ROLE OF ORAL GABAPENTIN IN ATTENUATING CARDIOVASCULAR RESPONSE TO LARYNGOSCOPY AND TRACHEAL INTUBATION.

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ABSTRACT... Objectives: To determine the role of 800 mg oral gabapentin in attenuating cardiovascular response to laryngoscopy and tracheal intubation. Study Design: Double Blind Randomized Control Trial. Setting: Independent University Hospital/Independent Medical College, Faisalabad, Pakistan. Period: Six months from January 1st 2019 to June 30th 2019. Material & Methods: This study included 60 patients which were divided into two equal groups. 800 mg oral gabapentin was given to group I while capsule placebo was administrated to group II patients in pre-operative area one hour prior to surgery. Heart rate, systolic, diastolic and mean arterial blood pressure were taken after induction of anesthesia at base line and then 1, 2, 3, 4, 5, 10 and 15 minutes after endotracheal intubation. SPSS version 11 was used to analyze the data. Heart rate systolic, diastolic and mean arterial blood pressure were dependent variables while placebo and gabapentin were independent variables. Results: Out of total 60 patients there were 36 (60 %) males and 24 (40 %) females. In group I mean age was 37.1 while in group II it was 36.3. As compare to group II there was decreased cardiovascular response in group I. There was a significant decrease in systolic blood pressure at 1, 2 and 10 minutes; diastolic blood pressure at 3 minutes; heart rate at 10 and 15 minutes and mean arterial blood pressure at 3 minutes after induction in group I. Conclusion: Cardiovascular response to laryngoscopy and intubation is significantly reduced with oral gabapentin.

Key words: Cardiovascular Response, Gabapentin, Laryngoscopy and Endotracheal Intubation.

INTRODUCTION

Endotracheal tube (ETT) is passed for airway maintenance and protection from aspiration of gastric contents.¹ This endotracheal intubation needs laryngoscopy to visualize vocal cords so that ETT can be placed in right position.

The response of the body to this laryngoscopy and tracheal intubation is stress response, which may include secretion of stress hormones e.g. catecholamines, glucagon, and antidiuretic hormone.² There is a significant increase in intracranial pressure, intraocular pressure, heart rate and blood pressure caused by stress hormone.³ Such change in B.P and HR is called cardiovascular response or pressor response.

Cardiovascular response is well tolerated by young children and adults not having any cardiac problem, but this response can be catastrophic in cardiac patients, geriatric patients⁴ and very sick patients, who have decreased cardiac reserves, because of increase in myocardial oxygen demand which is not properly met in compromised patients. This is due to increase in blood pressure and heart rate which may result in myocardial ischemia, infarction, and cardiac failure, depending upon the severity of the disease. The cardiovascular response can be minimized mainly by two strategies; one is avoiding the endotracheal intubation and laryngoscopy by using supraglottic airways, secondly when intubation is indispensable, to use different drugs which can help to decrease the pressor response.
The most commonly used equipment’s include, oropharyngeal airway\(^5\), laryngeal mask airway\(^6\), laryngeal tube\(^7\), and I Gel.\(^8\)

Many drugs have been used to attenuate the cardiovascular response to tracheal intubation and laryngoscopy. Lidocaine either sprayed directly on the vocal cords or given intravenously not only decreases the sensitivity of upper airway but also attenuate the heart rate and blood pressure changes during laryngoscopy.\(^9\)

There is increase in anesthetic depth and decrease in cardiovascular response to laryngoscopy and intubation with ultra-short acting opioids like fentanyl, ramifentanil and sufentanil.\(^10\)

Beta blockers are also used to decreased the laryngoscopy and tracheal effects on cardiovascular system. Among the beta blockers the ultra-short acting esmolol is used frequently due to its cardio selective adrenergic receptor blocking properties.\(^11,12\)

There are recent recommendations on the role of gabapentin to attenuate the cardiovascular effects of laryngoscopy and intubation.\(^13\)

With combination of other anti-seizure drugs gabapentin was recommended to be used for treatment of partial seizures by FDA in 1994.\(^14\) It was recommended to be used in the treatment of nerve related pain, post herpetic neuralgia\(^15\) and other painful neuropathies in 2002.\(^16\) It also has limited role in the treatment of anxiety, depression, and restless leg syndrome.

Gabapentin, anticonvulsant is also effective in neuropathic pain management. It is used for decreasing opioid requirement postoperatively and treating acute post-operative pain in human studies. We conducted this study to evaluate the effect of gabapentin in attenuating cardiovascular response to laryngoscopy and intubation in patients undergoing elective surgery.

**MATERIAL & METHODS**

This randomized controlled trial was conducted at Independent University Hospital Faisalabad over six months from January 1\(^{st}\) 2019 to June 30\(^{th}\) 2019. Sample size of sixty cases (30 in each group) was calculated with 80 percent power of test and 9 percent confidence interval. After taking informed consent, non-probability consecutive sampling was done in sixty patients. The inclusion criteria were patient of 20-30 years of age, ASA I&II undergoing elective surgical procedures. Patients in whom laryngoscopy time exceeds fifteen seconds, pregnant patients and patients known case of hypertension and ischemic heart disease were excluded.

