Journal of Cardiovascular Disease Research

ISSN:0975-3583,0976-2833 VOL15,ISSUE06,2024

Original Research Article

A Comparative Study of Oral Clonidine and Oral Midazolam as Premedications for General Anaesthesia in Elective Open Abdominal Surgery

Dr. Sanjib Paul[1], Dr. Pradip Kumar Mandal[2], Dr. Burulukui Hembram[3], Dr. Arindam Kumar Das[4]

[1]Assistant Professor Department of Anaesthesiology, Malda Medical College and Hospital, Malda, West Bengal, India.
[2]Associate Professor, Department of Anaesthesiology, Malda Medical College and Hospital, Malda, West Bengal, India.
[3]Associate Professor, Department of Anaesthesiology, Diamond Harbour Government Medical College, Diamond Harbour, West Bengal, India.
[4]Tutor, Department of Anaesthesiology, Malda Medical College and Hospital, Malda, West Bengal, India.

Corresponding Author
Dr. Arindam Kumar Das, Tutor, Department of Anaesthesiology, Malda Medical College and Hospital, Malda, West Bengal, India.

Received: 30-03-2024 / Revised: 05-04-2024 / Accepted: 12-05-2025

ABSTRACT

Background
This study was conducted to evaluate oral clonidine and oral midazolam as premedications for general anaesthesia in elective open abdominal surgery.

Methods
This was a hospital-based study conducted among 100 patients undergoing elective open abdominal surgery carried out in the General Surgery and Gynaecology OT and in the Department of Anaesthesiology of a Tertiary care teaching Hospital over a period of 1 year. Patients were randomly divided into 2 groups of 50 each. Group M(n=50) patients received Tablet Midazolam 7.5mg per orally and Group C(n=50) patients received Tablet Clonidine 150 µg (0.15mg) per orally 60 minutes before the induction of anaesthesia.

Results
At 60 minutes following the administration of oral midazolam, patients in Group M had extremely significant changes in their sedation scores (SedSco). Changes in sedation score [SedSco] in Group C patients were statistically significant (but less than midazolam) sedation at 60 minutes after administration of oral clonidine. There was statistically extremely significant anxiolysis at 60 minutes after oral midazolam administration in the group M patients' changes in anxiety score (AnxSco). At 60 minutes following the administration of oral clonidine, Group C patients had noticeable anxiolysis (although less than midazolam) according to the changes in their anxiety score [AnxSco]. It was also found that oral Clonidine decreased both the heart rate and Blood Pressure more than oral Midazolam. Clonidine effectively attenuated the cardiovascular stress response associated with laryngoscopy & intubation and following extubation

Conclusion
Oral clonidine may be considered to be a superior premedication.

ISSN:0975-3583,0976-2833 VOL15,ISSUE06,2024

Keywords: Oral Clonidine, Oral Midazolam, Premedications, General Anaesthesia, Elective Open Abdominal Surgery

INTRODUCTION

Alpha-2 agonists are safe and effective alternatives to benzodiazepines, which are the most often used drugs for this purpose, this includes midazolam. During general anaesthesia due to laryngoscopy and intubation there is a stress response resulting in intense sympathetic stimulation, causing hypertension and tachycardia. Compared to endotracheal intubation, laryngoscopy causes more intense stimulation so far as cardiovascular effects are concerned.[1] The changes usually recorded include a rise in SBP by about 30-50 mm Hg, and DBP by about 20-30 mm Hg above the baseline blood pressure, resulting in a rise in MAP. About 20–40 more beats per minute are added to the heart rate above the baseline. Five to ten percent of patients may experience different cardiac dysrhythmias. The majority of these, nevertheless, are benign and temporary.[2,3] A certain population of patients, such as those with ischemic heart disease who may experience an acute myocardial infarction, may suffer negative health effects from sympathetic-adrenal activation. Such an increase in heart rate can cause heart failure in patients with damaged hearts. Patients who have cerebral aneurysms may experience hypertensive haemorrhage in the brain. Therefore, one must attempt to reduce sympathoadrenal activation in order to avoid these casualties.[4] Due to this observation, various methods and medications were used, with varying degrees of success, to reduce the cardiovascular responses to tracheal intubation and laryngoscopy. These methods included the deeper plane of anaesthesia, local anaesthetics (applied both locally and intravenously), narcotics, vasodilators, calcium channel antagonists, beta-1 adrenoreceptor blockers, alpha-2 adrenoreceptor agonists, and their combinations.[5,6]

