

Efficacy of Oral Clonidine Versus Oral Midazolam as Premedication Among Adults: A Comparative Study

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Abstract:

Background: Premedication is a vital step before giving anaesthesia to any patient. They are used to provide pain relief, sedation, anxiolysis and muscle relaxation. Midazolam is a benzodiazepine with a short duration of action. Clonidine is an alpha-2 agonist that causes a decrease in anaesthetic and analgesic requirements, apart from producing sedation, haemodynamic stability, anti-sialogogue effect. In the view of less studies in the Indian context, the current study was undertaken.

Aim: To compare the efficacy of oral premedication with 200mcg of clonidine versus 15mg of midazolam regarding sedation, and reduction in haemodynamic response to intubation among adults undergoing general anaesthesia.

Materials and Methods: The current study was done on 50 patients belonging to American Society of Anaesthesiologists (ASA) grade I, II under general anaesthesia at our tertiary care center named NRI Medical College and Hospital from August 2022 to January 2023. Patients aged above 18 years of either gender who provided informed consent to participate in the study were included. They were divided into two groups (C and M), each group containing 25 patients by randomization.

Results: Most of the patients were aged 51 to 60 years. Most of the patients were females. Most of the patients belonged to ASA grade I. Sedation score was significantly more in M group patients. Antisialagogue effect was significantly more in C group patients. Mean VAS score was significantly less in M group patients. Heart rate was significantly less in C group patients. There is no significant difference in the mean arterial pressure between two groups. Hypotension is the most common adverse effect seen.

Conclusion: Our study results provided oral midazolam acts as a better pre-anaesthetic medication compared to oral clonidine among adults scheduled for various surgeries under general anaesthesia.

Key Words: Comparative study, Clonidine, Midazolam, Premedication, Adults

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I. Introduction

Premedication is a vital step before giving anaesthesia to any patient. They are used to provide pain relief, sedation, anxiolysis and muscle relaxation. Midazolam is a benzodiazepine, with a short duration of action. It causes muscle relaxation, anxiolysis and amnesia in lower doses and sedation, hypnosis at higher doses. Intravenous midazolam helps in the induction of anaesthesia and in the treatment of acute seizures. Due to its water-soluble nature, it has a rapid onset of action and can help to manage status epilepticus when IV administration of other medications is not feasible. The response to induction dose is more variable compared to thiopentone. It is superior to thiopentone in the maintenance of anaesthesia due to less requirement for adjunct drugs. It is an adjunct medication to regional and local anaesthesia for various diagnostic and therapeutic procedures with greater physician and patient acceptance.¹⁻³ The mechanism of action is related to an increase in the inhibitory neurotransmitter named GABA and its affinity to benzodiazepine receptors. It increases the frequency of opening of chloride channels. This leads to membrane hyperpolarization and neuronal inhibition. Muscle relaxation effect is due to its action on glycine receptors. Hepatic and renal insufficiency may also affect pharmacokinetics of midazolam.⁴⁻⁷

Clonidine is an alpha-2 agonist that causes a decrease in anaesthetic and analgesic requirements, sedation, haemodynamic stability, and antisialogogue effect.

Clonidine is approved for treating hypertension, attention deficit hyperactivity disorder (ADHD), Tourette syndrome, adjunct therapy for cancer-related pain and opioid withdrawal syndrome.⁸⁻¹¹ In view of less studies in Indian context, the current study was undertaken.

Aim:

To compare the efficacy of oral premedication with 200mcg of clonidine versus 15mg of midazolam regarding sedation, and reduction in haemodynamic response to intubation among adults undergoing general anaesthesia for various surgeries.

Material And Methods

This study was carried out at a tertiary care centre in India from August 2022 to January 2023.

Study Design: Randomized, interventional, single-centred study.

Study Location: This study was done at a tertiary care teaching institute in the Department of anaesthesia at NRI medical college and Hospital, Mangalagiri, Guntur, Andhra Pradesh, India.

Study Duration: August 2022 to January 2023

Sample size: 50 patients

Sample size calculation: Sample size was calculated based on the pilot study done at our tertiary care center, the prevalence of surgeries under general anaesthesia was around 10%. At confidence intervals of 75%, with an error of 5%, the minimum sample size came to be 48. Hence, we included 50 subjects in our study.

