# EVALUATION OF ORAL PREGABALIN PREMEDICATION FOR ATTENUATION OF PRESSOR RESPONSE DURING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

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***Abstract: A prospective, randomized study was performed after acceptance by the Ethics Committee and informed consent of 60 patients seeking elective surgery at the Krishna Hospital and the Medical Research Centre, Karad. The study objective is to evaluate haemodynamic consistency through attenuation of the pressure reaction during laryngoscopy and endotracheal intubation. Group A obtained pregabalin orally with water sips before induction and Group B served as control group, received multivitamin orally with sips of water 1hr before induction. Both groups were uniform in their distribution of age, weight and gender. They had similar physical status with no coexisting disease. Both groups were managed with same anesthetic protocol. It was concluded that the preoperative sedation before giving premedication in control and pregabalin groups are comparable, whereas pregabalin produced better preoperative sedation after one hour of premedication, as evidenced by higher Ramsay sedation score.***

***Keywords: Pregabalin, Premedication, Attenuation, Laryngoscopy, Endotracheal, Hemodynamic***

## 1. INTRODUCTION

Preoperative sedation and cardiovascular stability during anesthesia, laryngoscopy, intubation and after operation is the most important aspect of anaesthesia for a successful patient result. Anxiety is a big concern for many patients throughout the preoperative period. Laryngoscopy and endotracheal intubation are very essential tools in hand of anaesthesiologist in the maintenance of airway and prevention of aspiration. Hemodynamic pressure response to airway devices is a dangerous condition in general anaesthesia as these are associated with hypertension and tachycardia, transient and often unwanted body response[1]. These disturbances when they occur in normal patients are well tolerated, in absence of cardiovascular disease or disturbed intracranial pressure[2]. Most medications, such as midazolam, barbiturates, alpha 2 agonist, opioids, etc., have been utilized as a premedication for airway instrumentation to relapse these adverse hemodynamic reactions[3,4].

Gabamimetic drugs such as Gabapentin and Pregabalin have been utilized by numerous authors[5-12] as oral premedication to attenuate pressure reaction during airway instrumentation, to relieve preoperative discomfort and to minimize perioperative opioid consumption. With the above pharmacological profile Pregabalin, like its pharmacological predecessor gabapentin, can be a drug to attenuate hemodynamic response associated with direct laryngoscopy and intubation.

## 2. AIM AND OBJECTIVES

To evaluate haemodynamic stability through attenuation of pressor reaction during laryngoscopy and endotracheal intubation with pregabalin 150 mg, including its impact on pregabalin on preoperative anxiety and sedation.

## 3. REVIEW OF LITERATURE

Anatomy of upper airway and larynx:

Successful direct laryngoscopy and intubation needs knowledge of anatomy. In the following chapter, only the relevant anatomy is discussed. There are two openings leading to the human airway the nose which leads to the nasopharynx and the mouth which leads to the oropharynx and subsequently leading to laryngopharynx and ultimately the larynx.

It is a branch of superior laryngeal nerve. It is entirely sensory and autonomic apart from few fibers that are motor to the arytenoid muscles. It passes under the greater cornu of hyoid bone to penetrate the thyrohyoid membrane. The upper branches of internal laryngeal nerve pass into periglottic tissue to supply the vallecula, posterior surface of epiglottis and pyriform sinuses. Lower branches travel in the aryepiglottic fold supplying till the level of true vocal folds. Few terminal fibres pass through inferior constrictor to unite with ascending fibres from recurrent laryngeal nerve. It is a branch of superior laryngeal nerve. It accompanies the laryngeal branch of the inferior thyroid artery. It stays superficial to larynx until it submerges under the cricothyroid articulation to supply the cricothyroid muscle. It also supplies the pharyngeal plexus, connects with superior cardiac nerve (branch of vagus) and also superior cervical sympathetic ganglion.

Recurrent laryngeal nerve: This has different points of origin from the vagus on two sides. The right recurrent laryngeal nerve originates from the right vagus, as the superior subclavic artery is penetrated by the hand. The recurrent left laryngeal nerve is generated from left vagus, when it crosses over aortic arch, near the insertion of ligametum arteriosum. Both nerves curve under the respective arteries and travel up the neck between trachea and esophagus.