But while each strategy has advantages and disadvantages of its own, no single approach has been widely adopted. Numerous fresh studies are continually being conducted while reviewing earlier ones. This idea was investigated in order to determine whether oral midazolam and clonidine work as a premedication to lessen cardiovascular responses to direct laryngoscopy and endotracheal intubation. The level of preoperative sedation, reduction of preoperative anxiety and postoperative nausea and vomiting were also evaluated. Premedication with α2-adrenergic agonist drugs produces sedation and anxiolysis while decreasing the heart rate and blood pressure during anaesthesia and opioid requirements after surgery.[7]

Oral clonidine, the prototypical α2-agonist, has been successfully used for premedication and may reduce intraoperative blood loss,[8] as well as the anaesthetic and analgesic requirements. Clonidine has also been shown to have potential analgesic properties when administered by the extradural or intrathecal route.[9] When compared with oral midazolam, clonidine was less effective in reducing anxiety but more effective in haemodynamic stability.[10,11]

AIMS AND OBJECTIVES

- To evaluate the comparative clinical efficacy of oral midazolam and oral clonidine as preanaesthetic agents.
- To compare the haemodynamic effects (systolic blood pressure, diastolic blood pressure, mean arterial pressure, and heart rate) due to laryngoscopy and endotracheal intubation with oral clonidine and oral midazolam.
- To compare the haemodynamic changes following endotracheal extubation in both study drugs.
- To compare the sedative effects of oral midazolam and oral clonidine as preanaesthetic drugs.

ISSN:0975-3583,0976-2833 VOL15,ISSUE06,2024

- To compare the effects of the pre-anaesthetic drugs oral clonidine and oral midazolam in relation to anxiety.
- To compare the incidence of nausea and vomiting in the postoperative period in both study groups.

MATERIALS & METHODS

This was a hospital-based study conducted among 100 patients undergoing elective open abdominal surgery carried out in the General Surgery and Gynaecology OT in the Department of Anaesthesiology of a Tertiary care teaching Hospital over a period of 1 year, after obtaining clearance from the institutional ethics committee and written informed consent from the study participants.

100 patients were randomly divided into 2 groups of 50 each:
Group M(n=50): All patients were received Tablet MIDAZOLAM 7.5mg per orally.
Group C(n=50):All patients were received Tablet CLONIDINE 150 µg (0.15mg**)** per orally.

Inclusion Criteria

All the ASA I & II patient of either sex, age between 25-60 years, weight between 45 kg and 60 kg undergoing elective surgical procedure under general anaesthesia with controlled ventilation by endotracheal tube, duration of surgery ≤ 90 minutes.

Exclusion Criteria

ASA status III or more, history of hypersensitivity, allergy, any neurological, cardiovascular, pulmonary, hepatic, renal, endocrinal or metabolic disorders or bleeding diathesis or contraindication to any of the two study medicines, history of any drug treatment known to affect heart rate, blood pressure or hormonal stress responses.

Study Technique

Patients were given the study drug in powder form in a paper wrap with sips of water, about 60 minutes prior to the induction of anaesthesia. The patients were unaware of the nature of the study drug. Assessment of sedation was done just before the administration of the study drug which was 60 minutes before to the induction anaesthesia. [Time point-1] and just before induction anaesthesia. [Time point-2] using University of Michigan Sedation Scale (0-Awake/Alert,1-Minimally Sedated: Tired/sleepy, appropriate response to verbal conversation and/or sounds, 2- Moderately Sedated: Somnolent/sleeping, easily aroused with light tactile stimulation, 3- Deeply Sedated: Deep sleep, arousable only with significant physical stimulation,4-Unarousable). Assessment of anxiety was also done just before the administration of the study drug [Time point-1] and just before induction anaesthesia. [Time point-2] using Anxiety Score (0- Patient quiet and comfortable,1-Patient uneasy, 2- Patient worried or anxious, 3-Patient very worried or very upset, 4- Patient very frightened or terrified). After preoxygenation for 3 minutes, induction of anaesthesia was done with Inj. Thiopentone Sodium (5mg/kg) and Inj. Fentanyl (2µg/kg). Intubation was facilitated by Inj. Succinyl Choline (1mg/kg). Laryngoscopy and orotracheal intubation were done when adequate jaw relaxation was achieved. Controlled ventilation was instituted by using of Bain's coaxial breathing circuit and Boyle's machine. Maintenance of anaesthesia was done by N_2O:O_2 (60:40). I.V infusion of Propofol @2mg/kg/hour and as per requirement intermittent dose of Vecuronium were given. Inj.Tramadol @ 2mg/kg was given as analgesic agent. At the end of surgery, the patients were adequately reversed with Inj. Neostigmine 50 µg/ kg and Inj. Glycopyrrolate 10 µg /kg intravenously, then the patients were extubated. After oxygenation for about 5 minutes

