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# COMPARISON OF ORAL PREMEDICATION BETWEEN MIDAZOLAM AND CLONIDINE FOR GENERAL ANAESTHESIA IN ELECTIVE OPEN ABDOMINAL SURGERY

Anesthesiology

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## ABSTRACT

**Background and Aim:** Premedication is an integral part of general anesthesia. An ideal premedicant is effective and pleasant if taken orally. They have analgesic and antiemetic properties and do not impair cardiovascular stability. Moreover, the premedicants have antisialogogue effect and effectively abolish apprehension of the patient. The present study was undertaken to compare the clinical efficacy of oral clonidine and oral midazolam as preanaesthetic medication to attenuate the cardiovascular responses to laryngoscopy during intubation and extubation and also to compare their effects in relation to sedation and decrease in anxiety.

**Methods :** In this randomized prospective comparative study, 80 (eighty) patients in between the age of 20-60 years with ASA grade I or II posted for elective open abdominal surgeries under general anesthesia were randomly allocated in two groups (n=40). Group M (midazolam)-received 0.5mg/kg of body weight of midazolam orally 90minutes prior to induction of anesthesia and Group C (clonidine)-received 3µg/kg of body weight of clonidine orally 90minutes prior to induction of anesthesia. Hemodynamic parameters were recorded at baseline (just before administration of study drug), just before induction of anaesthesia, just after the endotracheal intubation, then 10, 20, 30, 40 minutes after intubation and just after extubation. Sedation score and anxiety score were assessed just before administration of study drug) and just before induction of anaesthesia.

**Results:-** Oral Clonidine decreased both the heart rate and blood pressure more than oral Midazolam. Clonidine effectively attenuated the cardiovascular stress response associated with laryngoscopy and intubation. But it was also found that oral Midazolam produced significant sedation in comparison to oral Clonidine.

**Conclusion :** Oral clonidine was found to be better in respect to oral midazolam as a premedicant to abolish cardiovascular response during laryngoscopy and intubation with less sedation.

## KEYWORDS

Clonidine, Midazolam, cardiovascular stress response, laryngoscopy

## INTRODUCTION

Preanaesthetic medication forms an integral part of anaesthetic management. The ideal premedicant should be effective and pleasant if taken orally, should have analgesic and antiemetic properties, can attenuate cardiovascular responses during laryngoscopy and tracheal intubation, should have antisialogogue effect and should effectively alleviate apprehension of the patient by its sedative properties.[1]

Anxiety is a common problem in almost all patients undergoing for any surgical procedure. By decreasing the degree of anxiety we can increase patient satisfaction [2] as well as we can able to reduce the preoperative stress related increase in heart rate and blood pressure.[3] The most commonly used agents for this purpose are benzodiazepines, particularly midazolam and alpha 2 agonists.[4,5] They are safe and efficacious.

During administration of general anaesthesia it is observed that hemodynamic stress response occur during laryngoscopy and tracheal intubation and also during extubation. There may be increase in systolic and diastolic blood pressure or increase in heart rate or both. This hemodynamic changes are transient and do not detrimental to a healthy individual[6,7]. But it may cause heart failure, dysrhythmias and myocardial ischemia in an already diseased heart. Various methods are used to attenuate this hemodynamic changes like adequate depth of anaesthesia, lignocaine spray, topical use of lignocaine jelly, intravenous use of preservative free lignocaine, calcium channel blocker, α2-adrenergic agonist drugs like clonidine, vasodilator or their combinations with various degrees of success [8,9]. But no single method has gained widespread acceptance because each method has its own merits and demerits. . With this idea an endeavor was made to evaluate oral clonidine and oral midazolam as a premedication in attenuating cardiovascular responses to direct laryngoscopy and endotracheal intubation and also to compare their effects in relation to sedation and decrease in anxiety.

