

# Effectiveness Of Oral Clonidine As Anxiolytic And For Attenuation Of Haemodynamic Responses To Laryngoscopy And Intubation.

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## Abstract

Background – Oral Clonidine premedication for attenuation of haemodynamic response to laryngoscopy and intubation. Methods : 50 Patients of ASA I & II in age group of 20-50 years undergoing elective surgery were included. Patients were randomly categorized to two groups. Group A receiving tab clonidine 4 ug/Kg 90 minutes prior to induction and Group B receiving placebo. Heart rate and blood pressure were measured and recorded before, immediately after 1 min and then every 5 minutes after intubation until 15 minutes. Results and conclusion – Clonidine decreases anxiety, systolic blood pressure, diastolic blood pressure, mean blood pressure and heart rate at 90 minutes. Clonidine group showed a significant superiority over placebo in the prevention of increase in systolic blood pressure as well as heart rate over the intubation. Clonidine blunts the stress response to laryngoscopy. Preoperative clonidine is also an effective anxiolysis and hence this study suggest that orally administered clonidine in preanaesthetic period provides more haemodynamic stability and attenuates the stress response to laryngoscopy and intubation.

## INTRODUCTION

Clonidine, an  $\alpha_2$  adrenergic receptor agonist attenuates adrenergic, hormonal and haemodynamic stress response to surgery, reduces anxiety and leads to sedation (Kulka et al., 1995). The hemodynamic responses due to sympathetic stimulation to laryngoscopy and tracheal intubation and their hazards have been well documented (Edward et al 1994 Fox et al., 1997). Various pharmacological agents which have been used to attenuate the pressor responses are  $\alpha_2$  adrenergic agonists like clonidine,  $\beta$  blockers, calcium channel blockers, gabapentine etc. Preanaesthetic medication form an integral part of anaesthetic management and some form of premedication is universally administered before any anaesthesia. The ideal premedicants should be effective and pleasant to be taken orally, have analgesic and non emetic properties, should effectively alleviate apprehensions of the patients.

However, it has been revealed that in comparison with other medications, clonidine has beneficial effects on the hyperdynamic responses during stressful conditions like laryngoscopy and endotracheal intubation. (Abo et al.,

1990; Carabine et al., 1991; Flincke et al., 1987; Ghignone et al., 1986; Mikawa et al., 1993; Nishikawa et al., 1991; Orko et al., 1987; Pouttuet et al., 1987, Raval & Mehta 2002, Zalunardo et al., 1997).

The objective of this, prospective, placebo controlled study was to evaluate the effects of oral clonidine premedication on the haemodynamic response to laryngoscopy and tracheal intubation.

## METHODS AND MATERIALS

Data Source – informed consent from all patients was obtained.

This was a randomized placebo – controlled study in which 50 patients of ASA I and II aged 18-50 years (mean 35 + 8 years) of both sexes. Male – 28 female – 22 were scheduled for elective surgery under general anaesthesia. Two groups Group A clonidine and Group B control were taken Patients with ischaemic heart diseases or myocardial infarction, history of cerebrovascular accidents, heart block, pregnancy, emergency surgical procedures, h/o of respiratory, hepatic and renal diseases, h/o of drug or alcohol abuse, h/o of

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allergy to clonidine, patients on  $\beta$ -blockers, antidepressant, anticonvulsant or antipsychotic drugs and prolonged laryngoscopy time (more than 30 seconds) were excluded.

Patients were randomly divided into two groups (25 each). Oral clonidine was given 90 minutes before admission to the operating room.

Group A – patients received – 4 ug/Kg of tab clonidine,  
Group B – patients received Placebo.

The patients were assessed for anxiety score in the preoperative room after 90 minutes. Following insertion of I/V cannulae, all patients were infused with 5ml/kg normal saline. Routine monitoring comprised of E.C.G., pulse oximetry, Etco<sub>2</sub>, and non-invasive blood pressure. Patients were preoxygenated for 3 minutes with oxygen 100% and anaesthesia was induced with Inj Propofol 1-1.5mg/kg and 0.5mg/Kg atracurium., fentanyl 1 ug/kg. Three minutes later, laryngoscopy using Macintosh blade size 3 and intubation using E.T.T. (Size 7.5-8) was performed. After successful intubation, anaesthesia was maintained with Isoflurane 1-1.2 MAC, N<sub>2</sub>O : O<sub>2</sub> (66%:33%) and atracurium 0.2 mg/Kg. Diastolic and mean arterial blood pressure were recorded before induction of anaesthesia, before laryngoscopy, just after and then every 5 minutes until 15 minutes. Data are expressed as mean SD or number of patients. A two way repeated measures ANOVA (Time x Haemodynamic Variables) was used. The two groups as the between subjects factor group and the five measurements (during Induction, intubation and maintenance of Anaesthesia) as within subjects factor (time were considered. This was done for heart rate and systolic blood pressure. In addition, to compare, two groups at baseline and at each time, independent sample t-test was used.

