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A Randomized Single Blinded Study Comparing the Effects of Oral Melatonin with Oral Alprazolam Used as Premedication in Adult Patients Undergoing Surgery Under General Anaesthesia

Article History:

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Abstract: Background: Preoperative anxiety is a common problem among surgical patients and may adversely affect perioperative hemodynamic stability, anesthetic requirements, recovery profile, and patient satisfaction. Benzodiazepines such as alprazolam are widely used for anxiolysis but are associated with sedation, cognitive impairment, and delayed recovery. Melatonin has emerged as a potential alternative premedicant with anxiolytic and sedative properties and fewer adverse cognitive effects.**Objectives:**To compare the effects of oral melatonin and oral alprazolam as premedicants in adult patients undergoing elective surgery under general anesthesia.
Methods: This prospective randomized single-blinded comparative study included 90 adult patients (ASA I and II) scheduled for elective surgeries under general anesthesia. Patients were randomly allocated into two groups of 45 each. Group M received oral melatonin 9 mg and Group A received oral alprazolam 0.5 mg, administered 120 minutes before surgery. Anxiety was assessed using the Visual Analogue Scale (VAS), sedation using Ramsay Sedation Score (RSS), orientation using orientation scores, and cognitive function using Digit Symbol Substitution Test (DSST). Hemodynamic parameters and adverse effects were also recorded.**Results:**Both groups showed significant reduction in anxiety after premedication; however, melatonin produced greater anxiolysis (VAS: 2.3 ± 0.8 vs 3.1 ± 0.9; p=0.001). Alprazolam produced deeper sedation (RSS: 3.5 ± 0.6 vs 2.9 ± 0.5; p=0.003) and greater cognitive impairment (DSST: 52.1 ± 6.3 vs 60.7 ± 5.2; p=0.0001). Melatonin demonstrated better orientation, improved hemodynamic stability, and fewer adverse effects.**Conclusion:**Oral melatonin is an effective and safer alternative to alprazolam as a premedicant, providing superior anxiolysis with better preservation of cognitive and psychomotor function and fewer adverse effects.

Keywords: Melatonin; Alprazolam; Premedication; Preoperative anxiety; General anesthesia; Cognitive function; Sedation; Psychomotor performance.

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INTRODUCTION

Preoperative anxiety is a common and significant psychological response experienced by patients awaiting surgery and anesthesia. It is characterized by feelings of fear, apprehension, uncertainty, and tension regarding the surgical procedure, anesthetic administration, postoperative pain, potential complications and overall outcomes. Studies have demonstrated that a large proportion of patients undergoing elective surgeries experience varying degrees of anxiety before operation, which may adversely influence both physiological and psychological well-being[1]. The stress response induced by anxiety leads to increased sympathetic nervous system activity and catecholamine release, resulting in tachycardia, hypertension, arrhythmias, increased myocardial oxygen demand and altered endocrine responses. Excessive perioperative anxiety may also contribute to increased anesthetic requirements, delayed recovery, poor postoperative pain control, prolonged hospital stay and reduced patient satisfaction[2].

Premedication before surgery is therefore an important component of anesthetic management aimed at reducing anxiety, providing sedation, ensuring patient comfort, and facilitating smooth induction of anesthesia. Benzodiazepines have traditionally been the most commonly used agents for preoperative anxiolysis due to their anxiolytic, sedative, amnesic, and hypnotic properties[3]. Alprazolam, a triazolobenzodiazepine, is widely used because of its rapid onset of action, short duration and effective anxiolytic effect. Oral alprazolam has been shown to reduce preoperative anxiety and improve patient cooperation before induction of anesthesia. However, despite its clinical utility, alprazolam may be associated with several undesirable effects including excessive sedation, respiratory depression, psychomotor impairment, delayed recovery, cognitive dysfunction, impaired orientation and postoperative drowsiness[4]. These adverse effects may negatively affect perioperative patient safety and postoperative recovery profiles.

In recent years, melatonin has emerged as a promising alternative premedicant in anesthesia practice. Melatonin (N-acetyl-5-methoxytryptamine) is an endogenous neurohormone secreted primarily by the pineal gland and plays a central role in regulation of circadian rhythm and sleep-wake cycles. Apart from its chronobiotic effect, melatonin possesses anxiolytic, sedative, analgesic, anti-inflammatory, antioxidant, and immunomodulatory properties[5]. Unlike benzodiazepines, melatonin has the unique advantage of producing anxiolysis and sedation without significantly impairing psychomotor performance or cognitive functions. This makes it particularly attractive in perioperative settings where rapid recovery, preservation of cognitive abilities, and minimal residual sedation are highly desirable.