ISSN:0975-3583,0976-2833 VOL15,ISSUE06,2024

postoperatively patients were sent to the recovery room. Assessment of Pulse rate/heart rate (beats/minute), Systolic, diastolic and mean arterial blood pressure (mm of Hg) was Just before the administration of the any study drug which was 60 minutes before the induction of anaesthesia. [Time point-1], just before induction of anaesthesia. [Time point-2], Just after the orotracheal intubation. [Time point-3], just after extubation [Time point-4],1 hour after extubation. [Time point-5]. Patients were observed during the operation at an interval of 5 min upto 30 min then at an interval of 10 min up to the end of the operation. After the operation patient were observed up to 1 hour.

Statistical Methods

Regular descriptive statistics were used to summarize the data. Both the Mann-Whitney U test and the Student's unpaired t test were used to compare numerical variables between groups. Numerical variables were compared within groups using the Wilcoxon matched pairs signed rank test, repeated measure ANOVA, and Tukey's multiple comparison test. For the intergroup comparison of categorical variables, Fisher's exact test was used. A statistically significant result was considered to be $p<0.05$ in all two-tailed analyses. The following common statistical software was used to examine the data that was entered into a Microsoft Excel database:

1. Statistical Version 6 [Tulsa, Oklahoma: Stat Soft Inc., 2001]
2. Graph Pad Prism version 5 [San Diego, California: Graph Pad Software Inc., 2007]

RESULTS

There was no significant differences in respect to age, sex, body weight distribution among the two groups.

	Time Points				
	SBP-1 (mm of Hg)	**SBP-2 (mm of Hg)**	**SBP-3 (mm of Hg)**	**SBP-4 (mm of Hg)**	**SBP-5 (mm of Hg)**
Range	112-142	110-148	116-160	112-150	106-144
Mean ± SD	127.44 ±8.21	127.16 ±10.50	137.64 ±10.75	134.76 ±9.89	121.32 ±9.30
SE	1.61	1.48	1.52	1.40	1.32
P-Value		NS	**<0.001**	**<0.001**	**<0.001**
(A) : Changes of Systolic Blood Pressure [SBP] in the Group M [Midazolam] Patients (n = 50) of the Present Study					
	Time Points				
	SBP-1 (mm of Hg)	**SBP-2 (mm of Hg)**	**SBP-3 (mm of Hg)**	**SBP-4 (mm of Hg)**	**SBP-5 (mm of Hg)**
Range	118-152	114-148	128-154	126-150	108-140
Mean ± SD	136.44 ±9.47	133.24 ±9.18	144.48 ±8.07	140.92 ±7.15	126.76 ±7.77
SE	1.34	1.30	1.14	1.01	1.10
p value		**<0.001**	**<0.001**	**<0.001**	**<0.001**
(B) : Changes of Systolic Blood Pressure [SBP] in the Group C [Clonidine] Patients (n = 50) of the Present Study					
	Time Points				
	2	**3**	**4**	**5**	
Group M	-0.28	10.20	7.32	-6.28	
Group C	-3.20	8.04	4.48	-9.68	
(C) : Changes [Increase (+) or Decrease (-)] of Mean Systolic Blood Pressure in Comparison to Time point-1[Basal Level]					
Table 1: (A), (B) and (C)					

ISSN:0975-3583,0976-2833 VOL15,ISSUE06,2024

About 60 minutes after the oral midazolam dose [time point-2] for the patients in Group M [midazolam], SBP was nearly the same and this was statistically insignificant. Group M patients showed a rise in SBP after laryngoscopy, intubation and extubation [time points 3 and 4] and it was significantly lower 1 hour after extubation [time point 5]. During the operations, there were no significant changes in SBP from the baseline value.

About 60 minutes after the oral clonidine was administered, patients in Group C [clonidine] experienced a statistically significant decline in SBP [time point 2]. Patients in Group C [clonidine] had a statistically significant rise in SBP after laryngoscopy, intubation and extubation [time points 3 and 4] but a statistically significant reduction occurred 1 hour after extubation [time point 5].

During the operations, there were no significant changes in SBP from the baseline value.

Table C shows a decrease in SBP in Group C and almost unchanged in Group M at time point-2.

It also shows an increase in SBP in both groups at time points 3 and 4, with a maximum in Group M and a minimum in Group C. At time point 5 SBP decreased in both patient group; the maximum decrease was observed in the clonidine group.

C shows changes in mean systolic blood pressure in Group M and C.