Autonomic nervous system is the biological house keeper of the internal milieu of the body. The adrenal medulla secretes around 0.2mcg/kg/minute adrenaline and 0.05mcg/kg/minute noradrenaline everyday. The sympathetic nervous system plays an important role in flight and fight response. In stress, the hypothalamus stimulates the sympathetic nervous system,which in turn releases catecholamines leading to an increase in heart rate, blood pressure, cardiac output, bronchodilatation, shunting of blood away from skin, muscles to brain, heart and kidney. Laryngoscopy and intubation are stimuli of different intensity leading to different responses. Laryngoscopy alone, without intubation provides a supraglottic pressure stimulus causing increases in both systolic and diastolic pressures above the pre-induction control levels. Increases in heart rate are slight and are not significant due to laryngoscopy alone. Intubation and placement of an endotracheal tube or a catheter in the trachea, stimulates infraglottic receptors and evokes an additional cardiovascular response with a further increase in catecholamines. The hemodynamic response is much greater, increasing by 36% from pre-induction control levels. The heart rate also significantly increases by about 20% with tracheal intubation, where as there is little rate response to laryngoscopy alone.[13,14]

In 1950, Burstein et al [15] studied the effects of laryngoscopy and intubation on the E.C.G in 109 patients - found out that transient E.C.G changes have occurred in 68% of the cases at the time of intubation.Though the type of anaesthesia had very little role in the occurrence of these disturbances insufficient depth of anaesthesia prolonged laryngoscopy, multiple attempts at intubation and respiratory depression do have increased the occurrence of these disturbances. Burstien in the same year had shown that procaine hydrochloride (100 mg) administered 3-5 minutes before intubation had reduced the incidence of arrhythmias to 24% off in a series of 114 patients.

The usage of halogenated hydrocarbons like halothane and enflurane (Bedford RF, Lt. Marshal, 1984) vastly improved the use of inhalational anaesthetic agents for blunting the laryngoscopic responses, as induction was smooth, rapid and these were not inflammable. It was found that 1.5 MAC of halothane or enflurane sufficiently blunted the laryngoscopic responses. However, as the depth of anesthesia increased, the myocardial depression caused by these agents also increased, leading to increased risk of bradycardia, hypotension and dysrhythmias (King et al, Crowhurst et al).

1951, King and Harris [16] anaesthetised 46 normal individuals with thiopentone, nitrous oxide, cycloprapane, ether, tubocurarine and decamethonium and found that direct laryngoscopy and intubation that were uncomplicated by hypoxia, hypercarbia and coughing were capable of producing tachycardia and hypertension. These were initiated by the blade of the laryngoscope pressing at the base of the tongue or lifting the epiglottis. Laryngoscopy alone does cause the pressor response brought about by the insertion of the endotracheal tube into the trachea, leading to cardiac arrythmias.

## 4. METHODOLOGY & METHODS

A prospective, randomized study was carried out and agreed upon after approval of the Ethical Committee on 60 patients undergoing elective surgery under General Anesthesia at Krishna Hospital and Medical Research Centre, Karad, from the academic year October 2014 to May 2016. 60 patients undertaking significant surgical procedures. Patients were granted clear and signed permission. Outcome values were recorded using a predetermined proforma.

Patient was premedicated on the night before surgery with Tablet Diazepam 5mg. On the day of surgery, on arrival in preoperative room, intravenous line was secured with 18 gauge cannula.

## 5. OBSERVATION AND RESULTS

Table 1: Distribution of patients by age

| **Age in years** | **Group A** | | **Group B** | |
|---|---|---|---|---|
| | **No** | **%** | **No** | **%** |
| **21-30** | 4 | 13 | 3 | 10 |
| **31-40** | 3 | 10 | 2 | 7 |
| **41-50** | 20 | 67 | 19 | 63 |

| | | | | |
|---|---|---|---|---|
| **51-60** | 3 | 10 | 6 | 20 |
| **Total** | 30 | 100 | 30 | 100 |
| **Mean ± SD** | **43.66±8.31** | | **44.76±7.76** | |

Table no. 1 shows the comparison of distribution of patients by age in both the groups. The mean age in group A and B were 43.66±8.31 and 44.76±7.76 respectively. The both groups are comparable.