Several studies have evaluated the role of melatonin in anesthesia and perioperative medicine. Oral melatonin has been shown to effectively reduce preoperative anxiety, attenuate hemodynamic responses to laryngoscopy and intubation, improve sleep quality, reduce postoperative pain, and decrease anesthetic requirements[6]. Furthermore, melatonin is associated with minimal respiratory depression and a favorable safety profile. The sedative effect of melatonin resembles natural sleep and patients remain easily arousable, which is advantageous in perioperative care. Various clinical trials comparing melatonin with midazolam have demonstrated comparable anxiolytic efficacy with fewer cognitive and psychomotor side effects. However, limited literature exists comparing melatonin directly with alprazolam in adult patients undergoing surgeries under general anesthesia[7].

The assessment of preoperative anxiolytic agents should not be limited to reduction in anxiety alone. An ideal premedicant should provide adequate sedation while preserving orientation, cognitive abilities and psychomotor performance. Cognitive dysfunction and impaired psychomotor coordination in the perioperative period can affect patient safety, delay discharge and reduce functional recovery. Therefore, objective assessment tools such as the Digit Symbol Substitution Test (DSST), Ramsay Sedation Score (RSS), and Visual Analogue Scale (VAS) for anxiety are valuable in evaluating the overall efficacy and safety profile of premedicants.

Melatonin has also attracted interest due to its potential role in reducing oxidative stress and inflammatory responses associated with surgery and anesthesia. Surgical stress can trigger release of inflammatory mediators and free radicals, contributing to tissue injury and delayed recovery. The antioxidant property of melatonin may provide additional perioperative benefits by scavenging free radicals and stabilizing cellular function[8]. Moreover, melatonin has been reported to have a favorable hemodynamic profile with less fluctuation in heart rate and blood pressure during perioperative stress responses.

Hence, the present study was designed to compare the effects of oral melatonin and oral alprazolam when administered as premedication in adult patients

undergoing elective surgery under general anesthesia. The study aims to evaluate and compare their effects on preoperative anxiety, sedation, orientation and cognitive function using standardized assessment scales. It is hypothesized that melatonin may provide adequate anxiolysis and sedation comparable to alprazolam while preserving cognitive and psychomotor performance with minimal adverse effects. The findings of this study may help identify a safer and more effective alternative premedicant that improves perioperative patient comfort and recovery while minimizing undesirable side effects associated with conventional benzodiazepines.

Materials and Methods

Study Design and Setting

This prospective randomized single-blinded comparative study was conducted in the Department of Anaesthesiology, Critical Care and Pain Medicine at KLE JGMM Medical College and KLE Hubli Co-operative Hospital, Hubballi. The study duration was four months following approval from the Institutional Ethics Committee. The study aimed to compare the efficacy of oral melatonin and oral alprazolam as premedicants in adult patients undergoing elective surgical procedures under general anesthesia. The study followed a randomized controlled design in which eligible participants were randomly allocated into two equal groups. Patients were blinded to the intervention administered, while the attending anesthesiologist responsible for drug administration was aware of the group allocation.

Study Population

The study population composed of adult patients aged between 18 and 60 years belonging to the American Society of Anesthesiologists (ASA) physical status classes I and II who were scheduled for elective surgical procedures lasting more than one hour under general anesthesia.

All eligible patients undergoing pre-anesthetic evaluation during the study period were screened for participation. A detailed history, physical examination, and routine preoperative investigations was performed before inclusion in the study.

Sample Size Calculation

The total sample size for the study were 90 patients, with 45 patients in each study group. The sample size was determined based on the seed article by Khare et al. comparing oral melatonin and oral alprazolam as premedicants in adult surgical patients under general anesthesia. Equal allocation of patients in both groups will ensure adequate comparison and statistical validity.

Sampling Technique and Randomization

Patients fulfilling the inclusion criteria were recruited using computer-generated randomization. Random allocation was performed using computer-generated random numbers to ensure unbiased assignment into the two study groups.
Group M: Patients received oral melatonin 9 mg (three tablets of 3 mg each) administered 120 minutes before induction of anesthesia.
Group A: Patients received oral alprazolam 0.5 mg administered 120 minutes before induction of anesthesia.
Allocation concealment were maintained using sealed opaque envelopes opened only at the time of administration of study medication.