Subjects & selection method:

The study included 50 patients who were scheduled for various surgeries under general anaesthesia at our tertiary care center.

Patients were randomized by computer-generated software into groups C and M.

Group C: 25 patients received oral clonidine 200mcg as premedication 90min before surgery.

Group M: 25 patients received oral midazolam 15mg as premedication 90 min before surgery.

Eligibility criteria:

Inclusion criteria:

1. Patients aged above 18 years of either gender, posted for elective surgeries under general anaesthesia.
2. Patients who provided informed consent to participate in the study.
3. Patients with ASA grade I, II.

Exclusion criteria:

1. Pregnant and lactating women
2. Patients with BMI above 30 kg/m².
3. Patients with Hypertension
4. Patients with hepatic, cardiac, pulmonary and renal dysfunction
5. Patients with bradycardia
6. Patients with psychiatric disorders.
7. Patients with known allergies to midazolam or clonidine

II. Methodology:

After complete preanesthetic assessment, vitals like heart rate, mean arterial pressure and oxygen saturation were recorded at baseline before premedication in surgery room for all the patients. Pulse oximeter, ECG, non-invasive BP monitoring were attached. IV access was secured using 18gauge IV cannula. All patients were given ondansetron 4mg by intravenous route. Patients were preoxygenated using 100% oxygen for five minutes. Induction was done using IV thiopentone sodium 2.5%. Patients given 60% nitrous oxide and 40% oxygen for 3 min.

Muscle relaxation was maintained using IV vecuronium. For analgesia, IV fentanyl was used. Iv paracetamol infusion was given towards the end of surgery. Neuromuscular blockade was reversed with IV neostigmine.

Patients were monitored for side effects like bradycardia, hypotension, dysrhythmias, respiratory depression and grade 5 sedation.

Parameters assessed:

Age

Gender

ASA grade

Sedation score

Heart rate

Mean arterial pressure

Mean VAS score- anxiolytic effect

Antisialagogue effect

Side effects

Anxiolytic effect was assessed using 11-point Visual Analog Scale (VAS).¹²

Sedative effect was assessed using a five-point sedation score:¹³

Grade 1-awake; grade

Grade 2-drowsy but easily arousable to alert state by oral commands;

Grade 3- asleep, no reaction to speech but immediate reaction to tactile stimuli;

Grade 4- reaction only to stronger tactile stimuli;

Grade 5- difficulty in arousing patient immediately falling asleep again.

Antisialagogue effect was assessed by knowing oral secretions and graded as normal secretions or dry mouth for all patients.

Statistical analysis:

Data was analyzed using SPSS software version 25.0. Results were expressed as percentages and mean with standard deviation. Numerical values between the two groups were compared using student t test and categorical parameters using chi-square analysis. P value below 0.05 is considered significant statistically.

Ethical considerations:

Informed consent was taken from every patient participated in the study.

III. Results

The current study included 50 patients scheduled for elective surgeries under general anaesthesia.

Age distribution:

Most of the patients were aged 51 to 60 years.

Table 1 shows age distribution of patients

Age distribution	Group M	Group C
8-30 years	7	6
31-40 years	4	7
41-50 years	5	3
51 -60 years	7	10
Above 60 years	1	0

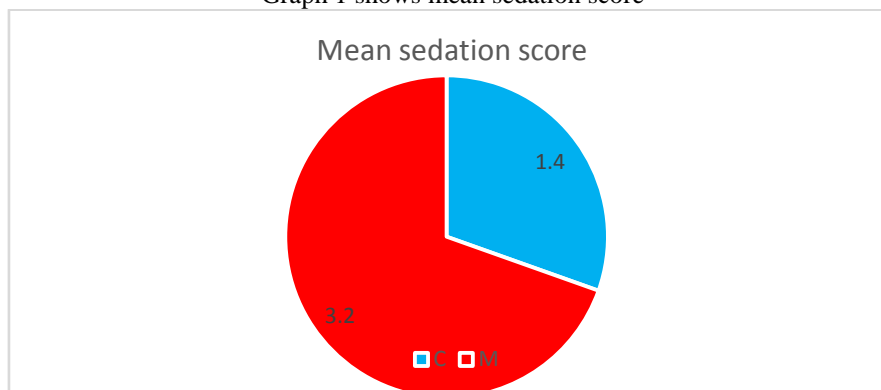
Gender distribution: Most of the patients were females in the current study (58%).