The baseline mean of systolic BP in the midazolam group and the clonidine group differs, but they are in the same physiological range

	Time Points				
	DBP-1 (mm of Hg)	**DBP-2 (mm of Hg)**	**DBP-3 (mm of Hg)**	**DBP-4 (mm of Hg)**	**DBP-5 (mm of Hg)**
Range	70-90	72-94	76-98	74-96	68-84
Mean ± SD	80.40 ±5.25	82.16 ±5.74	87.28 ±5.37	85.48 ±4.74	74.92 ±4.02
SE	0.74	0.81	0.76	0.67	0.56
p value		**<0.01**	**<0.001**	**<0.001**	**<0.001**
(A): Changes of Diastolic Blood Pressure [DBP] in the Group M [Midazolam] Patients (n = 50) of the Present Study					
	Time Points				
	DBP-1 (mm of Hg)	**DBP-2 (mm of Hg)**	**DBP-3 (mm of Hg)**	**DBP-4 (mm of Hg)**	**DBP-5 (mm of Hg)**
Range	76-92	70-90	78-94	76-90	68-88
Mean ± SD	85.16 ±4.68	82.04 ±5.12	88.08 ±4.28	84.80 ±3.81	76.12 ±4.52
SE	0.66	0.72	0.60	0.54	0.64
p value		**<0.001**	**<0.001**	NS	**<0.001**
(B): Changes of Diastolic Blood Pressure [DBP] in the Group C [Clonidine] Patients (n = 50) of the Present Study					
	Time Points				
	2	**3**	**4**		**5**
Group M	1.76	6.88	5.08		-5.48
Group C	-3.12	2.92	-0.36		-9.04
(C): Changes [Increase (+) or Decrease (-)] of Mean Diastolic Blood Pressure in Comparison to Time Point-1[Basal Level]					
Table 2: (A),(B),and (C)					

Patients in the midazolam group showed a statistically significant rise in DBP just before induction, after laryngoscopy and intubation and after extubation [time points 2, 3 and 4] there was a statistically significant reduction from baseline at time point 5.

ISSN:0975-3583,0976-2833 VOL15,ISSUE06,2024

Patients in the clonidine group had a statistically significant fall in DBP just before induction [time point 2]. But after laryngoscopy and intubation [time point 3], there was a significant rise in DBP. After extubation, there was almost no change from the basal value [time point 4]. At time point 5, DBP was lower than baseline and statistically significant.

During the operations, there were no significant changes in DBP from the baseline value.
C shows a decrease in DBP in Group C and a little increase in Group M at time point 2.
C also shows an increase in DBP in both groups at time points 3 and 4. At time point 4, there was a rise in DBP in Group M and almost no change from baseline in Group C. At time point 5, SBP decreased in both patient groups; the maximum decrease was observed in the clonidine group.

C shows changes in mean diastolic blood pressure in Groups M and C.

The baseline mean of diastolic BP in the midazolam group and the clonidine group differ, but they are in the same physiological range.

	Time Points				
	MAP-1 (mm of Hg)	**MAP-2 (mm of Hg)**	**MAP-3 (mm of Hg)**	**MAP-4 (mm of Hg)**	**MAP-5 (mm of Hg)**
Range	86.6-107.3	84.6-112	89.3-116.6	86.6-114	80.3-103.3
Mean ± SD	96.02 ±5.42	97.02 ±6.57	103.89 ±6.36	101.85 ±5.66	90.37 ±5.19
SE	0.77	0.93	0.90	0.80	0.73
p value		**<0.001**	**<0.001**	**<0.001**	**<0.001**
(A): Changes of Mean Arterial Pressure [MAP] in the Group M [Midazolam] Patients (n = 50) of the Present Study					
	Time Points				
	MAP-1 (mm of Hg)	**MAP-2 (mm of Hg)**	**MAP-3 (mm of Hg)**	**MAP-4 (mm of Hg)**	**MAP-5 (mm of Hg)**
Range	94-110	89.3-107.3	98.6-114	96.6-108.6	81.3-100.6
Mean ± SD	102.22 ±5.43	99.15 ±7.70	106.85 ±4.81	103.55 ±4.15	92.94 ±5.03
SE	0.77	0.81	0.68	0.59	0.71
p value		**<0.001**	**<0.001**	**<0.05**	**<0.001**
(B): Changes of Mean Arterial Pressure [MAP] in the Group C [Clonidine] Patients (n = 50) of the Present Study					
	Time Points				
	2		**3**	**4**	**5**
Group M	1.00		7.88	5.83	-5.64
Group C	-3.07		4.63	1.32	-9.28
(C): Changes [Increase (+) or Decrease (-)] of Mean of Mean Arterial Pressure in Comparison to Time Point-1[Basal Level]					
Table 3: (A),(B) and (C)					

Patients in the midazolam group had a statistically significant rise in MAP before induction, just after intubation, and just after extubation [time points 2, 3, 4]. They showed a significant reduction in MAP at time point – 5.