Inclusion Criteria

1. Patients aged between 18 and 60 years.
2. Patients belonging to ASA physical status grade I or II.
3. Patients scheduled for elective surgical procedures lasting more than one hour under general anesthesia.
4. Patients willing to participate and provide informed written consent.

Exclusion Criteria

1. Patients with ASA physical status grade III and above.
2. Patients younger than 18 years or older than 60 years.
3. Patients with known hypersensitivity or allergy to melatonin or alprazolam.
4. Pregnant or lactating women.
5. Patients with psychiatric illness or cognitive impairment.
6. Patients receiving steroids, sedatives, or antipsychotic medications.
7. Patients unable to understand or perform assessment scales and cognitive tests.
8. Patients with uncontrolled hypertension, diabetes mellitus, or major systemic illness.
9. Patients refusing consent for participation.

Preoperative Assessment

All patients underwent a detailed pre-anesthetic check-up prior to surgery. The anesthetic procedure, perioperative course, and study protocol was explained thoroughly to all participants. Written informed consent was obtained from each patient.

Patients were advised fasting according to standard preoperative fasting guidelines, including fasting for solid foods for eight hours and clear liquids for two hours prior to surgery.

Baseline demographic data including age, sex, weight, ASA status, diagnosis, and surgical procedure were recorded. Baseline vital parameters including heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, respiratory rate, and oxygen saturation was noted.

Assessment Tools

Preoperative anxiety was assessed using the Visual Analogue Scale (VAS) for anxiety. The scale consisted of a 10 cm linear scale ranging from 0 indicating "no anxiety" to 10 indicating "worst imaginable anxiety." Patients was asked to indicate their anxiety level on the scale.

Sedation was assessed using the Ramsay Sedation Score (RSS):

1 – Patient anxious, agitated, or restless
2 – Patient cooperative, oriented, and tranquil
3 – Patient responds to commands only
4 – Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
5 – Patient exhibits sluggish response to light glabellar tap or loud auditory stimulus
6 – Patient exhibits no response

Orientation was evaluated using a three-point orientation scale:

0 – No orientation
1 – Orientation to either time or place
2 – Orientation to both time and place

Cognitive and psychomotor function was assessed using the Digit Symbol Substitution Test (DSST). Patients were provided with a sheet containing a numerical key associated with specific symbols. They were instructed to fill corresponding symbols in blank boxes within 90 seconds. The number of correctly completed symbols were recorded as the DSST score.

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Study Procedure

After shifting the patient to the preoperative holding area, baseline assessment of anxiety, sedation, orientation, and cognitive function was performed prior to administration of the study medication.

Patients received the allocated oral medication with a sip of water exactly 120 minutes before induction of anesthesia.

Following drug administration, patients were reassessed after 120 minutes using the same scales and tests. Any side effects such as nausea, dizziness, excessive sedation, headache, or allergic reactions were documented.

In the operating room, intravenous access were secured using an 18-gauge cannula and Ringer lactate infusion were initiated. Standard monitoring including electrocardiography, pulse oximetry, non-invasive blood pressure, and heart rate monitoring were instituted.

All patients received intravenous glycopyrrolate 0.004 mg/kg and fentanyl 2 µg/kg as premedication. Preoxygenation with 100% oxygen were carried out for three minutes.

General anesthesia was induced using intravenous propofol 2 mg/kg administered slowly until loss of verbal response and eyelash reflex. Succinylcholine 2 mg/kg was administered to facilitate endotracheal intubation.

Anesthesia was maintained using sevoflurane 2% with nitrous oxide and oxygen in a 40:60 ratio along with atracurium 0.5 mg/kg loading dose followed by maintenance doses of 0.1 mg/kg as required.

Fifteen minutes before completion of surgery, intravenous paracetamol 20 mg/kg diluted in 100 ml normal saline will be administered slowly for postoperative analgesia.

At the completion of surgery, neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.008 mg/kg intravenously. Patients was extubated after adequate recovery from anesthesia and restoration of protective airway reflexes.

Outcome Measures

- **Primary Outcome:**
  • Preoperative anxiety score assessed using the Visual Analogue Scale.

  Secondary Outcomes:
  • Sedation score using Ramsay Sedation Score.
  • Orientation score.
  • Cognitive and psychomotor function assessed by DSST.
  • Hemodynamic parameters including heart rate and blood pressure.
  • Incidence of adverse effects and complications.

