ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 01 | January - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

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

Anaesthesiology

Shibani Chakraborty Sr. Resident, Anaesthesiology

Sagar Rai PGT, Anaesthesiology

Harpreet Kaur Assistant Professor, Anaesthesiology

Gautam Piplai* Professor, Anaesthesiology. *Corresponding Author

ABSTRACT

Anxiety is common in patients undergoing even minor surgery and it increases as the surgical event approaches. Treating anxiety not only improves patient satisfaction but it also decreases the hospital stay and offers good recovery. It decreases the surgical stress response, incidences of post-operative nausea and vomiting. The most commonly used agents for anxiolysis in Premedication are Benzodiazepines and Alpha 2 agonists. This study is a double blinded comparison of oral Midazolam and Clonidine as anxiolytic and sedative agent for general anaesthesia in elective open abdominal surgery. Laryngoscopy and intubation cause intense sympatho-adrenal stimulation resulting in tachycardia, rise of systolic BP, diastolic BP, Mean Arterial Blood Pressure, decrease in coronary perfusion due to decrease in diastole duration, increase in various cardiac dysrhythmias. In cardiac compromised patients this stress reaction may result in myocardial infarction and heart failure. Also there is a chance of bleeding in brain following rupture of any pre-existing cerebral aneurysm. The multi modal approach of GA encompasses use of anti-anxiety medication, opioids, volatile anaesthetics, local anaesthetics (locally , intravenously, regionally), vasodilators, CCB, Beta 1 adrenoceptor blocker, Alpha 2 adrenoceptor agonists, in combination, with varying degrees of success. METHOD: In this randomized prospective double blinded comparative study 80 patients were randomly divided into 2 groups namely Group M and Group C. Group M received Tablet Midazolam 7.5 mg while Group C received Tablet Clonidine 150 mcg, given orally, preoperatively 90 minutes before induction. Group M showed better sedation after induction, however, Group C showed better hemodynamic stability therefore had better attenuation of sympatho-adrenal response. Conclusion: Considering all parameters, it was observed that Group C was significantly more efficacious in attenuation of sympatho-adrenal response whereas Group M showed significantly better sedation.

KEYWORDS

midazolam, clonidine, sympatho-adrenal response, sedation score, comparative study, premedication.

INTRODUCTION

Laryngoscopy and intubation cause profound haemodynamic changes in patients' body. These changes include increase in heart rate, rise in SBP, DBP, MAP .[1, 2, 3] These changes occur as a result of sympatho-adrenal stimulation [4] and can have immense adverse effects in patients with compromised heart e.g. IHD, Hypertension. [5]

Balanced anaesthetic approach was adopted to attenuate the sympatho-adrenal stimulation during laryngoscopy and intubation. 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 the use of oral clonidine and midazolam as premedication to mitigate the effect of these changes. [6, 7]

Oral clonidine, the prototypical alpha 2 agonist has been successfully used to reduce the intraoperative blood loss [8, 9, 10] as well as the anaesthetic and analgesic requirements. Oral midazolam, which works by facilitating GABA action in CNS, has also been a popular choice because of good anxiolysis, sedation, anterograde amnesia and anticonvulsant effect. [9]

Oral administration has been preferred over injectable drug because it causes less anxiety. [11]

We undertook this study to compare the effects and variations in haemodynamic parameters that take place upon using these two drugs and thereby to determine the better option between the two.

MATERIAL AND METHODS

The aim of our study was to compare the two drugs in relation to changes in HR, SBP, DBP, and MAP after intubation and following extubation. We also compared sedation score. The study design was a double blinded prospective randomized comparative study.

After obtaining institutional ethics committee approval and patient consent, a total of 80 patients were randomly allocated into two groups of 40 each, using computer generated numbers. The patients included in the study were those: of age 18 to 45 years, ASA I, Mallampati score 1 and 2, body weight 45 to 60 kg, scheduled to undergo elective abdominal surgery of approximately 90 minutes duration, under GA, were assessed in this study.

The exclusion criteria are any criteria more than inclusion criteria; to mention especially pregnancy, patient taking multiple medicines for comorbidities like cardio respiratory diseases, hypertension and coagulation disorder, psychiatric illness, chronic alcoholics, heavy smokers, patients on beta blocker treatment, known allergy to midazolam or clonidine.

