

**COMPARISON OF ORAL CLONIDINE AND ORAL MIDAZOLAM AS PRE-MEDICATION FOR PEDIATRIC SURGERY IN CHILDREN**KARISHMA DHALWANI<sup>1\*</sup>, PALLAVI JAIN<sup>2</sup>, SURUCHI SIKARWAR<sup>3</sup>, DEEPTI SAXENA<sup>2</sup>

<sup>1</sup>Department of Anaesthesia, Maa Vindhyavasini Autonomous State Medical College, Mirzapur, Uttar Pradesh, India. <sup>2</sup>Department of Anaesthesia, MGM Medical College, Indore, Madhya Pradesh, India. <sup>3</sup>Department of Anaesthesia, Medanata Hospital, Gurgaon, Haryana, India.

\*Corresponding author: Dr. Karishma Dhalwani; Email: dhalwanikarishma@gmail.com

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**ABSTRACT**

**Objectives:** The objectives of the study are to compare the efficacy and safety of oral midazolam (0.5 mg/kg) and oral clonidine (3 µg/kg) as pre-medication in pediatric age children undergoing surgical intervention.

**Methods:** The present study was conducted at the Department of Anesthesiology and Critical Medicine, Sri Aurobindo Medical College and Postgraduate Institute, Indore (M.P.). We had included 60 children undergoing pediatric surgical intervention during the study period of 1-1/2 years of age 2-10 years. These children were randomized to receive either midazolam or clonidine. After obtaining consent from the parents, these children were included in the study. Pediatric separation anxiety score (PSAP) was used for the assessment of anxiety and mask acceptance scale was used for the assessment of mask acceptance. Comparison of means between the two groups was done using unpaired "t" test, and association between two non-parametric variables was done using Pearson Chi-square test. A p<0.05 was taken as statistically significant.

**Results:** The mean age in midazolam group was 5.50±3.18 years and in clonidine group was 5.56±4.44 years. The mean age was comparable between the two groups (p=0.954). In both groups, there was male predominance. Mask acceptance was also better in clonidine group compared to midazolam group (p=0.001). Sedation was more in clonidine group compared to midazolam group, but it was not statistically significant (p=0.136). Wake-up behaviors of the patients were comparable between the two groups (p=0.777). The hemodynamics were comparable between the two groups at majority of the time intervals (p>0.05). We found clonidine to be better in comparison to midazolam in providing sedation and patients were easily consolable compared to midazolam group patients.

**Conclusion:** We conclude that clonidine as a pre-medication in patients undergoing pediatric surgical intervention is better as compared to midazolam with slightly higher sedation in clonidine group. We recommend the use of clonidine as a pre-medication in patients undergoing pediatric surgical intervention.

**Keywords:** Clonidine, Midazolam, Pre-medication, Pediatric surgery, Mask acceptance scale, PSAP.

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**INTRODUCTION**

Children undergoing surgical procedures can experience significant anxiety and distress during the perioperative period [1]. Children are prone to significant stress and anxiety due to hospitalization and surgery. Of all the procedures to be conducted on them during hospitalization, induction of anesthesia is the most distressing one [2]. Age is found to be one of the major factors that interfere in the occurrence of anxiety in the pre-operative period [3]. The use of sedative pre-medication may help to reduce anxiety, minimize emotional trauma, and facilitate a smooth induction of anesthesia for surgery [4]. Midazolam is most commonly used as a pre-medication agent in children. Clonidine is a central sympatholytic that provides sedation, anxiolysis, and analgesic effects without causing respiratory depression [5]. Hence, in this study, we made an effort to compare oral clonidine and oral midazolam for pre-medication in pediatric patients undergoing surgeries. Hence, this study was conducted with the aim to compare the efficacy of oral clonidine (3 µg/kg) and oral midazolam (0.5 mg/kg) for pre-medication in pediatric age group undergoing surgery.