Data Collection Procedure

All observations and study-related data was entered into a predesigned data collection proforma. Data including demographic details, vital parameters, anxiety scores, sedation scores, orientation scores, and DSST scores before and after drug administration was recorded systematically.

Confidentiality of patient information was maintained throughout the study. Data collection were supervised by the principal investigator and co-investigators to ensure accuracy and completeness.

Statistical Analysis

Data obtained from the study was entered into Microsoft Excel and analyzed using appropriate statistical software. Quantitative variables was expressed as mean ± standard deviation, while

qualitative variables were expressed as frequencies and percentages. Comparison between the two groups for quantitative variables was performed using Student's independent t-test. Categorical variables was analyzed using Chi-square test or Fisher's exact test wherever appropriate. A p-value less than 0.05 was considered statistically significant.

Ethical Considerations

The study will commence only after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants after explaining the purpose, procedure, benefits, and risks of the study. Patient confidentiality was strictly maintained. Participation in the study was entirely voluntary, and participants will have the right to withdraw from the study at any point without affecting their medical care.

OBSERVATIONS AND RESULTS

Ninety patients satisfying inclusion criteria were enrolled in the present study and randomly allocated into two groups of 45 patients each. Group M received oral melatonin 9 mg whereas Group A received oral alprazolam 0.5 mg 120 minutes before surgery. The observations were recorded and statistically analyzed.

Table 1: Demographic Profile

Table 1 demonstrates the demographic comparability between Group M (melatonin) and Group A (alprazolam). The mean age, body weight, gender distribution, and ASA physical status were statistically similar between both groups, with all p values greater than 0.05. This indicates that the study groups were homogeneous at baseline and that subsequent differences observed in study outcomes can be attributed to the effects of the premedication drugs rather than demographic variations. The comparable distribution of male and female patients as well as ASA grading further strengthens the validity of intergroup comparisons.

Variable	Group M	Group A	P value
Age (years)	38.4 ± 10.2	39.1 ± 9.7	0.74
Weight (kg)	64.8 ± 8.5	66.1 ± 9.1	0.52
Male/Female	24/21	26/19	0.66
ASA I/II	28/17	30/15	0.64

Both groups were statistically comparable with respect to demographic characteristics.

Table 2: Comparison of VAS Anxiety Scores

Table 2 compares the Visual Analogue Scale (VAS) anxiety scores before administration of the study drug and 120 minutes after premedication. Baseline anxiety scores were similar in both groups, confirming comparable preoperative anxiety levels. Following drug administration, both groups demonstrated significant reduction in anxiety; however, Group M showed a markedly greater decline in anxiety scores compared to Group A. The statistically significant p value (0.001) suggests that melatonin provided superior anxiolytic efficacy compared with alprazolam in the preoperative period.

Time	Group M	Group A	P value
Before Drug	6.9 ± 1.2	7.0 ± 1.1	0.82
120 min After Drug	2.3 ± 0.8	3.1 ± 0.9	0.001

A significant reduction in anxiety scores was observed in both groups, with greater reduction in Group M.

Table 3: Ramsay Sedation Scores

Table 3 presents the Ramsay Sedation Scores observed at baseline and after 120 minutes of premedication. Baseline scores were comparable between groups. Following administration of the study drugs, sedation increased significantly in both groups, but the increase was more pronounced in Group A. The higher sedation scores in the alprazolam group indicate deeper sedative action, whereas melatonin produced mild to moderate sedation while maintaining better patient responsiveness and cooperation.

Time	Group M	Group A	P value
Baseline	1.8 ± 0.4	1.9 ± 0.3	0.58
120 min	2.9 ± 0.5	3.5 ± 0.6	0.003

Sedation scores were significantly higher in the alprazolam group.

Table 4: DSST Scores

Table 4 compares Digit Symbol Substitution Test (DSST) scores, which assess psychomotor and cognitive function. Baseline scores were comparable in both groups. After premedication, Group M maintained near-

baseline cognitive performance, whereas Group A showed a substantial reduction in DSST scores. The highly significant p value indicates that alprazolam caused greater psychomotor impairment and cognitive slowing compared to melatonin. These findings suggest that melatonin preserves cognitive function more effectively during the perioperative period.

Time	Group M	Group A	P value
Before Drug	62.4 ± 5.8	61.9 ± 5.5	0.71
120 min	60.7 ± 5.2	52.1 ± 6.3	0.0001

Melatonin preserved cognitive function better than alprazolam.