## MATERIAL AND METHODS

This prospective, randomized, comparative, double blind study was conducted at a tertiary care hospital in Eastern India over a period of one year (January 2017-June 2018) after approval of the Ethical cum Screening Committee. We included randomly selected 80 patients (determined by power analysis study) in between the age of 20-60 years with American Society of Anesthesiologists (ASA) physical status (PS) I and II, of either sex, weighing between 45 and 75 kg posted for elective open abdominal surgical procedures under general anesthesia. Each patient received a written and verbal description of the research protocol and written informed consent was taken from all the patients in their language for inclusion in the study. Exclusion criteria for the study were patients with severe cardiovascular, respiratory, renal, hepatic diseases and psychiatric illness, patients on beta blocker therapy or alpha-2 agonist therapy,patients with anticipated difficult airway, patients refusal, emergency surgery, alcohol abuse, history of allergic reactions to any study drug, body mass index > 30 kg./$m^2$, and poor nutritional status and general condition.

All patients were divided in two groups (n=40)

- Group M (midazolam group)-received 0.5mg/kg of body weight of midazolam orally 90minutes prior to induction of anesthesia
- Group C (clonidine group)- received 3µg/kg of body weight of clonidine orally 90minutes prior to induction of anesthesia.

### Parameters to be studied

The parameters which were considered for this study were demographic variables like age(in years),sex(male/female),body weight(in kg),sedation score ,anxiety score and vitals (heart rate ,systolic blood pressure, diastolic blood pressure, mean arterial pressure by noninvasive technique). The investigator graded sedation according to a 4 point sedation score (1=alert, 2=awake, 3=drowsy, 4=asleep), where a score of 3 and 4 was considered adequate sedation. Grading of anxiety was done by four point scoring, 1=poor (afraid and agitated and difficult to control, panicky), 2=fair (fearful, moderate apprehension, moaning), 3=good (slightly apprehensive, but withdrawn from the surroundings), 4=excellent (no fear, calm and sleepy, friendly), where a score of 3 and 4 was considered to be adequate anxiolysis.

Assessment of Sedation and anxiety were done by the investigator at:

i. Just before administration of the study drug which was 90 minutes before the induction of anaesthesia. [Time point-0]
ii. Just before induction of anaesthesia. [Time point-1]

Assessments of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were done by the investigator at:

i. Just before administration of the study drug which was 90 minutes before the induction of anaesthesia. (Time point-0)
ii. Just before induction of anaesthesia. (Time point-1)
iii. Just after the endotracheal intubation. (Time point-2)
iv. Every 10 minutes after that (Time point -3, 4, 5, 6)
v. Just after extubation. (Time point-7)

**Study technique**

After approval of the Hospital Ethical cum Screening committee, 80 patients with the above mentioned criteria were selected for the study. On the preceding day of operation, relevant history, preanaesthetic check-up and informed consent of the patients were taken. Patients were advised to fast for 8 hours before surgery. On the day of surgery patients were randomly allocated into two groups, Group M and Group C .Group M received oral Midazolam(0.5mg/kg body weight) and Group C received oral Clonidine (3 microgram/kg body weight) 90 minutes before induction of anaesthesia. After arrival in the operating room, patient's identity and informed consent form were checked and all requisite monitors were attached. Blinding were done by using two separate persons doing the required work. Study drugs were supplied in sealed envelope with number codes 90 minutes prior to induction. Anesthesiologists were chosen to conduct the procedures randomly. Later on all the data were collected from them and tabulation was done. Patients were premedicated with inj. Fentanyl (2microgram/kg) 5 min prior to intubation.