Table 2: Distribution of patients by gender

| **Gender** | **Group A** | | **Group B** | |
|---|---|---|---|---|
| | **No** | **%** | **No** | **%** |
| Female | 19 | 63 | 20 | 67 |
| Male | 11 | 37 | 10 | 33 |
| Total | 30 | 100 | 30 | 100 |

In the above table 2, it is seen that statistically there is no significant change in the gender, with females predominating in both groups.

Table 3: Sedation score before induction

| **Sedation Score** | **Before Premed** | **After1 hr ofpremed** | | **Sedation Score** | **Before Premed** | **After 1hr of premed** |
|---|---|---|---|---|---|---|
| 1 | 13 | 0 | | 1 | 24 | 22 |
| 2 | 17 | 3 | | 2 | 6 | 8 |
| 3 | 0 | 10 | | 3 | 0 | 0 |
| 4 | 0 | 17 | | 4 | 0 | 0 |
| 5 | 0 | 0 | | 5 | 0 | 0 |

Group A(PREGAB)n=30 Group B(CONTROL)n=30

The change in Ramsay sedation score after 1 hour of premed as compared to before premed is greater in the pregabalin group as compared to the control group. Before premedication, all the patients in both the groups were having sedation score of equal or less than 2.

After one hour of premedication, 90% of patients (27/30) in pregabalin group were having sedation score of more than 2 (Fischer exact test, p <0.00001), while in control group, all the patients were having score less than or equal to 2.(As shown in table no. 3)

## 6. DISCUSSION

The current study was undertaken to know the effectively of pregabalin (150mg) in blunting the haemodynamic response to laryngoscopy and intubation by comparing it with a placebo in the study. The study population consisted of 60 patients divided into two groups with 30 patients in each group. Group A (PREGAB group) consisted of 30 patients who were given pregabalin 150mg and Group B(control) consisted of 30 patients served as control who were given multivitamins, 60 minutes before intubation as pre-treatment to blunt the haemodynamic response to laryngoscopy and intubation. All the studies including the present study are prospective, double blind, randomized controlled comparative studies done in the years 2009-2015. All studies used 150 mg of pregabalin to attenuate hemodynamic response. The above studies used pregabalin in the oral form, 60 to 90 minutes pre-operatively. In study by K Gupta et al [8], comparison was done between control, pregabalin and clonidine for onset time of different sedation levels in which pregabalin had better sedation level similar to our study. As Sundar A S et al [7] studied pregabalin in patients undergoing off pump CABG , these patients were on preoperative beta blockers and anaesthetic induction was done with higher doses of fentanyl (5mcg/kg), midazolam (50mcg/kg), thiopentone (4 mg /kg) .These drugs may play a role in producing a relatively lesser rise in heart rate when compared to other studies. In control group, there is initial rise in the diastolic blood pressure in the present study as well as in the study done by Sundar A S et al [15] at 1 and 3 min. At 5min, there was fall in diastolic blood pressure in the present study as compared to the study done by Sundar A S et al [16] in which diastolic blood pressure was still above the baseline.

## 7. CONCLUSION

Study concluded that a Single, Oral dose of pregabalin (150 mg) given 60 minutes pre-operatively successfully attenuates the hemodynamic response associated with direct laryngoscopy and endotracheal intubation. The preoperative sedation before giving premedication in control and pregabalin groups are comparable, whereas pregabalin produced better preoperative sedation after one hour of premedication, as evidenced by higher Ramsay sedation score. The intraoperative requirement of analgesic is significantly lower in the pregabalin group when compared to the control group. Hence, pregabalin may have an opioid sparing effect thereby minimizing postoperative opioids related side effects. The requirement of analgesic top up in 1st 24hrs of postoperative period in pregabalin group is significantly much less when compared control group. Hence, pregabalin reduces the requirement of analgesia in postoperative period.

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