**METHODS**

This study was undertaken in the Department of Anaesthesiology and Critical Care, Sri Aurobindo Medical College and PG Institute, after valid approval of ethics committee of the institution on 60 pediatric patients of either sex scheduled to undergo surgery. Pediatric patients having

age between 2 and 10 years of either sex belonging to American Society of Anesthesiology (ASA) grade I and II and patients posted for pediatric surgery under general anesthesia and those patients' parents/guardians giving consent for getting included in the study were included in the present study. Patients belonging to ASA grades III and IV and patient's parent refusal, patients with a known history of hypersensitivity or contraindications to clonidine or midazolam, patients of age <2 years and >10 years, patients with history of nausea, vomiting, or retching 24 h before anesthesia, and patients with active infection or history of motion sickness were excluded from the present study. Pre-anesthetic checkup was done for all patients before the procedure as routine. Informed consent was taken from the relatives/guardians explaining them the whole procedure and the aim behind conducting the study. Patients kept nil by mouth for 6 h before the procedure as per guidelines. Sixty patients were randomly allocated into 2 groups of 30 patients each: Group A: Oral Clonidine 3 mcg/kg and Group B: Oral Midazolam 0.5 mg/kg.

**In group A for clonidine**

Oral clonidine was given to child 60 min before shifting the patient to the operating room (OR).

**In group B for midazolam**

As oral midazolam is commercially not available in most of the countries. In this study, we mixed the calculated dose of injectable preparation (5 mg/mL) of midazolam in mango juice.

Patients were shifted to the OR and all mandatory monitors were attached such as pulse-oximetry, blood pressure (BP) cuff, venturi mask for oxygen administration, and a large gauge i.v. line secured. Following parameters are been evaluated in this study, PSAS, Mask acceptance scale (MAS), and hemodynamic variables: Heart rate (HR), BP, oxygen saturation (SPO<sub>2</sub>), wake-up behavior, and sedation score.

#### Pediatric separation anxiety score (PSAS)

Parental separation anxiety was assessed using the Parental Separation Anxiety Scale (PSAS), which is a 4-point scale.

1. Easy separation
2. Whimpers but easily reassuring
3. Cries and cannot be easily reassured but not clinging to parents
4. Crying and clinging to parents.

A PSAS score of 1 or 2 is classified as an acceptable separation, and score of 3 or 4 is considered as difficult separation.

#### MAS

1. Excellent (unafraid, cooperative, accept mask readily)
2. Good (slight fear of mask, easily reassured)
3. Fair (moderate fear of mask, not calmed with reassurance)
4. Poor (terrified, crying, or combative).

Subjects with score of 1 or 2 are considered as satisfactory acceptance of mask, and scores of 3 or 4 are considered unsatisfactory.

#### Sedation score

- Does not respond to mild protruding or shaking
- Responds only to mild protruding or shaking.

#### Wake-up behavior

1. Calm and cooperative
2. Not calm but could be easily calmed
3. Not easily calmed, moderately agitated, or restless
4. Combative, excited, disoriented.

Subjects with score of 1 or 2 are considered as satisfactory for wake-up behavior of a child, scores of 3 or 4 are not considered satisfactory.

Data were collected and entered into the Excel sheet; the analysis was done using the 16.0 software. The mean of systolic BP, diastolic BP, HR, and SPO<sub>2</sub>, between different groups at the same time interval was analyzed using chi-square test. Unpaired t-test was used to compare the parent separation anxiety and mask acceptance in both the groups. Pearson Chi-square test was used to compare the sedation and wake-up behavior between both groups.  $p \leq 0.05$  was considered as statistically significant.

#### OBSERVATION AND RESULTS

The mean PSAS in oral clonidine group was  $1.00 \pm 0.00$ , while in the oral midazolam group was  $2.10 \pm 0.31$ . The difference was found to be statistically significant ( $p=0.000$ ), showing a higher mean PSAS in oral midazolam group in comparison to the oral clonidine group (Graph 1).

The mean MAS in oral clonidine group was  $1.00 \pm 0.00$ , while in the oral midazolam group was  $2.13 \pm 0.35$ . The difference was found to be statistically significant ( $p=0.000$ ), showing a higher mean MAS in oral midazolam group in comparison to the oral clonidine group

The comparison of mean HR between the two groups showed that the mean HR was comparable between the two groups till 60 min ( $p>0.05$ ). The mean HR in oral clonidine group from 75 min till the end of 160 min was significantly lower than that in the oral midazolam group ( $p<0.05$ ).