ASA Grade: Most of the patients belonged to ASA grade I(64%) in this study.

Mean sedation score:

There is significant difference in the mean sedation score between two groups of patients(p=0.001). It was more in Midazolam group patients.

Graph 1 shows mean sedation score



Heart rate:

Heart rate was significantly less in group C patients compared to group M patients after induction and intubation.

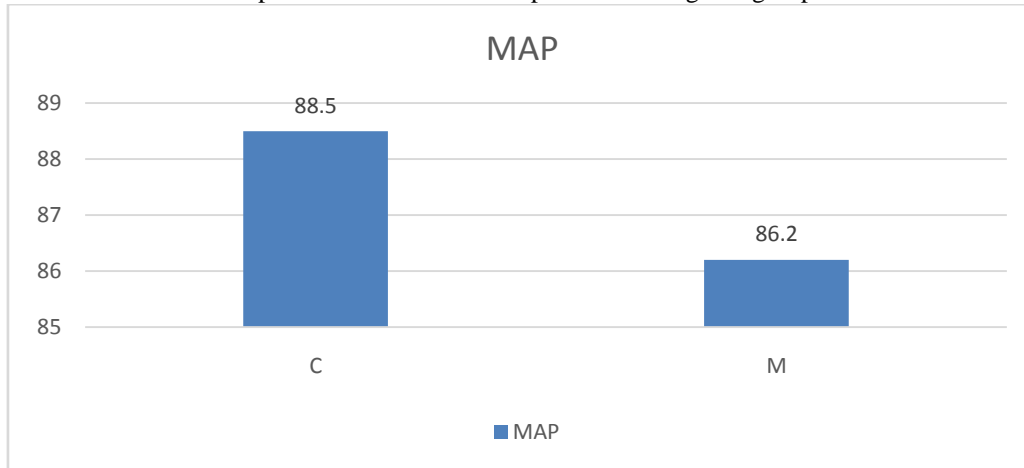
Table 2 shows heart rate after induction and after intubation among two groups

Heart rate	Group C	Group M	P value
After induction	68±5.2	78±7.1	0.0001
After intubation	66±5.9	77±4.8	0.0001

Mean arterial pressure:

There was no significant difference in the mean arterial pressure in between two groups($p>0.05$).

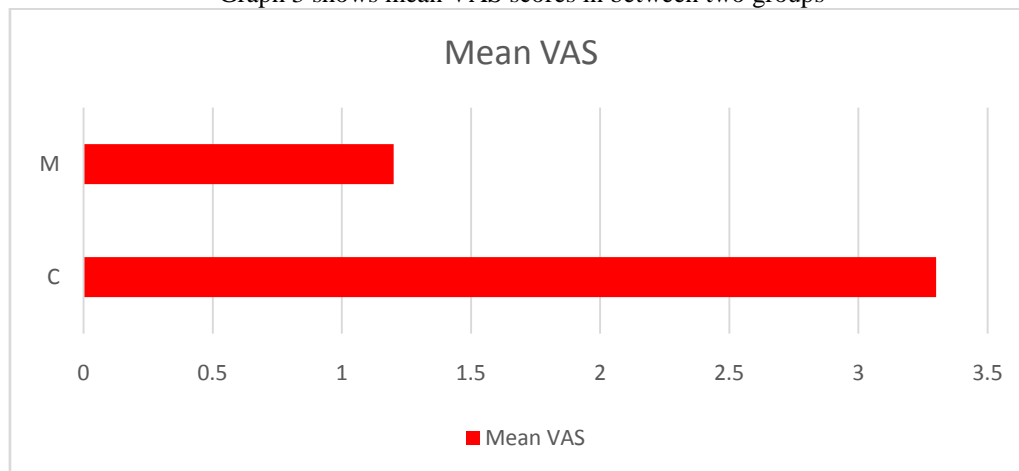
Graph 2 shows mean arterial pressure among two groups



Mean VAS score:

Mean VAS score was significantly more in M group patients($p=0.001$) during 6hrs of postoperative period.