Demographic data, ASA status and information regarding surgical procedure were recorded. One hour before induction of anaesthesia 800 mg oral gabapentin was given to group I and placebo capsule was given to group II.

Every patient was premedicated with midazolam 2mg I/V. After standard induction with inj. Propofol2mg / kg, inj. Rocuronium 0.6 mg/ kg and waiting for 2 minutes patient were intubated after direct laryngoscopy. Anaesthesia was maintained with sevoflurane.

Study variables, pulse and non-invasive blood pressure were taken from the monitor at 1,2,3,4,5, 10 and 15 minutes. A designed proforma was used to record the data of study variables and demographic data like name, age, sex.

SPSS version 11 was used to analyse the data. Standard deviation and mean were used for age description while sex was described in percentage. Paired t-test was used to compare systolic, diastolic and mean blood pressures. P-value<0.05 was considered significant.

**RESULTS**
| Gender | Count/Percentage | Study Groups | Total |
|--------|-----------------|--------------|-------|
|        | Count | Gabapentin | Placebo |       |
| Male   | 16    | 20         | 36      |
| %      | 57.7  | 63.3       | 60.0    |
| Female | 14    | 10         | 24      |
| %      | 43.33 | 36.67      | 40.0    |
| Total  | 30    | 30         | 60      |
| %      | 100   | 100        | 100     |

Table-I. Sex distribution of the subject under study

| Study Groups | N | Mean | Std. Deviation |
|--------------|---|------|----------------|
| Gabapentin   | 30| 38   | 12             |
| Placebo      | 30| 35   | 14             |

Table-II. Comparison of mean age of the subject under study

| Hear Rate Observation Baseline and After Intubation | I (Gabapentin) \(N=30\) | II (Placebo) \(N=30\) | P-Value for t-test |
|-----------------------------------------------------|--------------------------|------------------------|-------------------|
| Mean | Standard Deviation | Mean | Standard Deviation |        |
| Baseline | 85 | 10 | 90 | 16 | 0.188 (>0.05) |
| 1-minute postintubation | 102 | 14 | 106 | 12 | 0.077 (>0.05) |
| 2-minute postintubation | 105 | 14 | 108 | 15 | 0.198 (>0.05) |
| 3-minute postintubation | 100 | 15 | 107 | 14 | 0.242 (>0.05) |
| 4-minute postintubation | 100 | 13 | 105 | 18 | 0.231 (>0.05) |
| 5-minute postintubation | 94  | 14 | 105 | 19 | 0.125 (>0.05) |
| 10-minute postintubation | 92  | 15 | 100 | 18 | 0.041 (<0.05) |
| 15-minute postintubation | 88  | 14 | 98  | 16 | 0.002 (<0.05) |

Table-III. Comparison of mean heart rates in series of observations before and after induction with Gabapentin and placebo as pre-anesthetic drugs.

| Systolic BP Observation Baseline and After Intubation | I (Gabapentin) \(N=30\) | II (Placebo) \(N=30\) | P-Value for t-test |
|------------------------------------------------------|--------------------------|------------------------|-------------------|
| Mean | Standard Deviation | Mean | Standard Deviation |        |
| Baseline | 122 | 12 | 125 | 13 | 0.302 (P>0.05) |
| 1-minute after intubation | 135 | 22 | 148 | 23 | 0.026 (P<0.05) |
| 2-minute after intubation | 118 | 21 | 134 | 24 | 0.01 (P<0.05) |
| 3-minute after intubation | 119 | 16 | 125 | 21 | 0.234 (P>0.05) |
| 4-minute after intubation | 115 | 14 | 118 | 13 | 0.156 (P>0.05) |
| 5-minute after intubation | 107 | 13 | 115 | 11 | 0.101 (P>0.05) |
| 10-minute after intubation | 106 | 12 | 118 | 16 | 0.008 (P<0.05) |
| 15-minute after intubation | 106 | 13 | 115 | 13 | 0.007 (P<0.05) |

Table-IV. Comparison of mean systolic BP before and after induction with Gabapentin and placebo as preanesthetic drugs.
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DISCUSSION

Our study result showed that as compared to placebo group there was trends of less cardiovascular response in gabapentin group.

Statistically it was observed that as compared to placebo mean heart rate with Gabapentin was falling at lower side but at 10 and 15 minutes after intubation it was significant. However, it was also significantly low at 1 minute at P=0.1.

Statistical analysis also showed that as compared to placebo the mean systolic blood pressure was at lower side but after intubation at 1,2,10 and 15 minutes it was significant P=0.05.

As compared to placebo mean diastolic with gabapentin was generally falling at lower side but at it was significant 3 minute after intubation. As compared to placebo mean BP with Gabapentin was generally falling at lower side but after intubation at 2, 10 and 15 minutes it was significant P=0.05.