Group M (n= 40) received tablet midazolam (Mezolam) 7.5 mg orally. Group C (n=40) received tablet clonidine (Catapres) 150 mcg.

A thorough preanaesthetic check-up was done and routine informed risk consent was taken. Fasting for 6 hours before surgery was suggested. On the day of surgery, 90 minutes before induction patients were given tablet midazolam 7.5 mg for Group M and tablet clonidine 150 mcg for Group C.

On the OT table a 20G i.v. cannula was secured and Ringer Lactate infusion was started. Multi-channel monitors were attached to periodically record HR, SBP, DBP, MAP, SpO2, EtCO2 at 3 minute intervals. Patient was induced with Inj. Propofol and intubated after giving Inj. Succinylcholine. Inj. Fentanyl citrate was given as analgesic. After bolus dose of Inj. Vecuronium 4 mg, maintenance was done on TOF guided further incremental doses, oxygen 30 % and nitrous oxide 70 % and volatile anaesthetic Isoflurane guided by haemodynamic parameters. Isoflurane was stopped 10 minutes before skin closure. After surgery, the patients were given TOF guided reversal containing Inj. Neostigmine plus Inj. Glycopyrrolate and were extubated after proper suction. Patients were observed on OT table for 5 minutes with oxygen inhalation and then sent to PACU. Any adverse events were managed appropriately.

The parameters studied were:

1. Demographic variables (Age, Sex, Body Weight)
2. Sedation score
3. Haemodynamic parameters by non-invasive methods (HR, SBP, DBP, MAP)

To assess sedation, Rating Scale of Sedation Intensity was used [12]

1. No Sedation, Patient awake.
2. Moderate Sedation. Patient drowsy, immediate reaction to speech.
3. Marked sedation. Patient asleep, no reaction to speech but

immediate reaction to tactile stimuli.
4. Strong sedation. Reaction only to stronger to tactile stimuli.
5. Somnolent. Difficult to arouse, immediately falling asleep again.

The recorded values taken into consideration were as follows:

- Reading_0 (Variable_0): Recorded just before administrations of the study drug which was 90 minutes before the induction of anaesthesia. (Baseline value.)
- Reading_1: Immediately before the induction of anaesthesia.
- Reading_2: Immediately after the oro-tracheal intubation and fixation of tube
- Reading_3: 10 minutes after intubation
- Reading_4, 5, 6: Every 10 minutes after that.
- Reading_7: Just after the oro-tracheal extubation.

Statistical analysis was done using Pearson's Chi square test, Fisher's Exact test as appropriate, continuous variables like mean and standard deviation using Mann-Whitney U Test. SPSS version 20 was used for analysis. P value <0.05 was considered as significant.

RESULT

Total 80 patients were studied. The following tables represent the findings.

Table 1: Demographic parameters

Demographic data	Group M	Group C	P value
Age (years)	41.45 ± 7.86	38.93 ± 7.54	0.167
Sex- M/F	21/19	22/18	0.823
Height (cm)	167.95 ± 9.21	166.83 ± 8.80	0.398
Weight (kg)	52.65 ± 4.92	53.23 ± 4.77	0.555
P value shows no significant variation in these parameters.			

Table 2: Heart Rate

	Group M	Group C		
	Mean ± Std. Deviation	Mean± Std. Deviation	p Value	Significance
HR_0	91.18±8.83	94.05± 6.14	0.125	Not Significant
HR_1	86.28± 5.55	75.33± 4.55	<0.001	Significant
HR_2	89.18± 5.55	77.05± 4.80	<0.001	Significant
HR_3	91.18± 5.98	69.20± 3.67	<0.001	Significant
HR_4	78.68± 5.35	65.40± 4.28	<0.001	Significant
HR_5	81.30± 5.14	65.55± 4.85	<0.001	Significant
HR_6	88.15± 3.69	67.95± 4.16	<0.001	Significant
HR_7	100.20± 4.59	84.70± 3.86	<0.001	Significant

Table 2 shows, When the preoperative baseline Heart Rate was compared between two groups (HR_0) no statistically significant difference was found (p value >0.05). The Heart Rate after laryngoscopy & intubation was significantly lower in clonidine compared to midazolam. The Heart Rate just after extubation was also lower in clonidine group.