During the operations, there were no significant changes in MAP from the baseline value.

Patients in the Clonidine group showed a statistically significant fall in MAP before induction [time point 2]. They showed a significant rise in MAP after intubation and after extubation [time points -3, 4]. There was a significant decrease in MAP at time point 5.

During the operations, there were no significant changes in MAP from the baseline value.

ISSN:0975-3583,0976-2833 VOL15,ISSUE06,2024

C shows a significant decrease in MAP in group C and a significant increase in MAP in group M [time point 2]. There was a significant increase in MAP in both groups at time points 3 and 4. At time point 5, the decrease in MAP in Group C is greater than that in Group M.

Changes in mean arterial pressure in Groups M and C

The baseline mean of the mean arterial BP of the midazolam group and the clonidine group differ, but they are in the same physiological range.

	Time Points				
	PR-1 (beats/min)	**PR-2 (beats/min)**	**PR-3 (beats/min)**	**PR-4 (beats/min)**	**PR-5 (beats/min)**
Range	72-96	76-98	78-102	76-100	70-90
Mean ± SD	81.44 ±6.96	84.96 ±6.12	90.76 ±6.17	88.76 ±5.43	78.20 ±5.65
SE	0.98	0.86	0.87	0.77	0.80
p value		**<0.001**	**<0.001**	**<0.001**	**<0.001**
(A): Changes of Pulse Rate [PR] in the Group M [Midazolam] Patients (n = 50) of the Present Study					
	Time Points				
	PR-1 (beats/min)	**PR-2 (beats/min)**	**PR-3 (beats/min)**	**PR-4 (beats/min)**	**PR-5 (beats/min)**
Range	76-96	72-92	82-102	82-104	70-90
Mean ± SD	85.60 ±4.88	80.68 ±5.34	89.76 ±4.69	89 ±5.05	79.80 ±4.61
SE	0.69	0.76	0.66	0.71	0.65
p value		**<0.001**	**<0.001**	**<0.001**	**<0.001**
(B): Changes of Pulse Rate [PR] in the Group C [Clonidine] Patients (n = 50) of the Present Study					
	Time Points				
	2		**3**	**4**	**5**
Group M	3.52		9.32	7.32	-3.24
Group C	-4.92		4.16	3.40	-5.80
(C)Changes [Increase (+) or Decrease (-)] of Mean of Pulse Rate in Comparison to Time Point-1[Basal Level]					

Table 4: (A),(B),and (C)

Before induction, following laryngoscopy and intubation, and after extubation (time points 2, 3, and 4), patients in group M experienced a significant elevation in heart rate. They were statistically significant increases. At time point 5, there was a considerable decrease in pulse rate.

During the operations, there were no significant changes in pulse rate from the baseline value.

The pulse rate in Group C significantly decreased at time point two, then increased at time points 3 and 4. Time point 5 showed a decrease in pulse rate. All changes in pulse rate were statistically significant.

During the operations, there were no significant changes in pulse rate from the baseline value.

C shows an increase in pulse rate in group M and a decrease in pulse rate in group C at time point 2. At time points 3 and 4, the pulse rate increases in both groups, but more so in Group M. The pulse rate of both groups decreases below the base line at time point 5.

Changes in mean of pulse rate in Groups M and C

The baseline mean of pulse rate in the midazolam group and the clonidine group differs, but they are in the same physiological range.

ISSN:0975-3583,0976-2833 VOL15,ISSUE06,2024

	Time Points	
	SedSco1	**SedSco2**
Range	0 - 2	0 – 3
Mean ± SD	0.18 ± 0.44	1.18 ± 0.87
Median	0	1
SE	0.06	0.12
P value		**<0.001**
(A): Changes of Sedation Score [SedSco] in the Group M [Midazolam] Patients (n = 50) of the Present Study		
	Time Points	
	SedSco1	**SedSco2**
Range	0 - 1	0 – 2
Mean ± SD	0.22 ± 0.42	0.40 ± 0.57
Median	0	0
SE	0.06	0.08
P value		**0.028**
(B): Changes of Sedation Score [SedSco] in the Group C [Clonidine] Patients (n = 50) of the Present Study		
Table 5: (A) and (B)		

At 60 minutes after receiving oral midazolam, patients in the midazolam group were statistically significantly sedated.