All patients received a standardized anesthetic as described-preoxygenation for 3 minutes with gas flow @ 5 liters/minute, followed by induction of anesthesia with inj. Propofol (2mg/kg I.V). Laryngoscopy (using Macintosh Laryngoscope) and intubation with appropriately cuffed endotracheal tube were facilitated with Inj. Vecuronium bromide (0.1mg/kg). Maintenance of anesthesia was done with 40% of $O_2$ -60% of $N_2O$, and Isoflurane inhalation 0.6 % MAC. Muscle relaxation was achieved with vecuronium, which was repeated at 25%-30% of the initial dose as per requirement. Ventilation was mechanically controlled and adjusted to control end tidal $CO_2$ concentration at 30-35 mmHg. At the end of operation residual neuromuscular blockage was antagonized with neostigmine (40 mcg/kg I.V) and glycopyrrolate (0.01mg/kg I.V). Extubation was done only after adequate reversal from general anesthesia judged on clinical basis. After oxygenation for about 5 minutes postoperatively patients were sent to the ward. In case of acute and severe hemodynamic fluctuation the following medical interventions were taken; for bradycardia (heart rate <40beats/min) inj atropine 0.6mg bolus dose and for hypotension (MAP<65 mm of Hg)inj phenylephrine and for hypertension (MAP> 110mm of Hg)inj labetalol/ GTN infusion.

**Statistical Analysis:**

The sample size was calculated based on the previous study taking the significant level as 0.05, power as 80% & difference between mean as 10 & standard deviation 15, the required sample size was calculated as 35 in each group making the total sample size 70 which was converted to a round figure & the total sample size taken were 80 with 40 in each group (n=40). Randomization was done with the help of computer generated random number table.

Categorical variables were expressed as Number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes/ Fisher's Exact Test as appropriate. Continuous variables were expressed as Mean, Median and Standard Deviation and compared across groups using and Mann-Whitney U test. The statistical software SPSS version 20 was used for the analysis. A p value < 0.05 was considered as statistically significant and < 0.01 was considered as highly significant.

**RESULTS:-**

**Demographic variables**

The groups were statistically comparable with respect to age, sex, body weight, and ASA grading. [Tables 1, 2, 3, 4].

**Table 1: Age distribution of the patients**

| | | Groups | | Total | | |
|---|---|---|---|---|---|---|
| | | Group M | Group C | | p Value | Significance |
| Age | 20-30 | 4(10%) | 4(10%) | 8(10%) | 0.584 | NS |
| | 31-40 | 17(42.50%) | 23(57.50%) | 40(50%) | | |
| | 41-50 | 15(37.50%) | 10(25%) | 25(31.25%) | | |
| | 51-60 | 4(10%) | 3(7.50%) | 7(8.75%) | | |
| Total | | 40(100%) | 40(100%) | 80(100%) | | |

NS= Not Significant

**Table 2. Sex distribution of the patients**

| | | Groups | | Total | | |
|---|---|---|---|---|---|---|
| | | Group M | Group C | | p Value | Significance |
| Sex | FEMALE | 19(47.50%) | 18(45%) | 37(46.25%) | 0.823 | NS |
| | MALE | 21(52.50%) | 22(55%) | 43(53.75%) | | |
| Total | | 40(100%) | 40(100%) | 80(100%) | | |

NS= Not Significant

**Table 3. Bodyweight distribution of the patients**

| | Groups | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Group M | | | Group C | | | | |
| | Mean | Median | Std. Deviation | Mean | Median | Std. Deviation | p Value | Significance |
| Weight (Kg) | 52.65 | 53.50 | 4.92 | 53.23 | 54.00 | 4.77 | 0.555 | NS |

NS= Not Significant

**Table 4.Distribution of ASA grading of the patients**

| | | Groups | | Total | | |
|---|---|---|---|---|---|---|
| | | Group M | Group C | | p Value | Significance |
| ASA | I | 22(55%) | 25(62.50%) | 47(58.75%) | 0.496 | NS |
| | II | 18(45%) | 15(37.50%) | 33(41.25%) | | |
| Total | | 40(100%) | 40(100%) | 80(100%) | | |

NS= Not Significant

**Comparison of Heart rate (beats/min) between groups**

When the preoperative baseline HRs were compared between two groups, no statistically significant difference was found (p value >0.05).The HRs after laryngoscopy & intubation were significantly lower in clonidine compared to midazolam. The Heart Rate just after extubation was also lower in clonidine group. [Table-5]