Table 3: Systolic Blood Pressure (SBP)

Systolic Blood Pressure	Midazolam	Clonidine		
	Mean± Std. Deviation	Mean± Std. Deviation	p Value	**Significance**
SBP_0	133.20± 8.78	136.60± 7.91	0.089	Not Significant
SBP_1	131.35± 8.50	127.30± 6.74	0.034	Significant
SBP_2	134.45± 9.12	131.10± 6.50	0.045	Significant
SBP_3	138.55± 10.75	134.30± 3.94	0.029	Significant
SBP_4	135.53± 9.61	130.85± 4.07	0.015	Significant
SBP_5	134.45± 7.31	127.85± 2.91	<0.001	Significant
SBP_6	133.90± 6.82	127.40± 4.08	<0.001	Significant
SBP_7	139.30± 7.01	135.20± 2.16	<0.001	Significant

Table 3: it was observed that when the preoperative baseline SBP was compared between two groups, no statistically significant difference was found (p value >.05). The SBP after laryngoscopy & intubation showed less variation in clonidine group. The SBP just after extubation was also stable in clonidine group.

Table 4: Diastolic Blood Pressure (DBP)

Diastolic Blood Pressure	Midazolam	Clonidine		
	Mean± Std. Deviation	Mean± Std. Deviation	p Value	Significance
DBP_0	83.85± 4.84	83.30± 4.06	0.617	Not Significant
DBP_1	80.95± 5.34	77.05± 3.68	<0.001	Significant
DBP_2	85.15± 5.43	81.05± 3.79	0.001	Significant
DBP_3	87.45± 5.42	81.40± 3.36	<0.001	Significant
DBP_4	85.75± 4.84	80.50± 3.03	<0.001	Significant
DBP_5	80.65± 4.63	77.55± 2.29	<0.001	Significant
DBP_6	78.25± 4.69	75.15± 3.53	0.001	Significant
DBP_7	83.10± 3.39	80.95± 3.68	0.006	Significant

Table 4: It was observed that when the preoperative baseline DBP was compared between two groups, no statistically significant difference was found (p value >0.05). The DBP after laryngoscopy & intubation showed less variation in clonidine group. The DBP just after extubation were also stable in clonidine group.

Table 5: Mean Arterial Pressure (MAP)

Mean Arterial Pressure	Midazolam	Clonidine		
	Mean± Std. Deviation	Mean± Std. Deviation	p Value	Significance
MAP_0	100.33± 5.57	101.03± 4.38	0.521	Not Significant
MAP_1	97.73± 5.48	93.78± 3.87	0.002	Significant
MAP_2	101.58± 5.90	97.68± 3.87	0.001	Significant
MAP_3	104.45± 6.51	99.00± 2.95	<0.001	Significant
MAP_4	102.30± 5.45	97.30± 2.76	<0.001	Significant
MAP_5	98.55± 4.64	94.38± 1.64	<0.001	Significant
MAP_6	96.78± 4.09	92.48± 3.09	<0.001	Significant
MAP_7	101.85± 3.29	99.03± 2.84	<0.001	Significant

Table 5: It was observed that when the preoperative baseline MAP was compared between two groups, no statistically significant difference was found (p value >0.05). The MAP after intubation showed less variation in clonidine group compared to midazolam. The MAP just after extubation was stable in clonidine group.

Table 6: Sedation Score

	Drug		Total		
Sedation Score after 90 minutes of administration.	Midazolam	Clonidine		p Value	Significance
1	19 (47.50%)	34 (85%)	53 (66.25%)	0.00362	Significant
2	19 (47.50%)	6 (15%)	25 (31.25%)	0.00024	Significant
3	2 (5%)	0 (0%)	2 (2.5%)	0.0455	Significant
Total	40 (100%)	40 (100%)	80 (100%)		

Table 6: It was observed that patients in midazolam group showed significant difference in sedation score 2.

DISCUSSION

Laryngoscopy and endotracheal intubation has become the mainstay of modern anaesthesia because of its many advantages, however, it causes profound changes in hemodynamics due to sympatho-adrenal stimulation. [13] This stimulation causes rapid surge in blood pressure and heart rate which may precipitate many co-morbidities. It is also common to have fear associated with surgery which leads to anxiety before surgery which in turn increases heart rate and blood pressure.

