95.3±9.8	91.9±10.2	84.6±11.4	79.9±9.8
Gr C	7 9.6±8.88	89.73±11.2	86.13±11.2	81.3±10.5	76.3±9.5
SBP					
Gr P	122.43±12.84	124.3±15.2	117.5±137	111.6±12	108.6±10.6
Gr C	121.2±15.44	135.9±13.3	13.2. ±129	126±12	123±11.5
DBP					
Gr P	79.73±8.7	81.67±9.7	76.4±8.4	73.5±6.8	71.4±6.4
Gr C	79.8±9.05	91.3±7.3	85.6±7.8	82.2±7.2	77.4±6.9
MAP					
Gr P	93.96±9.29	95.8±11	90.1±96	86 ±8.5	83.9±7.6
Gr C	93.6±10	106.2±8.7	100.5±86	96±8.8	92.7±7.8
RPP					
Gr P	10413±1897	11902±2018	10842±1821	9463±47	8511±204
Gr C	9630±1731	12205±2022	10219±1727	9927±2324	9636±1366

Discussion

The present study assessed the effect of oral premedication with pregabalin or clonidine for haemodynamic stability following laryngoscopy and intubation. We observed the sedative effects of these premedicants without any respiratory depression. Haemodynamic responses following laryngoscopy and intubation were diminished with pregabalin and clonidine. The haemodynamic results of our study were in agreement with other studies done on pregabalin and clonidine. Both drugs possess many properties to make them valuable premedicants to attenuate the haemodynamic stressor response to laryngoscopy and intubation.

Tracheal intubation is a crucial skill in anaesthetic practice. It needs direct laryngoscopy to view the vocal cords for insertion of the tube. Both laryngoscopy and passage of a tracheal tube are noxious stimuli that can incite adverse events in the respiratory, cardiovascular and other physiologic systems.[1] The haemodynamic changes was first described by Reid and Brace.[15] Many techniques have been tried in an effort to offset these adverse hemodynamic responses to laryngoscopy and intubation like increasing the depth of anaesthesia, using aerosol or topical anaesthetics and using glossopharyngeal and superior laryngeal nerve blocks. Many pharmacological methods were evaluated to attenuate these adverse responses with controversial results. Narcotics such as fentanyl, remifentanyl or alfentanyl were found to have the most stable effect on these haemodynamic responses, but with a risk of prolonged respiratory depression. Intranasal nitroglycerin diminished the hypertensive response but tachycardia was noted. Administration of intravenous lidocaine, vasodilators (sodium nitroprusside, nitroglycerin), beta blockers (esmolol, propranolol) calcium channel blockers (nifedapine, verapamil) and α_2 adrenergic agonists (dexmedetomidine, clonidine) has been tried prior to laryngoscopy with varying results[4-6],[8-13].

Our study compares Clonidine a α2 adrenergic receptor agonist which is an established drug in diminution of hemodynamic responses to laryngoscopy and tracheal intubation with Pregabalin which is a GABA analogue and belongs to the class of anticonvulsants and is now being increasingly used for neuropathic pain, post-operative analgesia, generalized anxiety disorders as well as in control of perioperative stress responses including that of laryngoscopy and intubation[16,17]. We have compared Pregabalin with Clonidine which was better in attenuation of heart rate response. Pregabalin attenuates haemodynamic response to laryngoscopy and endotracheal intubation in a dose response manner. Attenuation is more with 150mg compared to 75mg.[14] We used Pregabalin in a dose of 150 mg 60 to 90 minutes prior to surgery and it was found to effectively attenuate the rise in SBP, DBP and MAP at 1, 3, 5 and 10 minutes after laryngoscopy and intubation. This correlates with the studies done by Gupta K and colleagues.[18] Fentanyl at a dose of 1 μg/kg has minimal effects on the hemodynamic responses.[1, 19] The anaesthetic agents can also attenuate the pressor response to laryngoscopy and intubation.[20,21]

Elderly patients were not included in the

study as the more often exhibit increased sensitivity to drugs and the cardiovascular effects of Pregabalin have not been studied extensively. Also multiple medications are used by elderly including antidepressants, hypnotics and antihypertensive. Separate studies are required to study the effect of pregabalin in elderly patients. Studies have shown that arterial pressure and heart rate responses are greater when the duration of laryngoscopy exceeds 30 seconds.[3] some studies which have studied the effect of pregabalin to attenuate the haemodynamic responses to laryngoscopy and intubation have not commented upon duration of laryngoscopy and intubation[14]. In the present study the mean duration of laryngoscopy and intubation did not exceed 15seconds.

In our study at 5th and 10th minute there was no significant differences between the two groups regarding heart rate changes but at 1 and 3 minutes heart rate response to laryngoscopy and intubation in the clonidine group was clinically lesser than Pregabalin group and was statistically significant. Hence clonidine group better attenuated the tachycardia response compared to Pregabalin group. The mean systolic blood pressure, diastolic blood pressure and mean arterial pressure at 1 minute, 3 minute, 5 minute and 10 minute time interval was clinically lesser in Pregabalin group than in the Clonidine group. Increase in the rate pressure product is less in Pregabalin group signifying lesser load on the myocardium compared to Clonidine. Sedation scores which was measured using four point scale described by Chernik et al showed the mean sedation scores to be clinically and statistically more in Pregabalin group than Clonidine group with p value<0.001. This correlates with the studies done by Gupta K, et al.[22] As patients with ASA physical status I and II were enrolled in the study, the results cannot be generalized to the patients with higher ASA physical status. Stress mediators like endogenous plasma catecholamines or cortisol values were not measured.

Conclusions

We conclude that Pregabalin is better compared to Clonidine to attenuate the pressor response associated with laryngoscopy and tracheal intubation, but the tachycardia response is not completely attenuated.

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