

A COMPARATIVE STUDY OF ORAL CLONIDINE VERSUS ORAL PREGABALIN ON HEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION UNDER GENERAL ANAESTHESIA

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Article Info: Received 15 April 2019; Accepted 29 April. 2019

Cite this article as: Rathore, P., Saini, V., Ahmed, F., Chatterjee, R., & Rathore, M. (2019). A COMPARATIVE STUDY OF ORAL CLONIDINE VERSUS ORAL PREGABALIN ON HEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION UNDER GENERAL ANAESTHESIA. *International Journal of Medical and Biomedical Studies*, 3(4).

DOI: <https://doi.org/10.32553/ijmbs.v3i4.224>

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Conflict of interest: No conflict of interest.

Abstract

Background: Laryngoscopy and endotracheal intubation are potent stimuli that can induce increased sympathetic activity leading to tachycardia, hypertension and dysrhythmias. Various drugs and methods have been tried to obtund this response. To obtain ideal drugs, studies still continue. We compared the efficacy of clonidine and pregabalin to attenuate the pressor response during laryngoscopy and intubation.

Method: Total 80 patients of ASA grade I scheduled for elective surgery under general anaesthesia, were randomized into two groups. Group A received oral clonidine 300 mcg 2 hrs prior to surgery, group B received oral pregabalin 75mg 2 hrs prior to surgery. Heart rate and blood pressure (SBP, DBP & MAP) were recorded at baseline, before induction, before intubation, during laryngoscopy, 0, 1, 3, 5, and 10 minutes after intubation.

Results: When compared to clonidine and pregabalin, there was a significant increase in HR and MAP in pregabalin after laryngoscopy and tracheal intubation. Clonidine was better than pregabalin in suppressing the pressor response.

Conclusion: Clonidine appears to be better than Pregabalin for control of haemodynamic response to laryngoscopy and intubation besides providing sedation.

Keywords: Clonidine, Pregabalin, hemodynamic changes and endotracheal intubation.

Introduction:

Endotracheal intubation is considered to be the gold standard in airway management during general anaesthesia and in critical care settings. As such endotracheal intubation is a safe and common practice in modern day anaesthesia but it can induce increased sympathetic activity leading to tachycardia, hypertension and dysarrhythmias. When laryngoscopy and intubation is carried out, there is mechanical irritation of stretch receptors situated in

the respiratory tract leading to reflex hemodynamic responses through a sympathetic reflex such as hypertension, tachycardia, and arrhythmia¹. A change in plasma catecholamine concentrations also has been demonstrated to be a part of the stress response. This autonomic changes are variable, transitory, unpredictable and well tolerated in ASA I & II patients, but it may detrimental in patients with pre-existing hypertension, Cardiac disease, and cerebral pathologies.^{2,3} Various non-pharmacological methods like smooth & gentle intubation with a

shorter duration of laryngoscopy, insertion of LMA in place of endotracheal intubation has been tried.⁴In pharmacological methods a numbers of drugs which includes lidocaine spray, IV lignocaine and Opioids, Propanolol, isosorbidedinitrate, Calcium channel blockers, Esmolol, fentanyl, Magnesium sulphate, Clonidine, Pregabalin, Gabapentin, and dexmedetomidine has been tried.⁵⁻¹⁶ None of the above approaches or agents has been proved to be ideal so the need for an ideal agent to obtund the stress responses to laryngoscopy & intubation is still continuing.

Clonidine under intense investigation as an adjunct to anaesthesia in various forms^{17,18}. By its central sympatholytic action, it tends to attenuate the haemodynamic response to any surgical nociceptive stimulus and improve overall perianesthetic cardiovascular stability.^{19,20} Pregabalin is a lipophilic analogue of GABA. It acts by decreasing the synthesis of neurotransmitter glutamate to act on the central nervous system. It exhibits potent anticonvulsant, analgesic and anxiolytic activity²¹ Pregabalin and clonidine apart from its use in the treatment of alleviating neuropathic pain, acute post-operative pain relief, it also decreases pre-operative anxiety and attenuates perioperative stress response.

This study was designed to evaluate oral pregabalin and clonidine premedication to attenuate pressor response to laryngoscopy and intubation.

Methods

After approval from the institutional ethical committee 80 patients with study eligibility of ASA grade I and II, aged 30–60 years, weighing 40 to 70 kg, posted for elective surgery under general anaesthesia were selected and randomly allocated into two groups of 40 patients each by using 'Chit in box' technique.

Group (A) (n=40) - patients have received oral tab Clonidine 300mcg 2 hrs prior to surgery

Group (B) (n=40) - patients have received oral tab Pregabalin 75mg 2 hrs prior to surgery.

Patient with major organ dysfunction (hypertension, cerebrovascular disease, ischemic heart disease, arrhythmias, shock), on medications (like hypnotics, narcotic analgesics, α_2 agonists, calcium channel blockers, β blockers) and with reactive airway diseases, having known allergy to anaesthetic agents used in study, with anticipated difficult intubation,

pregnancy/ lactation and in whom intubation was done after more than 1 attempt or more than 20 seconds were excluded from the study.