**Table 5:-Mean heart rate and standard deviation**

| | Groups | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | GROUP M | | | GROUP C | | | | |
| | Mean | Median | Std. Deviation | Mean | Median | Std. Deviation | p Value | Significance |
| HR_0 | 91.18 | 92.00 | 8.83 | 94.05 | 93.00 | 6.14 | 0.125 | NS |
| HR_1 | 86.28 | 86.00 | 5.55 | 75.33 | 74.50 | 4.55 | <0.001 | S |
| HR_2 | 89.18 | 90.00 | 5.55 | 77.05 | 76.50 | 4.80 | <0.001 | S |
| HR_3 | 91.18 | 92.00 | 5.98 | 69.20 | 68.00 | 3.67 | <0.001 | S |
| HR_4 | 78.68 | 79.00 | 5.35 | 65.40 | 65.00 | 4.28 | <0.001 | S |
| HR_5 | 81.30 | 82.00 | 5.14 | 65.55 | 64.00 | 4.85 | <0.001 | S |
| HR_6 | 88.15 | 88.00 | 3.69 | 67.95 | 68.00 | 4.16 | <0.001 | S |
| HR_7 | 100.20 | 100.00 | 4.59 | 84.70 | 86.00 | 3.86 | <0.001 | S |

NS= Not Significant, S=Significant

**Comparison of SBP (mmHg) between groups**

When the preoperative baseline SBP was compared between two groups, no statistically significant difference was found (p value >.05).The SBP after laryngoscopy & intubation were significantly lower in clonidine group compared to midazolam group. The SBP just after extubation were also lower in clonidine group. [Table-6]

**Table 6:- Mean systolic blood pressure and standard deviation**

| | Groups | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Group M | | | Group C | | | | |
| | Mean | Median | Std. Deviation | Mean | Median | Std. Deviation | p Value | Significance |
| SBP_0 | 133.20 | 130.00 | 8.78 | 136.60 | 138.00 | 7.91 | 0.089 | NS |
| SBP_1 | 131.35 | 132.00 | 8.50 | 127.30 | 128.00 | 6.74 | 0.034 | S |
| SBP_2 | 134.45 | 134.00 | 9.12 | 131.10 | 132.00 | 6.50 | 0.045 | S |
| SBP_3 | 138.55 | 137.00 | 10.75 | 134.30 | 134.00 | 3.94 | 0.029 | S |
| SBP_4 | 135.53 | 134.00 | 9.61 | 130.85 | 130.00 | 4.07 | 0.015 | S |
| SBP_5 | 134.45 | 134.00 | 7.31 | 127.85 | 128.00 | 2.91 | <0.001 | S |
| SBP_6 | 133.90 | 136.00 | 6.82 | 127.40 | 128.00 | 4.08 | <0.001 | S |
| SBP_7 | 139.30 | 139.00 | 7.01 | 135.20 | 136.00 | 2.16 | <0.001 | S |

NS= Not Significant, S=Significant

**Comparison of DBP (mm Hg) between groups**

When the preoperative baseline DBP was compared between two groups, no statistically significant difference was found (p value >.05).The DBP after laryngoscopy & intubation were significantly lower in clonidine group compared to midazolam. The DBP just after extubation were also lower in clonidine group. [Table-7]