Patients in the clonidine group were having statistically significant (but less than midazolam) sedation at 60 minutes after administration of oral clonidine.

	Time Points	
	AnxSco1	**AnxSco2**
Range	0 - 3	0 – 2
Mean ± SD	0.74 ± 0.90	0.26 ± 0.53
Median	1	0
SE	0.13	0.08
P value		**<0.001**
(A): Changes of Anxiety Score [AnxSco] in the Group M [Midazolam] Patients (n = 50) of the Present Study		
	Time Points	
	AnxSco1	**AnxSco2**
Range	0 - 3	0 – 2
Mean ± SD	0.56 ± 0.73	0.40 ± 0.57
Median	0	0
SE	0.10	0.08
P value		**0.025**
(B): Changes of Anxiety Score [AnxSco] in the Group C [Clonidine] Patients (n = 50) of the Present Study		
Table 6: (A) and (B)		

At 60 minutes after receiving oral midazolam, patients in the midazolam group began to exhibit statistically extremely significant anxiolysis.

ISSN:0975-3583,0976-2833 VOL15,ISSUE06,2024

Patients in the clonidine group were having significant anxiolysis (but less than midazolam) at 60 minutes after administration of oral clonidine.

DISCUSSION

In both groups, patients were between 15 and 60 years old. The mean age was 39.32 ± 8.08 in Group M and 39.16 ± 8.10 in Group C. Since their mean ages were similar, the slight difference between them was determined to be statistically unimportant ($p > 0.05$).

Among Group M, 26 were male and 24 were female (M:F = 1.08:1). Among Group C, there were 27 males and 23 females (M:F = 1.17:1).

All of them were in good nutritional status and free from systemic diseases. The mean weight was 53.08 ± 4.60 in Group M and 53.68 ± 40.70 in Group C. Those mean weights also have a very small difference and were found to be statistically insignificant ($p > 0.05$).

Kikuchi K., Konishi A., and Watanabe Y. [1995][12] conducted a study to show the efficacy of oral midazolam as a premedication in adults. They found that there were no remarkable changes in the blood pressure or pulse rate. On the other hand, Ahmed N. Khan FA [1995][13] conducted a study for evaluation of oral midazolam as a pre-medication in day-care surgery in adult Pakistani patients. They found that in premedication with 7.5mg oral midazolam there was a lesser rise in blood pressure and heart rate after laryngoscopy and intubation.

Raval DL and Mehta MK [2002][14] studied the effect of oral clonidine premedication on the attenuation of the hemodynamic response to laryngoscopy and intubation. They showed that Clonidine blunted the hemodynamic responses during laryngoscopy and endotracheal intubation. Again, in their investigation, Das M et al. [2007][15] discovered that clonidine has been demonstrated to lessen perioperative hemodynamic instability. The study's goal was to determine whether oral clonidine premedication is clinically effective at preventing the hemodynamic response associated with pneumoperitoneum. They found that a significant rise in heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were observed following pneumoperitoneum in the placebo group as compared to the clonidine group.

In our investigation, SBP for the patients in group M [midazolam] was nearly identical 60 minutes after midazolam was administered orally [time point 2]. However, it was statistically unimportant ($p > 0.05$). About 60 minutes after receiving oral clonidine, patients in Group C (clonidine) observed a statistically significant decrease in systolic blood pressure (SBP) ($p < 0.00l$). [Time point: 2].

Both groups experienced a peak rise in systolic blood pressure right after the laryngoscopy and orotracheal intubation [time point-3] that was statistically highly significant ($p<0.001$). Group M had a higher increase (10.20 mm of Hg) than Group C (8.04 mm of Hg). Both groups saw a rise in systolic blood pressure right after the extubation [time point 4], which was statistically highly significant ($p < 0.001$). But 1 hour after extubation, there was a fall in SBP below the baseline, and the fall was more in the case of clonidine [time point 5].

Before induction, DBP increased in the case of the midazolam group while it decreased in the case of the clonidine group. "Time Point 2." Following the laryngoscopy and intubation [time point 3], there was a peak rise in diastolic blood pressure (DBP) in both groups. When compared to the baseline value, this rise was highly significant [$p<0.001$] in both groups. In Group M, the peak increase was higher (6.88 mm of Hg), while in Group C, it was lower (2.92 mm of Hg). Nearly no change in DBP from the baseline was seen in the clonidine group immediately after extubation, but the DBP in the midazolam group increased [time point 4]. However, diastolic blood pressure significantly decreased at time point 5 in both groups (with a greater reduction in the clonidine group).