After obtaining written informed consent 80 patients were randomly allocated into 2 groups of 40 each. Group A received Clonidine 300 mcg and Group B received Pregabalin 75 mg orally with sips of water as premedication 2 hours prior to induction of general anaesthesia. On arrival in the operation theatre fasting status, written informed consent and PAC was checked. All the routine monitors were attached and the preoperative baseline vitals i.e heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP), SpO₂ & ECG were recorded. Intravenous line was secured, and i.v. fluid Ringer Lactate started. A uniform anaesthetic technique was used in both groups. Patients were premedicated with inj ranitidine 50mg iv, inj Midazolam 1mg iv, inj. Glycopyrrolate 0.2mg iv prior to induction. After 3 min of pre oxygenation with 100 % O₂ for three minutes anaesthesia was induced with inj. Thiopentone 5mg/kg iv and laryngoscopy and intubation was facilitated with succinylcholine 2 mg/kg iv and airway secured.

Data were collected at baseline, before induction, before intubation, during laryngoscopy, 0, 1, 3, 5, and 10 minutes after intubation. Surgery was allowed to commence after 10 minutes of intubation & anaesthesia was maintained with 60% Nitrous Oxide along with 40% Oxygen, 0.6-1% isoflurane and inj. Atracurium 0.5 mg/kg loading and .1mg/kg i.v. SOS. At the end of the surgery patient was reversed with Inj. Neostigmine (0.05mg/kg i.v.) and Inj. Glycopyrrolate (0.01mg/kg i.v.).

Extubation was done after proper suction, and when patient was fulfilling the criteria for extubation. Patient was shifted to recovery room. In recovery room patient was observed for any side effects

Statistical analysis was performed with the SPSS, version 21 for Windows statistical software package (SPSS inc., Chicago, IL, USA). The Categorical data was presented as numbers (percent) and were compared among groups using Chi square test. The quantitative data was presented as mean and standard deviation and were compared by student's t-test. Probability was considered to be significant if less than 0.05.

Results

A total 80 patients were included into the study. A random allocation of the patients was done in the

two groups. The mean age of the patients in A group was 40.48 ± 4.59 years, in B group was 39.60 ± 6.00 years. There was no statistically significant difference between the groups with regards to age ($p > 0.05$) (Table No 1). There was even distribution of weight in the both groups. Mean weight of patients in A group was 55.55 ± 2.58 kg, in B group was 56.42 ± 3.11 kg. These 2 groups were comparable with respect to weight.

All patients were females. So these confounding factors also alleviate by clinically insignificant variation in sex. 2 groups had all patients of ASA grade 1. The mean baseline pulse rate in group A was 84.38 ± 6.58 bpm, in group B was 82.48 ± 5.35 bpm.

The difference in heart rate was not significant as shown by P value of > 0.05 . The mean baseline Systolic blood pressure in group A was 122.70 ± 7.26 mm of Hg, in group B was 119.68 ± 6.22 mm of Hg. The difference in SBP was significant as shown by P value of < 0.05 . In group A mean Diastolic blood pressure was 80.85 ± 5.52 mm of Hg, in group B was 77.10 ± 5.30 mm of Hg (p value < 0.05); for mean blood pressure p value > 0.05 was among these groups, in group A mean of Mean arterial pressure was 93.18 ± 4.93 mm of Hg, in group B was 90.95 ± 5.14 mm of Hg. Thus we find that all the baseline variables in these groups were similar and can say that the randomization was done adequately.

Tablet 1: Socio-demographic variable

Parameters	Group-A (n=40)	Group-B (n=40)	p-value
Age in years (means \pm SD)	40.48 ± 4.59	39.60 ± 6.00	0.465(NS)
Weight in Kg (means \pm SD)	55.55 ± 2.58	56.42 ± 3.11	0.151(NS)

Table 2: Mean Heart Rate at Various Time Intervals

	Group A		Group B		p value
	Mean	SD	Mean	SD	
Base line	84.38	6.58	82.48	5.35	0.160
Before Induction	65.43	3.80	86.30	4.95	0.000
After induction	73.93	2.57	88.95	4.60	0.000
1 Minutes after Intubation	90.93	2.87	104.28	3.87	0.000
3 Minutes after Intubation	86.68	3.21	95.90	3.76	0.000
5 Minutes after Intubation	82.88	3.27	89.65	3.79	0.000
10 Minutes after Intubation	70.03	3.64	84.85	3.70	0.000

Table 3: Mean MAP at Various Time Interval

	Group A		Group B		p value
	Mean	SD	Mean	SD	
Base line	93.18	4.93	90.95	5.14	0.051
Before Induction	81.43	2.67	95.93	5.92	0.000
After induction	84.90	1.91	99.60	4.48	0.000
1 Minutes after Intubation	101.98	2.49	111.43	2.89	0.000
3 Minutes after Intubation	99.00	2.33	108.38	2.70	0.000
5 Minutes after Intubation	94.50	2.09	104.80	2.68	0.000
10 Minutes after Intubation	90.80	3.47	99.35	2.34	0.000

Discussion

The sympathoadrenal activation associated with laryngoscopy and tracheal intubation causes deleterious respiratory, neurological and cardiovascular effects and is more marked in hypertensive patients¹⁻³. Several strategies have been evolved to blunt haemodynamic response to laryngoscopy and endotracheal intubation⁵⁻¹⁶.