The comparison of mean systolic BP between the two groups was comparable till 105 min ( $p>0.05$ ). The mean systolic BP in oral clonidine

group at 115 min till the end of 160 min was significantly lower than oral midazolam group ( $p<0.05$ ).

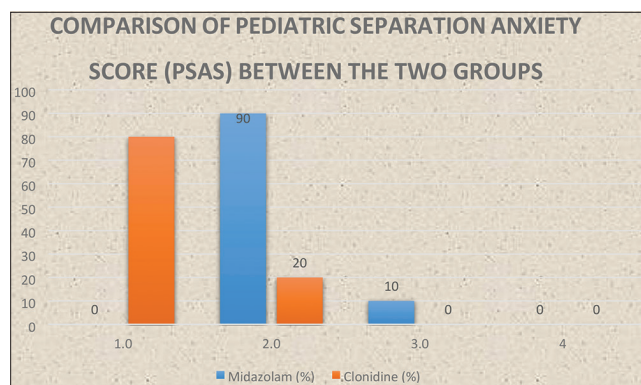
The comparison of mean diastolic BP between the two groups was comparable throughout the study period ( $p>0.05$ ). The mean diastolic BP in oral clonidine group was lower than oral midazolam (Graph 2).

The comparison of mean diastolic BP between the two groups was comparable throughout the study period ( $p>0.05$ ). The mean diastolic BP in oral clonidine group was lower than oral midazolam. In oral midazolam group, all the patients were having sedation grade 1 while in oral clonidine group, all the patients were having sedation grade 2. There was a statistically significant association seen between sedation grade and the groups ( $p=0.000$ ), showing that groups are dependent on the sedation group (Graph 3).

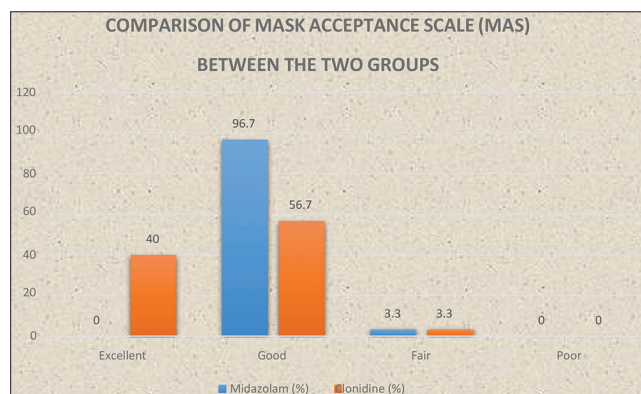
In oral midazolam group, all the patients were having wake-up behavior grade 1. In oral clonidine group, all patients were having wake-up behavior grade 2 (Graph 4).

#### DISCUSSION

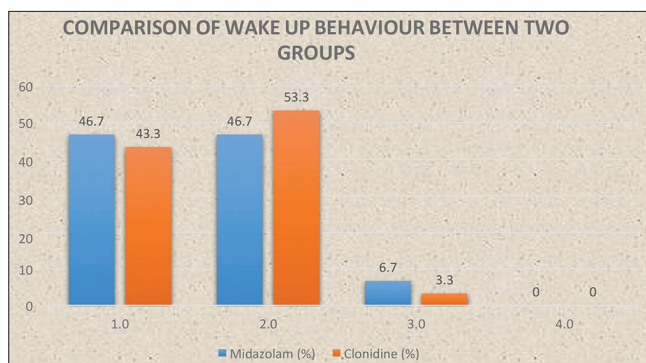
In our analysis, we found that oral clonidine is better and effective for parent separation anxiety and in comparison to midazolam. Mostafa and Morsy [2] conducted a randomized double-blind controlled trial in 96 children aged 2–8 years scheduled for bone marrow biopsy and aspirate. Patients with child–parent separation score grade 1 was significantly higher in clonidine group than. In our analysis, we found that oral clonidine is better and effective for mask acceptance. The comparison of mean systolic BP between the two groups was comparable till 105 min ( $p>0.05$ ). The mean systolic BP in oral clonidine group at 115 min till end of 160 min was significantly lower than oral midazolam