To alleviate these changes and relieve anxiety it is prevalent practice to give some form of premedication which would alleviate anxiety and attenuate sympatho-adrenal response of endotracheal intubation. Oral medication like midazolam and clonidine is commonly used. It has been seen that clonidine is better at maintaining haemodynamic stability. [14] Oral route is chosen as it causes less anxiety compared to injection and has better acceptance. [15]

Use of premedication not only relieves pre-operative anxiety but also provides better intraoperative circumstances and better post-operative outcome. Patients already suffering from diseases like IHD and Stroke can have adverse outcome if hemodynamic surge is not well controlled.

We observed that sedation was better with midazolam (p value <0.05). In terms of maintaining hemodynamic stability it was seen that clonidine was significantly better than midazolam (p value<0.05). However it should be noted that clonidine also provides sedation.

Considering all parameters it can be said that pre anaesthetic medication with oral clonidine is superior to oral midazolam. This result supports the findings of Paris, Andrea [13]

LIMITATION

Only two drugs have been taken into consideration for this study to compare the attenuation of sympatho-adrenal response, however, there are many drugs available for this purpose. Optimum dose of the drugs should be found after research work so as to administer them with minimum side effects but maximal cardiovascular stability. Effects of inhalational agents on intra operative hemodynamic parameters may vary between patients. Anxiety score has been omitted as we found no significant difference.

Conflict Of Interest: None
Funding: Nil
Ethical Approval: Approved by institutional ethics committee.

CONCLUSIONS

So to conclude we observed that midazolam had better sedation property however clonidine provided better hemodynamic stability.

REFERENCES:

1. Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Complications related to the pressor response to endotracheal intubation. Anesthesiology 1977; 47: 524-25
2. Okuyama K, Inomata S, Toyooka H: The effects of prostaglandin E1 or oral clonidine premedication on blood loss during paranasal sinus surgery. *Can J Anesth* 2005; 52: 546-7
3. Takeshima K. Nada K, Higachi M. Cardiovascular responses to rapid anaesthetic induction and endotracheal intubation. AnesthAnalg 1964; 43: 203
4. Forbes A, Dally FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. Br J Anaesth 1970; 42:618-24
5. King BD, Harris LC, Griefenstein FF et al. Reflex circulatory responses to direct laryngoscopy and endotracheal intubation performed during general anaesthesia. Anesthesiology 1951; 12: 556-66
6. Goel L, Dukle N V . A comparison of oral clonidine versus oral midazolam as premedication in adults .Indian Journal of Clinical Anaesthesia. 2017 ; 4(2);188-192
7. Kikuchi K, Konishi A, Watanabe Y. Efficacy of oral midazolam as premedication in adult. PMID: 7837398 [Pub Med - indexed for MEDLINE] J Pak Med Assoc. 1995 Sep; 45 (9): 239-41
8. Frank T, Thieme V, Radow L. Premedication in maxillofacial surgery under total intravenous anaesthesia. Effects of clonidine compared to midazolam on the perioperative course. Anaesthesiol Intensive med Notfallmed Schmerzther 2000; 35: 428- 434
9. Fazi L, Jantzen EC, Rose JB, et al: A comparison of oral clonidine and oral midazolam as preanesthetic medications in the paediatric tonsillectomy patient. AnesthAnalg 2001; 92:56
10. Raval DL, Mehta MK. Oral clonidine premedication for attenuation of haemodynamic response to laryngoscopy and intubation. Indian J Anaesth. 2002; 46(2): 124-129.
11. Comparison of oral and intramuscular preanesthetic medication for pediatric inpatient surgery S C Nicolson et al. Anesthesiology. 1989 Jul. 1989 Jul;71(1):8-10
12. H Heine, J Weindler, H H W Gabriel, W Kindermann, and K W Ruprecht Br J Ophthalmol. 2003 Aug; 87(8): 1020–1024
13. Russel WJ, Morris RG, et al. changes in plasma catecholamine concentrations during endotracheal intubation. Br J Anaesth 1981; 53: 837-79.
14. Paris, Andrea. Effects of clonidine and midazolam premedication on bispectral index and recovery after elective surgery. European Journal of Anaesthesiology: 2009 - Volume 26 - Issue 7 p 603-610
15. Bansal R, Khan Joad AS, Saxena M, Hemrajani M. Oral midazolam is a safe and effective premedication in adult outpatients undergoing brachytherapy for cancer cervix under general anaesthesia: A prospective randomised, double blind placebo-controlled study. Indian J Anaesth. 2015;59(7):437-439. doi:10.4103/0019-5049.160955