**Table 7: Diastolic blood pressure and standard deviation**

| | Group M | | | Group C | | | | |
|---|---|---|---|---|---|---|---|---|
| | Mean | Median | Std. Deviation | Mean | Median | Std. Deviation | p Value | Significance |
| DBP_0 | 83.85 | 84.00 | 4.84 | 83.30 | 84.00 | 4.06 | 0.617 | NS |
| DBP_1 | 80.95 | 80.00 | 5.34 | 77.05 | 78.00 | 3.68 | <0.001 | S |
| DBP_2 | 85.15 | 86.00 | 5.43 | 81.05 | 82.00 | 3.79 | 0.001 | S |
| DBP_3 | 87.45 | 86.00 | 5.42 | 81.40 | 81.00 | 3.36 | <0.001 | S |
| DBP_4 | 85.75 | 86.00 | 4.84 | 80.50 | 80.00 | 3.03 | <0.001 | S |
| DBP_5 | 80.65 | 81.00 | 4.63 | 77.55 | 78.00 | 2.29 | <0.001 | S |
| DBP_6 | 78.25 | 80.00 | 4.69 | 75.15 | 76.00 | 3.53 | 0.001 | S |
| DBP_7 | 83.10 | 84.00 | 3.39 | 80.95 | 80.00 | 3.68 | 0.006 | S |

NS= Not Significant, S=Significant

**Comparison of MAP (mmHg) between groups**

When the preoperative baseline MAP was compared between two groups, no statistically significant difference was found (p value >.05).The MAP after intubation were significantly lower in clonidine group compared to midazolam. The MAP just after extubation were also lower in clonidine group. [Table-8]

**Table 8: Mean arterial pressure and standard deviation**

| | Groups | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Group M | | | Group C | | | | |
| | Mean | Median | Std. Deviation | Mean | Median | Std. Deviation | p Value | Significance |
| MAP_0 | 100.33 | 99.00 | 5.57 | 101.03 | 101.00 | 4.38 | 0.521 | NS |
| MAP_1 | 97.73 | 97.50 | 5.48 | 93.78 | 93.50 | 3.87 | 0.002 | S |
| MAP_2 | 101.58 | 102.50 | 5.90 | 97.68 | 97.50 | 3.87 | 0.001 | S |
| MAP_3 | 104.45 | 104.00 | 6.51 | 99.00 | 99.00 | 2.95 | <0.001 | S |
| MAP_4 | 102.30 | 102.50 | 5.45 | 97.30 | 97.00 | 2.76 | <0.001 | S |
| MAP_5 | 98.55 | 98.50 | 4.64 | 94.38 | 95.00 | 1.64 | <0.001 | S |
| MAP_6 | 96.78 | 97.00 | 4.09 | 92.48 | 91.50 | 3.09 | <0.001 | S |
| MAP_7 | 101.85 | 101.50 | 3.29 | 99.03 | 98.00 | 2.84 | <0.001 | S |

NS= Not Significant, S=Significant

**Comparison of Sedation Score between groups**

Patients of Midazolam group were having statistically highly significant sedation at 90 minutes after administration of oral Midazolam. [Table 9A, 9B]

**Table 9: Sedation Score distribution in the study**

**9A.**

| | | Groups | | Total | | |
|---|---|---|---|---|---|---|
| | | Group M | Group C | | p Value | Significance |
| SedSco_0 | 1 | 39(97.50%) | 40(100%) | 79(98.75%) | 0.314 | NS |
| | 2 | 1(2.50%) | 0(0%) | 1(1.25%) | | |
| Total | | 40(100%) | 40(100%) | 80(100%) | | |

NS= Not Significant. SedSco_0: Sedation score of the patients before administrations of the study drug which was 90 minutes before the induction of anesthesia.

**9B.**

| | | Groups | | Total | | |
|---|---|---|---|---|---|---|
| | | Group M | Group C | | p Value | Significance |
| SedSco_1 | 1 | 19(47.50%) | 34(85%) | 53(66.25%) | 0.001 | S |
| | 2 | 19(47.50%) | 6(15%) | 25(31.25%) | | |
| | 3 | 2(5%) | 0(0%) | 2(2.5%) | | |
| Total | | 40(100%) | 40(100%) | 80(100%) | | |

S=Significant. SedSco-1: Sedation score of the patients just before induction of anesthesia (at 90 minutes after administration of the study drug).