Paired sample t-test was used for comparison of two subsequent measurements in each group. Differences were considered significant at  $P < 0.05$ .

## RESULTS

In our study, no patient was excluded. No significant differences were identified between patients randomly assigned to two groups with regards to age and sex.

There were no significant differences between the two groups at the baseline on the systolic blood pressure ( $p = 0.34$ ) and heart rate ( $p = 0.14$ ). However, both heart rate and systolic blood pressure were significantly higher in control group at three subsequent measurements following

Intubation. ( $P < 0.001$ )

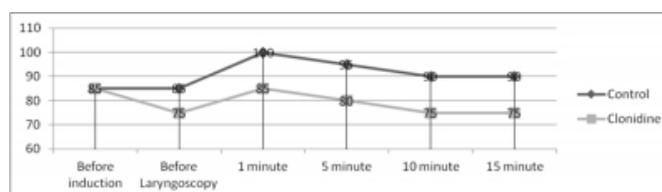
The differences in systolic blood pressure between the two groups were significant so were the differences in the heart rates. ( $P < 0.001$ )

Statistically significant difference were observed between control and clonidine group in the anxiety score.

## MEAN HEART RATE

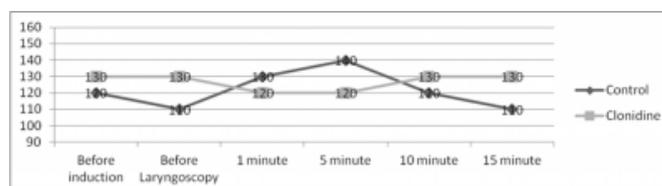
**Figure 1**

Plot of estimated Heart rate according to group and time



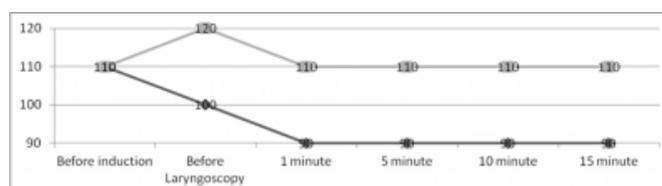
**Figure 2**

Plot of estimated means of SAP according to groups and time



**Figure 3**

Plot of estimated means of MAP according to groups and time



Anxiety Scoring Score

Score -0 Patient quiet and comfortable

Score – 1 Patient uneasy

Score – 2 Patient worried or anxious

Score – 3 Patient very worried or very upset

Score – 4 Patient frightened or terrified

## **DISCUSSION**

Clonidine, an  $\alpha_2$  adrenoreceptor agonist, prevents tachycardia and rise in blood pressure in response to laryngoscopy and intubation. It applies its properties through a complex underlying mechanism in which it interacts with the catecholaminergic neuronal system which modulates tonic and phasic (reflex) blood pressure control. Two different central and peripheral components have been considered for this achievement. In the central pathway, centrally activation of  $\alpha_2$  – adrenoreceptors causes both a reduction in peripheral sympathetic tone and an increase of vagally induced reflex bradycardia, which in turn results in the attenuation of heart rate acceleration. Peripherally acted, stimulation of presynaptic  $\alpha_2$  adrenoreceptors diminishes release of norepinephrine from the nerve endings towards the vasculature and to a reduction in a peripheral sympathetic tone towards the heart (Doxey 1979).

Sung et al., (2000) has shown that premedicated with oral clonidine helped to provide preoperative haemodynamic stability. Same has been revealed by DC Deyne et al., (2000) where better hemodynamical stability was seen preoperatively.

The rise in the pulse rate and blood pressure after noxious stimulus like laryngoscopy and endotracheal intubation is attributed to the sympathoadrenal activation. (Raval and Mehta, 2002).

De Dyne observed oral clonidine in a dose of 4ug/kg produced both sedation and anxiolysis. The degree of sedation is less as compared to diazepam. The sedative effect of clonidine may be due to decreased tonic activity of the locus coeruleus which modulates the stimuli arriving in the central nervous system. Sedation and anxiolysis caused by clonidine are elicited at central  $\alpha_2$  – adrenergic receptors., Same study done by Raval, Mehta in 2002 using clonidine and diazepam as premedication for attenuation of hemodynamic response to laryngoscopy and intubation.

Similarly Rudra A et al., (1994), . A.K. Rudra ® (1995) observed less sedation with 3 ug/kg oral clonidine, as compared to 0.2 mg/kg diazepam or no significant differences in anxiety score between two groups.

Our data confirmed that heart rate , systolic blood pressure,mean arterial pressure,significantly differ with regard to groups and to times (all the p-values < 0.05).

Between the group, the highest rate of heart rate., systolic blood pressure, mean blood pressure were in placebo group especially in 1 minute after layngoscopy. It follows that clonidine has effective role in blunting hemodynamic responses following laryngoscopy. Anxiety was decreased and significant difference was observed in clonidine group.

In conclusion, the results of this study showed that orally administration of 4ug/kg clonidine provides hemodynamic stability and attenuates the stress response to laryngoscopy and intubation and also act as an anxiolytic.

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