Table 5: Hemodynamic Parameters

Table 5 evaluates hemodynamic parameters including heart rate, mean arterial pressure (MAP), and oxygen saturation (SpO2). Patients receiving melatonin demonstrated lower heart rate and MAP values, indicating better hemodynamic stability and reduced sympathetic response to preoperative stress. Oxygen saturation remained stable and comparable in both groups. These findings suggest that melatonin provides a more stable cardiovascular profile during the perioperative period.

Parameter	Group M	Group A	P value
Heart Rate	76 ± 7	81 ± 8	0.01
MAP	89 ± 6	93 ± 7	0.03
SpO2	99 ± 1	99 ± 1	0.88

Group M showed greater hemodynamic stability compared to Group A.

Table 6: Orientation Scores after Premedication

Table 6 compares orientation scores between the two groups after premedication. A higher number of patients in Group M retained normal orientation scores compared with Group A, suggesting better preservation of orientation and alertness with melatonin. In contrast, alprazolam administration was associated with greater disorientation and impaired responsiveness. These results indicate that melatonin offers anxiolysis with minimal cognitive disturbance.

Orientation Score	Group M	Group A
0	2	5
1	8	15
2	35	25

Orientation was better maintained in the melatonin group.

Table 7: Incidence of Side Effects

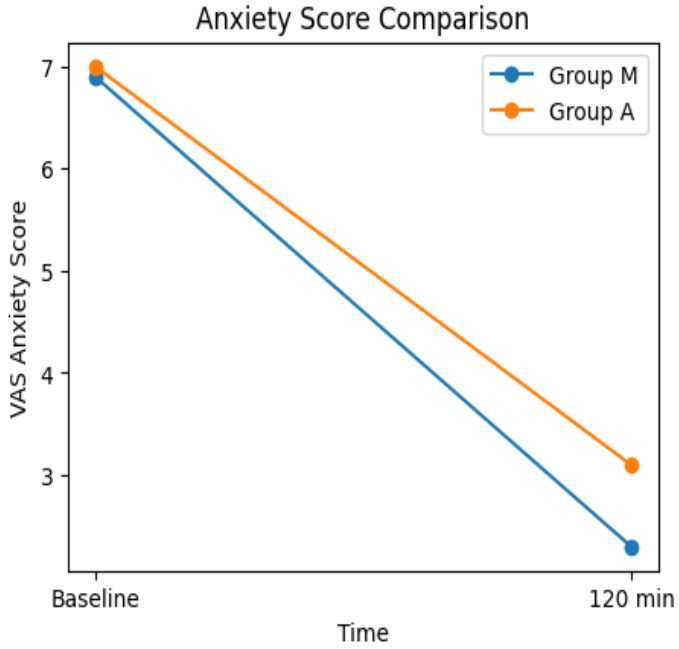
Table 7 summarizes the adverse effects observed in both study groups. The alprazolam group exhibited a higher incidence of dizziness, dry mouth, nausea, and excessive drowsiness compared to the melatonin group. The comparatively lower side-effect profile associated with melatonin suggests better tolerability and improved patient comfort. Reduced adverse effects may also contribute to enhanced postoperative recovery and patient satisfaction.

Adverse Effect	Group M	Group A
Dizziness	2	5
Dry Mouth	1	4
Nausea	1	2
Drowsiness	3	9

The incidence of adverse effects was higher in the alprazolam group.