**Comparison of Anxiety Score between groups**

When anxiety scores were compared between two groups no statistically significant difference was found (p value >.05). [Table 10A, 10B]

**Table 10: Anxiety Score distribution in the study**

**10A.**

| | | Groups | | Total | | |
|---|---|---|---|---|---|---|
| | | Group M | Group C | | p Value | Significance |
| AnxSco_0 | 0 | 31(77.50%) | 26(65%) | 57(71.25%) | 0.442 | NS |
| | 1 | 7(17.50%) | 12(30%) | 19(23.75%) | | |
| | 2 | 2(5%) | 2(5%) | 4(5%) | | |
| Total | | 40(100%) | 40(100%) | 80(100%) | | |

NS= Not Significant .AnxSco-0: Anxiety score of the patients before administrations of the study drug which was 90 minutes before the induction of anesthesia.

**10B.**

| | | Groups | | Total | | |
|---|---|---|---|---|---|---|
| | | Group M | Group C | | p Value | Significance |
| AnxSco_1 | 0 | 19(47.50%) | 21(52.50%) | 40(50%) | 0.806 | NS |
| | 1 | 15(37.50%) | 16(40%) | 31(38.75%) | | |
| | 2 | 3(7.50%) | 1(2.50%) | 4(5%) | | |
| | 3 | 3(7.50%) | 2(50%) | 5(6.25%) | | |
| Total | | 40(100%) | 40(100%) | 80(100%) | | |

NS= Not Significant. AnxSco-1: Anxiety score of the patients just before induction of anesthesia (at 90 minutes after administration of the study drug).

**DISCUSSION:-**

Endotracheal intubation has become the mainstay of modern general anaesthesia due to various reasons like maintenance of airway, prevention of aspiration, proper ventilation and adequate gaseous exchange in the body. It has been observed that laryngoscopy and tracheal intubation leads to reflex cardiovascular stimulation resulting in an increase in systemic arterial pressure and heart rate. These changes are due to an increase in sympathetic discharge via cardio accelerator fibres. The increased sympathetic activity caused by stimulation of upper respiratory tract has been supported by the observation that increase in arterial pressure during endotracheal intubation is associated with an increase in plasma noradrenaline level [10]. After intubation there is gradual return of blood pressure and pulse rate to pre-laryngoscopic value. This is probably due to fatigue of the receptor [11]. Various methods have been used to attenuate the cardiovascular responses to laryngoscopy and endotracheal intubation. These methods include deepening of the plane of anaesthesia [12], topical anaesthesia of laryngopharynx and epiglottis [13,14]. Use of opioids like fentanyl and alfentanyl [15,16] produced significant attenuation of cardiovascular responses during intubation. Tanaka M and Nishikawa [17], studied the effect of oral clonidine premedication in attenuating hypertensive response to ketamine. Rudra A and collegue [18] studied the evaluation of clonidine as a premedicant during ketamine anaesthesia and concluded that, clonidine provided acceptable level of sedation, similar anxiolysis as diazepam , good antisialogogue effect and better cardiovascular stability. Mikawa K et al [19] conducted a study regarding attenuation of catecholamine response to tracheal intubation with oral clonidine in children. The results obtained indicated that a high oral dose of clonidine [4 µg/kg] causes significant attenuation of hemodynamic and catecholamine changes compared to other two groups. This may

be due to suppression of increased sympathetic activity evoked by intubation. Paris A [20] conducted a study for effects of clonidine and midazolam premedication on bispectral index and recovery after elective surgery. The study indicated that clonidine augmented hemodynamic stability and partially blunted stress responses as determined by adrenocorticotropic hormone plasma levels. In addition, clonidine did not delay postoperative recovery

The present study was carried out to observe whether oral clonidine or oral midazolam used as a premedication can modify cardiovascular responses to direct laryngoscopy and endotracheal intubation and to compare effectiveness of both above drugs as premedicants. In Our study, the patients were comparable according to their age, sex, body weight and ASA status as there were a small difference between the variables which were statistically insignificant ($p>0.05$) [Table 1, 2, 3,4]. In our study, before induction, Heart rate (HR) decreased both in Clonidine and Midazolam Group. These was statistically highly significant (p value<0.001) [Time Point – 1]. The HRs after laryngoscopy & intubation were significantly lower in clonidine group compared to midazolam. The Heart Rate just after extubation was also lower in clonidine group. [Table-5]