Mean arterial pressure (MAP) significantly decreased in the clonidine group prior to induction, whereas the MAP in the Midazolam group barely changed [time point 2]. Mean arterial pressure (MAP) increased to a high value following laryngoscopy and intubation [time point 3] and following extubation [time point 4]. When compared to the baseline value, this rise

ISSN:0975-3583,0976-2833 VOL15,ISSUE06,2024

was statistically significant in both groups [p < 0.05]. Group M experienced greater peak growth than Group C. This result supports the research by Trevor et al. (2012). The statistically significant mean arterial pressure [MAP] drop was caused by both clonidine and midazolam at one hour following extubation. The fall was also greater in the case of clonidine. [Time point 5].

Prior to induction, the midazolam group's pulse rate (PR) increased while it decreased in the clonidine group. Both have very high statistical significance [time point 2]. After laryngoscopy and orotracheal intubation and after extubation, there was an increase in pulse rate in both groups of patients at time points 3 and 4. When compared to the basal value, this increase was highly significant in both groups (p<0.001). The increase in PR is higher in the midazolam group. 1 hour after extubation, there was a decrease in pulse rate, which was greater in the case of the clonidine group.

Arora A et al. [2014][16] looked at and compared how well midazolam, clonidine, and dexmedetomidine worked when given by mouth to kids for sedation before surgery, how they reacted to being away from their parents, how well they accepted a face mask, and how quickly they recovered. They came to the conclusion that parental separation and mask induction were not as good as midazolam, even though clonidine and dexmedetomidine were good at sedating patients before surgery (>90%). Again, Sahoo S et al. [2013][17] compared oral midazolam and oral clonidine as paediatric premedications. They concluded that under the conditions of this study, oral midazolam is a better medication than clonidine in children in the preoperative period, while clonidine is a better medication postoperatively with the added advantage of palatability, hemodynamic stability, and no significant side effects.

At 60 minutes following the administration of oral midazolam, patients in the midazolam group had statistically significant drowsiness (p < 0.001). Time point -2

60 minutes after the administration of oral Clonidine, it was seen that the sedation of the patients in the clonidine group was significantly less than that of the midazolam group [time point 2]. This finding corroborates with the studies of Sahoo S et al. (2013) and Arora S et al. (2014).

Trevor S et al. [2012][18] compared oral midazolam (0.5 mg/kg) to oral clonidine (4 μg/kg) in terms of sedation and anxiolysis in paediatric patients aged 2 to 12 years. They came to the conclusion that, in the study's settings, oral midazolam is more effective than clonidine as an anxiolytic in the paediatric population. When used as a premedicant during ketamine anaesthesia, clonidine offers an appropriate level of sedation and anxiolysis similar to diazepam (p > 0.1), according to research by Rudra A. et al. (1994).

At 60 minutes following the administration of oral midazolam in our investigation, patients in the midazolam group displayed statistically very significant anxiolysis (p < 0.001). Time point - 2

But at 60 minutes following the administration of oral clonidine [time point-2], patients in the clonidine group experienced less anxiolysis (in comparison to midazolam), which was also statistically significant (p = 0.025). This result supports the research by Trevor S. et al.

Zhao et al. [2005][19] conducted a randomised study to study the effects of clonidine and midazolam on post-operative shivering, nausea, and vomiting in 40 elderly patients undergoing elective surgery under general anaesthesia combined with epidural anaesthesia. They found that clonidine premedication decreased the incidence of shivering and nausea postoperatively. Taheri et al. [2010] studied the effect of oral clonidine premedication on nausea and vomiting after ear surgery. In that study, there was no need for rescue antiemetic medication; during the first 24 hours after anaesthesia, 33% received a placebo and 67% received clonidine (p <0.01).

In our study, out of 50 patients in the midazolam group, 12 (24%) suffered from post-operative nausea and vomiting (PONV) within 1 hour of the post-operative period. Only six (12%) patients in Group C suffered from PONV. So, there is better control of PONV in the case of clonidine. These findings corroborated the studies done by Zhao et al. and Taheri et al.[20]

ISSN:0975-3583,0976-2833 VOL15,ISSUE06,2024

There was never a dramatic decline in mean arterial pressure (MAP) to less than 70 mm Hg that called for medical attention. In none of the cases, the administration of an anticholinergic medication was necessary.

In comparison to oral midazolam, oral clonidine was more effective at reducing heart rate, systolic, diastolic, and mean arterial pressure. Post-operative nausea and vomiting (PONV) control is also better in the case of oral clonidine. But sedation and anxiolysis are better in the case of oral midazolam. It can be concluded that oral clonidine preanaesthetic medicine is better than oral midazolam when all factors are taken into account. The conclusions of Paris, Andrea (2009) are supported by this outcome.