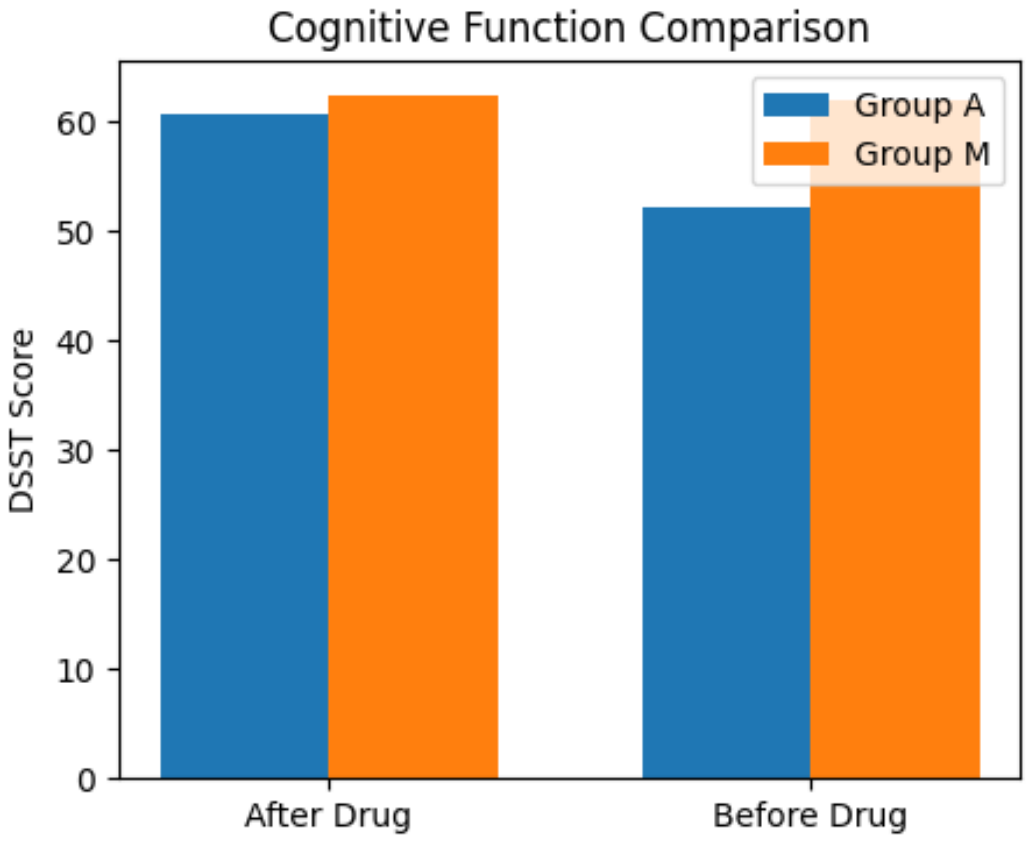
Graph 1: Line Graph Showing Anxiety Scores

Graph 1 illustrates the trend in anxiety scores before and after administration of the study drugs. Both groups demonstrated reduction in anxiety following premedication; however, the decline was steeper and more pronounced in the melatonin group. The graphical representation clearly highlights the superior anxiolytic effect of melatonin compared with alprazolam.



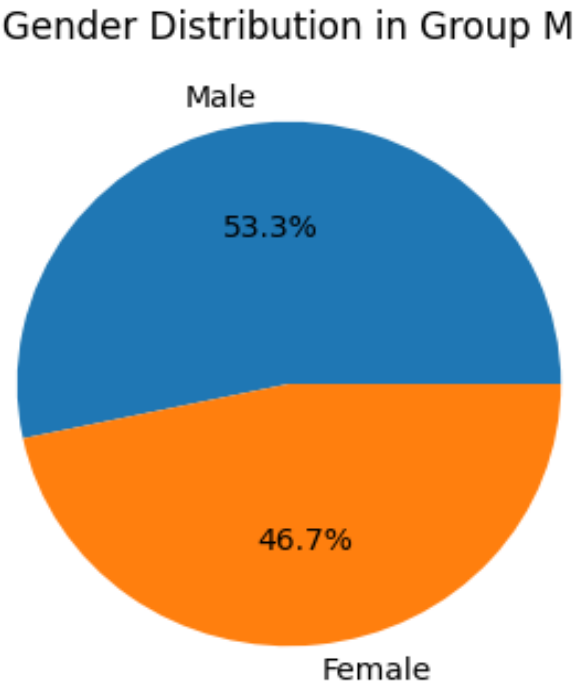
Graph 2: Bar Graph Showing DSST Scores

Graph 2 visually compares DSST scores between the two groups before and after premedication. While Group M maintained relatively stable scores, Group A showed a marked decline after drug administration. The graph emphasizes the better preservation of psychomotor performance and cognitive function with melatonin.



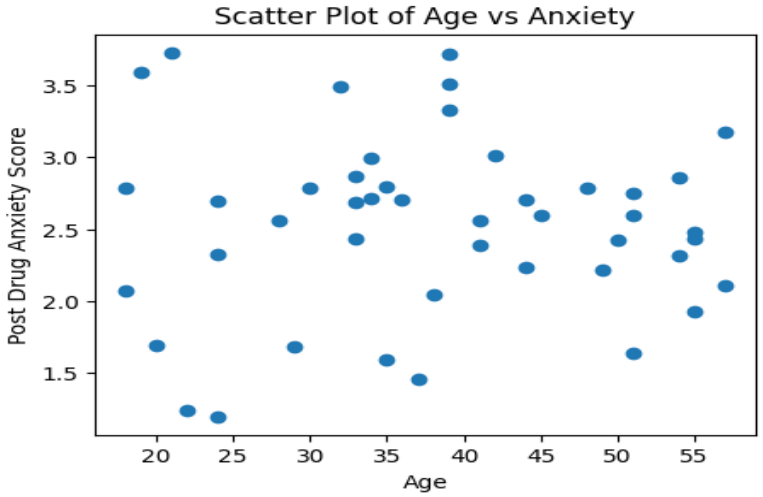
Graph 3: Pie Chart Showing Gender Distribution