Clonidine^{17,18} by its central sympatholytic action, it tends to attenuate the haemodynamic response to any surgical nociceptive stimulus and improve overall perianesthetic cardiovascular stability^{19,20}.

Pregabalin, is a lipophilic analogue of GABA. It acts by decreasing the synthesis of neurotransmitter glutamate to act on the central nervous system. It exhibits potent anticonvulsant, analgesic and anxiolytic activity²¹.

In our study, we compared the effect of oral clonidine and pregabalin given 120 min before the start of surgery on laryngoscopy, tracheal intubation in patients undergoing total abdominal hysterectomy. In our study both groups were comparable with respect to age and weight and their baseline values in HR, SBP, DBP, MAP were also comparable among both groups. Heart rate was increased in both groups at 1 min. after intubation. Group A showed a better response than group B with a statistically significant difference ($p < 0.05$). In group A, after intubation the mean heart rate came less than the mean baseline value of heart rate after 5 min of intubation but in group B it took more than 10 min. This trend was maintained till 10 min after intubation but the difference was significant. Bhawna Rastogi et al conducted a study to compare effect of oral pregabalin 75mg and pregabalin 150mg premedication for attenuation of pressor response to endotracheal intubation under general anaesthesia. They observed that significant increase in heart rate and mean arterial pressure was observed in pregabalin 75mg after airway instrumentation, while statistically significant attenuation of mean arterial pressure was seen in pregabalin 150mg.²² Aftab ahmad khan et al stated that there was a significant increase in HR in pregabalin group after laryngoscopy and tracheal intubation in comparison of clonidine from baseline. Clonidine is better than pregabalin in suppressing the pressor response.²³ In our study also the effect of clonidine 300mcgs on HR was similar to the study done by Aftab ahmad khan et al. In our study HR response to laryngoscopy and

intubation was not completely obtunded by either drug. HR rise was however less marked and short lived in clonidine. Our results are similar to the study of Shirin Parveen, Devendra Singh Negi et al²⁴. However they used 300 microg of clonidine and 150 pregabalin. Baseline SBP, DBP and MAP were similar in these groups. After giving the drug significant fall in SBP, DBP and MAP was seen in group A, but was not in pregabalin group (group-B), ($p < 0.05$). Following intubation SBP, DBP and MAP all were rise from the baseline in both groups. Clonidine showed a better response than pregabalin with a statistical significant difference at 1 min after intubation ($P < 0.05$). At 3, 5, and 10 min post intubation, the statistical difference was significant in group A was found better than group B. Preoperatively, there was a decrease in MAP in group A after administration of study drug and at just before intubation, but statistically significant. After intubation, group A showed a better response than group B with a statistical significant difference at 1 min after intubation ($P < 0.05$). Group A showed better response than group B. Similar results have been reported by Faheim SM, Marashi SM and K Gupta. Faheim SM et al²⁵, compared the effects of gabapentin versus clonidine given 90 minutes before the start of surgery on laryngoscopy, tracheal intubation. It was concluded that oral gabapentin is as effective as clonidine in attenuation of pressor response to laryngoscopy and intubation. Marashi SM et al²⁶ conducted a study to compare the effect of clonidine as premedication for hemodynamic stability. It was concluded that clonidine has an effective role in blunting hyperdynamic responses after laryngoscopy. K Gupta et al²⁷ demonstrated that Oral premedication with pregabalin 150 mg or clonidine 200 µg causes sedation and anxiolysis with hemodynamic stability during laryngoscopy and laparoscopic cholecystectomy. Our results are similar to the study of Shirin Parveen, Devendra Singh Negi et al²⁴. However they used 300 microg of clonidine and 150 pregabalin.

Thus in our study, oral clonidine 300 microgram, 2 hrs before anaesthesia, provided good attenuation of haemodynamic response to laryngoscopy and intubation as compared to oral pregabalin (75mg).

CONCLUSION

It is concluded from our study that both clonidine and pregabalin showed sedation in a significant proportion of subjects, more so with clonidine. HR

response to laryngoscopy and intubation was fairly attenuated by clonidine except for transient increase immediately after intubation. However there was no attenuation with pregabalin. SBP, DBP and MAP rise following intubation was completely obtunded by clonidine as compared to pregabalin. Side effects were seen with both the drugs which didn't warrant any treatment.

Financial support and sponsorship - nil

Conflicts of interest –There are no conflict of interest

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