CONCLUSION

When used as premedicants to lessen the cardiovascular reactions to laryngoscopy, intubation, and extubation, oral clonidine outperforms the other medication. Additionally, oral clonidine demonstrated a decrease in the frequency of post-operative nausea and vomiting. Compared to oral clonidine, oral midazolam induced a significant amount of drowsiness and anxiolysis. Bradycardia and hypotension never happened in any of the groups. Therefore, of the two medicines examined in this study, oral clonidine may be considered to be a superior premedication.

REFERENCES

[1] King BD, Harris LC, Griefenstein FF, Elder JD, Dripps RD. Reflex circulatory responses to direct laryngoscopy and endotracheal intubation performed during general anaesthesia. Anaesthesiology 1951;12(5):556-66.
[2] Takeshima K. Nada K, Higachi M. Cardiovascular responses to rapid anaesthetic induction and endotracheal intubation. Anaesth Analg 1964;43(2):201-8.
[3] Forbes A, Dally FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. Br J Anaesth 1970;42(7):618-24
[4] Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Complications related to the pressor response to endotracheal intubation. Anaesthesiology 1977;47(6):524-5.
[5] Joris JL, Hamoir EE, Hartstein GM. Haemodynamic changes and catecholamine release during laparoscopic adrenalectomy for pheochromocytoma. Anaesth Analg 1999;88(1):16-21.
[6] Bukhar SA, Naqash I, Zargar J, Nengroo S, Mir AW. Pressor responses and intraocular pressure changes following insertion of laryngeal mask airway: comparison with tracheal tube insertion. Indian J Anaesth 2003;47(6):473-5.
[7] Segal IS, Jarvis DJ, Duncan SR, White PF, Maze M. Clinical efficacy of oral-transdermal clonidine combinations during the perioperative period. Anaesthesiology 1991;74(2):220-5.
[8] Okuyama K, Inomata S, Toyooka H. The effects of prostaglandin E1 or oral clonidine premedication on blood loss during paranasal sinus surgery. Can J Anaesth 2005;52(5):546-7.
[9] Gordh TE, Tamsen A. A study of the analgesic effect of clonidine in man. Acta Anaesthesiol Scand 1983;27:72
[10] Fazi L, Jantzen EC, Rose JB, Kurth CD, Watcha MF. A comparison of oral clonidine and oral midazolam as preanaesthetic medications in the paediatric tonsillectomy patient. Anaesth Analg 2001;92(1):56-61.
[11] Inomata S, Kihara S, Miyabe M, Sumiya K, Baba Y, Kohda Y, et al. The hypnotic and analgesic effects of oral clonidine during sevoflurane anaesthesia in children: a dose-response study. Anaesth Analg 2002;94(6):1479-83.

ISSN:0975-3583,0976-2833 VOL15,ISSUE06,2024

[12] Kikuchi K, Konishi A, Watanabe Y. Efficacy of oral midazolam as premedication in adult. J Pak Med Assoc 1995;45(9):239-41.
[13] Ahmed N, Khan FA. Evaluation of oral midazolam as premedication in day care surgery in adult Pakistani patients. J Pak Med Assoc 1995;45(9):239.
[14] Raval DL, Mehta MK. Oral clonidine premedication for attenuation of haemodynamic response to laryngoscopy and intubation. Indian J Anaesth 2002;46(2):124-9.
[15] Das M, Ray M, Mukherjee M. Haemodynamic changes during laparoscopic cholecystectomy: effect of clonidine premedication. Indian J Anaesth 2007;51(3):205-10.
[16] Arora S, Saini K, Bhardwaj N. A comparative evaluation of midazolam, clonidine and dexmedetomidine as oral premedicants in children: A double blind randomized clinical trial. Anaesth Pain & Intensive Care 2014;18(4):355-60.
[17] Sahoo S, Kaur M,Tripathy HK, Kumar A, Kohli S, Nanda S. Comparative evaluation of midazolam and clonidine as pediatric oral premedication. Anaesth Essays Res 2013;7(2):221-7.
[18] Trevor S, Upadya M, Sinha C, Kaur M. A comparison of midazolam and clonidine as an oral premedication in pediatric patients. Saudi J Anaesth 2012;6(1):8-11.
[19] Zhao H, Ishiyama T, Oguchi T, Kumazawa T. Effects of clonidine and midazolam on post-operative shivering, nausea and vomiting. Masui 2005;54(11):1253-57.
[20] Taheri A, Javadimanesh MA, Ashraf H. The effect of oral clonidine premedication on nausea and vomiting after ear surgery. Middle East J Anaesth 2010;20(5):691-4.