Graph 3 presents the gender distribution of study participants in both groups. The nearly equal proportions of male and female participants demonstrate balanced recruitment and minimize gender-related bias. This balanced distribution contributes to the reliability and generalizability of the study findings.



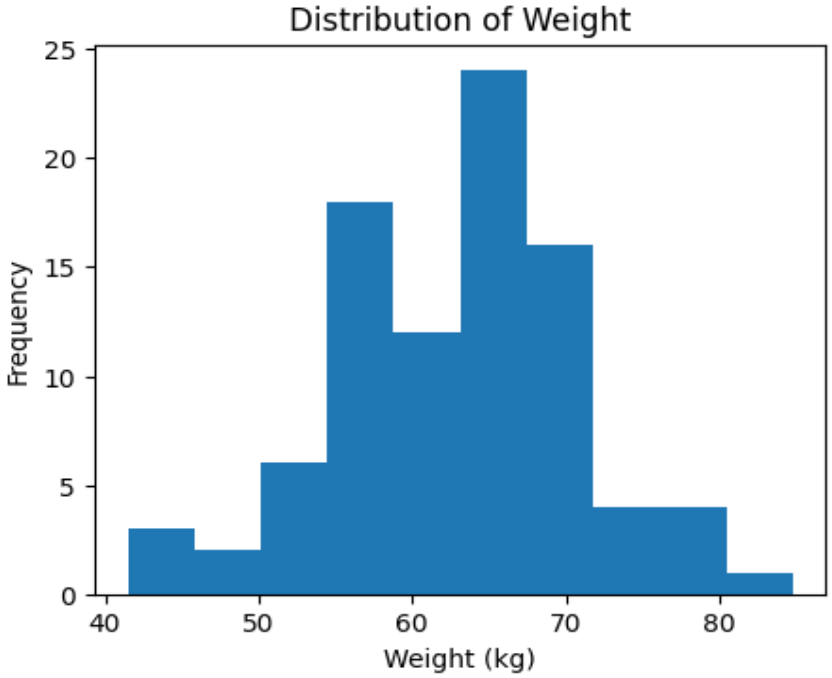
Graph 4: Scatter Plot of Age vs Anxiety

Graph 4 depicts the relationship between patient age and anxiety scores. The scatter plot demonstrates that anxiety levels were distributed across all age groups without a strong age-dependent correlation. This suggests that the anxiolytic effects observed were primarily related to the administered drugs rather than age-related variations.



Graph 5: Histogram Showing Weight Distribution

Graph 5 illustrates the distribution of patient body weight in the study population. Most participants were clustered around the mean weight range, indicating relatively normal distribution of body weight across both groups. The comparable weight distribution further supports the baseline similarity between the groups.



The study demonstrated that oral melatonin was associated with superior anxiolytic effect, better preservation of cognitive and psychomotor function, improved orientation, and greater hemodynamic stability compared to oral alprazolam. Although alprazolam produced deeper sedation, it was associated with increased psychomotor impairment and a higher incidence of side effects.

DISCUSSION

The present randomized single-blinded comparative study was conducted to evaluate and compare the effects of oral melatonin and oral alprazolam as premedicants in adult patients undergoing elective surgery under general anaesthesia. Preoperative anxiety is a common concern among surgical patients and effective anxiolysis forms an essential component of perioperative management. The ideal premedicant should reduce anxiety, provide adequate sedation, preserve cognitive and psychomotor function, maintain hemodynamic stability, and produce minimal adverse effects. The findings of the present study demonstrated that oral melatonin provided superior anxiolytic efficacy with better preservation of orientation and cognitive function compared with oral alprazolam.

In the present study, both groups were comparable with respect to demographic characteristics including age, weight, gender distribution, and ASA physical status. The absence of statistically significant differences between the two groups indicates that the study population was homogeneous and that the observed differences in outcomes were attributable to the pharmacological effects of the study drugs rather than demographic variations. Similar baseline comparability has been reported in previous studies evaluating melatonin and benzodiazepines as premedicants.