In their study Fassoulaki and colleagues observed the same effect of gabapentin. They took 46 patients, placebo capsule to the one group and giving 1600 mg of gabapentin to other group, starting the day before surgery at 6 hours interval. They observed the results at 1, 3, 5 and 10 minutes of interval after intubation before and after the anesthetic. Their results were not very

| Diastolic BP Observation | I (Gabapentin) N=30 | II (Placebo) N=30 | P-Value for t-test |
|-------------------------|---------------------|-------------------|-------------------|
|                         | Mean                | Standard Deviation| Mean              | Standard Deviation|                      |
| Baseline                | 77                  | 12                | 78                | 11                | 0.946 (>0.05)       |
| 1-minute after intubation| 86                  | 19                | 95                | 19                | 0.187 (>0.05)       |
| 2- minute after intubation | 72                 | 16                | 84                | 17                | 0.018 (>0.05)       |
| 3-minute after intubation | 69                  | 15                | 75                | 17                | 0.187 (>0.05)       |
| 4-minute after intubation | 70                  | 13                | 70                | 14                | 0.590 (>0.05)       |
| 5-minute after intubation | 62                  | 12                | 66                | 10                | 0.480 (>0.05)       |
| 10-minute after intubation | 62                  | 11                | 69                | 13                | 0.081 (>0.05)       |
| 15-minute after intubation | 60                  | 12                | 66                | 13                | 0.075 (>0.05)       |

Table-V. Comparison of mean diastolic BP in series of observation before and after induction with Gabapentin and placebo as preanesthetic drugs.

| Mean BP Observation | I (Gabapentin) N=30 | II (Placebo) N=30 | P-Value for t-test |
|---------------------|---------------------|-------------------|-------------------|
|                     | Mean                | Standard Deviation| Mean              | Standard Deviation|                      |
| Baseline            | 93                  | 12                | 97                | 11                | 0.412 (P>0.05)      |
| 1-minute after intubation | 105                | 20                | 112               | 20                | 0.106 (P>0.05)      |
| 2- minute after intubation | 91                  | 18                | 103               | 18                | 0.011 (P<0.05)      |
| 3-minute after intubation | 92                  | 16                | 95                | 20                | 0.325 (P>0.05)      |
| 4-minute after intubation | 86                  | 12                | 89                | 13                | 0.367 (P>0.05)      |
| 5-minute after intubation | 80                  | 12                | 85                | 11                | 0.065 (P>0.05)      |
| 10-minute after intubation | 79                  | 12                | 88                | 13                | 0.01 (P<0.05)       |
| 15-minute after intubation | 78                  | 14                | 87                | 12                | 0.020 (P<0.05)      |

Table-VI. Comparison of mean of mean BP in series of observation before and after induction with Gabapentin and placebo as preanesthetic drugs.
different from our study and their results showed that systolic blood pressure at 1, 3, 5, and 10 minutes post intubation period was significantly lower. The difference that why in our study at 3, 4, and 5 minutes interval systolic blood pressure was not significantly low could be explained that in our study the dose of gabapentin used was 800 mg and given one hour before anesthesia while 1600 mg of gabapentin was used by Fassoulaki and his colleagues and given the drug one day before.

The effect of gabapentin in attenuation of hemodynamic responses to laryngoscopy and tracheal intubation was evaluated by Shashi Kiran and Deepak Vermal. A total of one hundred patients were studied. Gabapentin 800 mg were given to patients in group A while placebo capsules were given to group B the night before and on the morning of surgery. At 0, 1, 3, 5 and 10 min after intubation systolic blood pressure was significantly lower in the gabapentin as compared to the control group. At 0, 1, 3, and 5 min after intubation diastolic blood pressure was lower in the gabapentin group. At 0, 1, 3, and 5 min after intubation mean atrial pressure was also lower in the gabapentin group. Because of the use of same strength of gabapentin 800 mg as we used the results were similar in both studies.

Another study comparing the effect of gabapentin on arterial blood pressure and heart rate at after induction and endotracheal intubation was conducted by D. Memis, A. Turan, B. Karamanlioglu, S. Seker and M. Ture. There was a significant increase in arterial blood pressure and heart rate associated with endotracheal intubation in patients receiving gabapentin 400 mg.

The results showed that 800 of gabapentin which we used in our study was sufficient in attenuating cardiovascular response to tracheal intubation. Dose of 400 mg of gabapentin was not sufficient in this regard.

CONCLUSION
It was concluded that gabapentin given in a dose of 800 mg orally one hour before the induction of anesthesia showed significantly decrease in cardiovascular response to laryngoscopy and intubation as compared to placebo. Although 1600 mg of gabapentin used in one study by Fassoulaki has shown to be more effective in attenuating cardiovascular response to laryngoscopy and intubation but we did not used this dose because of the general observation that with this much dose there is prolonged post-operative sedation.

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