Graph 3 shows mean VAS scores in between two groups



Antisialagogue effect:

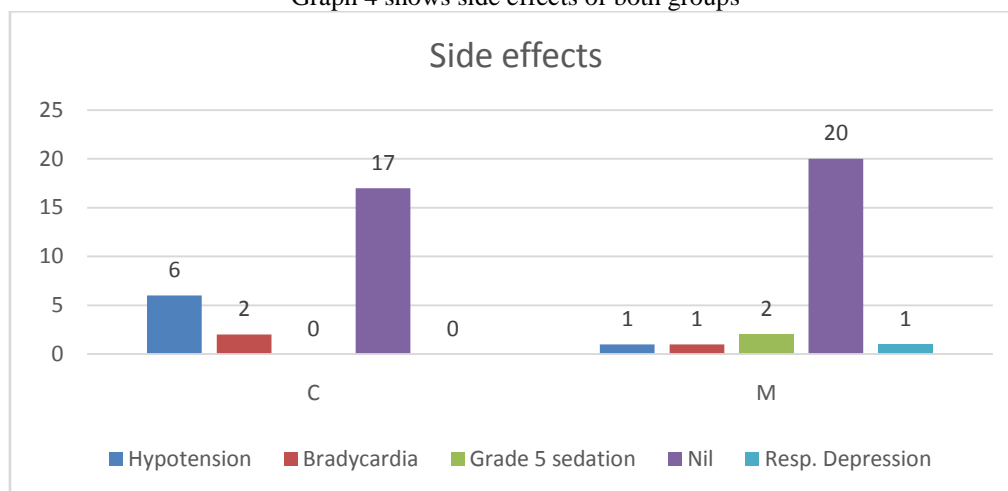
64% of patients in C group had dry mouth and only 4% of patients in M group had dry mouth. There is significant difference in the presence of anti sialagogue effect between two groups.

Table 3 shows anti-sialagogue effect

Dry mouth	Group M	Group C	P value
Yes	1	16	0.0001
No	24	9	

Side effects: Hypotension was the major side effect, which was seen mainly in C group patients.

Graph 4 shows side effects of both groups



IV. Discussion

The current study was done on 50 patients belonging to American Society of Anaesthesiologists (ASA) grade I, II, posted for various surgeries under general anaesthesia at our tertiary care center. Results showed that most of the patients were aged 51 to 60 years. Most of the patients were females. Most of the patients belonged to ASA grade I. Sedation score was significantly more in M group patients. Antisialagogue effect was significantly more in C group patients. Mean VAS score was significantly less in M group patients. Heart rate was significantly less in C group patients. There is no significant difference in the mean arterial pressure between two groups. Hypotension is the most common adverse effect seen in our study.

Trevor et al.¹⁴ did a study on sixty patients belonging to the ASA grade I and II scheduled for elective surgery. Patients were randomized to receive either oral midazolam or oral clonidine. Results showed that after premedication, % of patients who were sedated and calm raised on both the groups. Overall level of sedation was found to be better among patients in the clonidine group, in contrast to our study findings. Clonidine showed a fall in blood pressure, similar to our study.

Sahoo et al.¹⁵ did a study on 60 children of ASA physical status I, aged 2 to 12 years, who were scheduled for various elective surgeries. Children received either midazolam or clonidine before induction of anaesthesia. Results showed that oral midazolam to have better efficacy in the as a sedative and anxiolytic, similar to our study. Oral clonidine showed better hemodynamic stability, in contrast to our study findings.

Zickerman et al.¹⁶ concluded that there is no significant difference in the anxiety scale between midazolam and clonidine.

Studies done on children aged below two years showed clonidine to cause bradycardia.¹⁷ Doses of midazolam and clonidine used in our study were established as per the optimal pediatric pre-anesthetic sedation doses.¹⁸⁻¹⁹ Novel commercially prepared oral midazolam formulations are more palatable are not yet available in our center.

Finally, midazolam premedication resulted in a better suppression of anxiety. *Almenrader et al.*, and *Tazeroualti et al.*,²⁰⁻²¹ concluded that midazolam was less effective in producing more sedation compared to clonidine. *Lavrich et al.*, and *Frank et al.*²²⁻²³ found similar levels of sedation due to clonidine and midazolam.

V. Conclusion

Our study results provided oral midazolam acts as a better preanaesthetic medication compared to oral clonidine among adults scheduled for various surgeries under general anaesthesia.

The study is self-sponsored. There were no conflicts of interest.

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