Assessment of anxiety using the Visual Analogue Scale revealed that both melatonin and alprazolam significantly reduced preoperative anxiety scores after administration. However, the reduction in anxiety was significantly greater in the melatonin group. These findings suggest that melatonin possesses potent anxiolytic properties comparable or even superior to conventional benzodiazepines. The anxiolytic action of melatonin is believed to be mediated through interaction with melatonin receptors in the central nervous system and modulation of gamma aminobutyric acid (GABA) neurotransmission[9]. In addition, melatonin influences circadian rhythm and promotes a calming effect resembling physiological sleep.

The findings of the present study are in agreement with the study conducted by Khare et al., who demonstrated that oral melatonin effectively reduced preoperative anxiety and produced anxiolysis comparable to benzodiazepines with fewer adverse effects. Similarly, Naguib et al. reported that melatonin significantly reduced anxiety in surgical patients while maintaining better psychomotor performance. These observations support the growing evidence favoring melatonin as a safe and effective alternative anxiolytic agent in perioperative care[10].

Sedation assessment using the Ramsay Sedation Score demonstrated increased sedation in both groups after premedication. However, sedation scores were significantly higher in the alprazolam group.

Although deeper sedation may facilitate patient calmness, excessive sedation can impair responsiveness, delay recovery, and increase perioperative complications. Melatonin produced mild to moderate sedation while preserving patient cooperation and orientation. This characteristic may be advantageous in ambulatory and short-duration procedures where rapid postoperative recovery is desired[11].

An important finding of the present study was the preservation of psychomotor and cognitive function in patients receiving melatonin. Assessment using the Digit Symbol Substitution Test showed minimal decline in scores in the melatonin group, whereas a marked reduction was observed in the alprazolam group. This indicates that alprazolam caused greater cognitive impairment and psychomotor slowing. Preservation of cognitive function is clinically important because excessive psychomotor impairment may delay postoperative recovery, impair patient communication, and reduce discharge readiness. Melatonin appears to provide anxiolysis without causing significant cognitive dysfunction, thereby improving overall perioperative patient safety[12].

Orientation scores further supported the superior cognitive profile of melatonin. A larger proportion of patients in the melatonin group remained fully oriented after premedication compared with the alprazolam group. Benzodiazepines are known to impair memory and orientation due to central nervous system depression, whereas melatonin induces a more physiological form of sedation with easier arousability and preserved awareness[13].

The present study also demonstrated improved hemodynamic stability in the melatonin group. Patients receiving melatonin exhibited lower heart rate and mean arterial pressure compared with the alprazolam group. Preoperative anxiety activates the sympathetic nervous system leading to tachycardia and hypertension. By reducing sympathetic activation, melatonin may contribute to better cardiovascular stability during the perioperative period. Furthermore, the antioxidant and anti-inflammatory properties of melatonin may also play a role in attenuating stress responses associated with surgery and anesthesia.

The incidence of adverse effects was lower in the melatonin group. Patients receiving alprazolam experienced higher rates of dizziness, dry mouth, nausea, and excessive drowsiness. The favorable side-effect profile of melatonin is an important advantage because postoperative comfort and rapid recovery are increasingly emphasized in modern anesthesia practice. Reduced adverse effects may improve patient satisfaction and decrease postoperative morbidity[14].

Overall, the findings of the present study suggest that oral melatonin is an effective and safe alternative to oral alprazolam as a premedicant in adult surgical patients undergoing general anesthesia. Melatonin provided superior anxiolysis, better preservation of cognitive and psychomotor function, improved orientation, greater hemodynamic stability, and fewer adverse effects. Although alprazolam produced deeper sedation, it was associated with greater psychomotor impairment and postoperative drowsiness.

The present study has certain limitations. The sample size was relatively small and the study was conducted at a single center, which may limit generalizability of the findings. Long-term postoperative outcomes such as recovery profile, sleep quality, and patient satisfaction were not extensively evaluated. Further multicentric studies with larger sample sizes are required to establish optimal dosing regimens and evaluate long-term benefits of melatonin in perioperative practice.

In conclusion, the present study supports the use of oral melatonin as an effective preoperative anxiolytic and sedative agent with significant advantages over alprazolam. Melatonin may be considered a safer alternative premedicant because of its favorable cognitive profile, minimal adverse effects, and better hemodynamic stability.

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