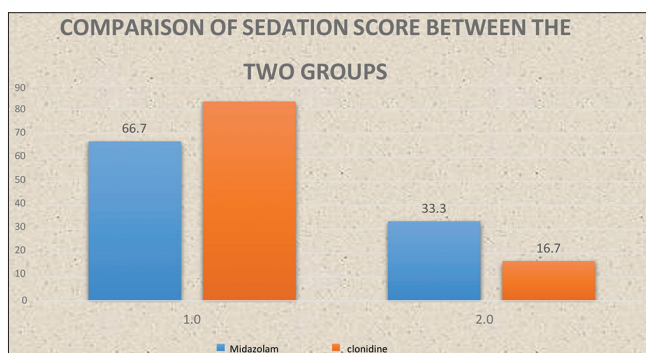
Graph 1: Comparison of pediatric separation anxiety score between the two groups



Graph 2: Comparison of mask acceptance scale between the two groups



Graph 3: Comparison of wake-up behavior between two groups



Graph 4: Comparison of sedation score between the two groups

group ( $p < 0.05$ ). The comparison of mean systolic BP between the two groups was comparable till 105 min ( $p > 0.05$ ). The mean systolic BP in oral clonidine group at 115 min till the end of 160 min was significantly lower than oral midazolam group ( $p < 0.05$ ). The comparison of mean diastolic BP between the two groups was comparable throughout the study period ( $p > 0.05$ ). The mean diastolic BP in oral clonidine group was lower than oral midazolam. In oral clonidine group, all the patients were having sedation grade 2. In oral midazolam group, all the patients were having sedation grade 1. There was a statistically significant association seen between sedation grade and the groups ( $p = 0.000$ ), showing that groups are dependent on the sedation group. In oral midazolam group, all the patients were having wake-up behavior grade 1. In oral clonidine group, all the patients were having wake-up behavior grade 2. There was a statistically significant association seen between wake-up behavior grade and the groups ( $p = 0.000$ ), showing that groups are dependent on the wake-up behavior grade.

In our analysis, we found that oral clonidine has better wake-up behavior and sedation score in comparison to oral midazolam. In our analysis, in oral clonidine hemodynamic variables, HR BP values were lowered in comparison of midazolam. Sheta *et al.* [6], seventy-two children of American Society of Anesthesiology classification (ASA) physical status (I and II), aged 3–6 years, were randomly assigned

to one of two groups equally. Group M received oral midazolam (0.5 mg/kg), and group C received oral clonidine (3  $\mu$ g/kg). The patients' hemodynamic parameters were recorded by an observer until anesthesia induction. There were no incidences of bradycardia, hypotension, in either of the groups during study observation. Singla *et al.* [3] conducted a prospective, randomized double-blind controlled trial on 60 children, 3–10 years of age with ASA physical status I, scheduled for elective surgery. In this study, mask acceptance score ( $p = 0.0472$ ) was significantly lower in group in clonidine as comparison to midazolam. Hence, oral clonidine is an effective and safe alternative and results in superior sedation. Kawanda *et al.* [7] conducted a study in which 80 children (median age 3 years) were recruited and 140 surgical procedures were performed and found similarly that oral clonidine has better sedation and wake-up behavior as compared to oral midazolam.

## CONCLUSION

Oral clonidine 3 mcg/kg is an effective and safe alternative for pre-medication in children undergoing surgery under general anesthesia. Oral clonidine decreases anxiety levels, allows better parent separation, and results in better mask acceptance at the time of induction when compared with oral midazolam 0.5 mg/kg. Oral clonidine has better sedation and wake-up behavior and works without causing many side effects or post-operative complications.

## CONFLICT OF INTEREST

None declared.

## FUNDING

Nil.

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