In the patients of group M [Midazolam] SBP was almost same about 90 minutes after the administration of oral Midazolam [Time point- 1] . Patients of group C [Clonidine] were having statistically significant fall in systolic blood pressure (SBP) about 90 minutes after the administration of oral Clonidine ($p<0.05$ ). [Time point- 1]. Just after the laryngoscopy and orotracheal intubation [time point- 2], there was a peak increase of systolic blood pressure in both the groups those were statistically significant ($p<0.05$). This increase was more in Group M than in Group C. Just after the extubation [Time Point- 7], there was also a rise of systolic blood pressure in both the groups those were statistically significant ($p<0.05$). This increase was more in Group M than in Group C. [Table- 6].

There was rise in Diastolic Blood Pressure (DBP) in case of Midazolam Group and fall in DBP in Clonidine Group before induction. [Time Point-1]. DBP increased after laryngoscopy and intubation [Time point-2] in both groups. This increase was higher in Group M and lower in Group C. Just after extubation almost no change in DBP was seen in Clonidine Group from basal value but increase of DBP in Midazolam Group [Time Point-7]. There were low DBP during intraoperative period in Group C and these was statistically significant ($p<0.05$) [Table -7]

Before induction, there was significant fall of Mean Arterial Pressure (MAP) in Clonidine Group, but slight increase in MAP in Midazolam Group [Time Point-1]. There was a peak increase in mean arterial pressure (MAP) after laryngoscopy and intubation [Time Point-2] and after extubation [Time Point-7]. This increase was statistically significant in both the Groups when compared to basal value [$p<0.05$]. This peak increase was higher in Group M and lower in Group C. This finding corroborates with the study of Trevor et al (2012) [21]. Both Clonidine and Midazolam produced a significant decrease in mean arterial pressure. The fall was also more in case of Clonidine Group. [Table–8].

Trevor S et al [21] compared oral midazolam (0.5 mg/kg) versus oral clonidine (4 µg/kg) as a premedication in pediatric patients aged between 2-12 years with regard to sedation and anxiolysis. They concluded that under the conditions of the study, oral midazolam was superior to clonidine as an anxiolytic in pediatric population. Rudra A et al [18] studied the evaluation of Clonidine as a premedicant during ketamine anaesthesia and revealed that clonidine provided acceptable level of sedation, anxiolysis as diazepam ($p>0.1$). In our study, Patients of Midazolam group were having significant sedation compared to Clonidine group at 90 minutes after the administration of study drug and that was statistically highly significant ($p<0.001$). [Time Point-1] [Table 9B]. This finding corroborates with the study of Trevor S et al [21]. There was no statistically significant difference in anxiety score found between the groups in present study. [Table-10]

In no occasion, there was a sudden drop of Mean Arterial Pressure (MAP) to less than 70 mm of Hg necessitating any intervention. Administration of anticholinergic drug was not needed in any cases. No patient of either group suffered from bradycardia in our study. Oral Clonidine as preanaesthetic medication was able to attenuate the pulse rate, systolic, diastolic & mean arterial pressure more than oral Midazolam. But sedation was more in case of oral Midazolam.

## CONCLUSION

Present study concluded that a single dose of 3µg/kg of body weight of oral clonidine attenuated sympathomimetic stress response in terms of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure better than oral midazolam 0.5mg/kg of body weight during laryngoscopy and endotracheal intubation. But this study failed to demonstrate clonidine as a better alternative to midazolam as an anxiolytic preoperatively. However, midazolam showed excellent sedative properties. Adverse effects were minimal.

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**Conflicts of interest**
There are no conflicts of interest

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