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RESEARCH ARTICLE

Clinical Observation of Effect of Oral Melatonin 10 Mg as Premedication

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ABSTRACT

Introduction: Preoperative anxiety has a significant impact on surgical outcomes. Oral melatonin, known for its anxiolytic and sedative properties, is used as a premedicant. This study aimed to evaluate the effects of administering 10 mg of oral melatonin two hours prior to elective surgery, focusing on its anxiolytic, sedative, amnestic, and perioperative effects.

Methodology: A prospective observational study was conducted at R. D. Gardi Medical College, Ujjain. The study included thirty patients, aged 18–75 years, with ASA physical status I–II, scheduled for elective surgery. Each patient received 10 mg of oral mouth-dissolving melatonin approximately 120 minutes before surgery. Perioperative measurements included anxiety and sedation levels.

Results: The mean age of participants was 40.44 ± 13.10 years, with 76.7% being male. Anxiety scores significantly decreased from 2.24 ± 1.39 at baseline to 0.00 postoperatively ($p < 0.001$). Sedation scores increased from 0.00 ± 0.00 to 1.32 ± 0.56 ($p < 0.001$), with all patients remaining arousable. Significant reductions were observed in pulse rate and blood pressure, while oxygen saturation remained stable. No instances of respiratory depression, haemodynamic and adverse events were reported.

Conclusion: Administering 10 mg of oral melatonin two hours before elective surgery effectively provided anxiolysis and mild sedation, maintaining haemodynamic and respiratory stability.

Keywords: Melatonin; Premedication; Preoperative anxiety; Sedation; Elective surgery.

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Introduction

Premedication involves administering drugs prior to anaesthesia to facilitate its administration, enhance patient comfort, and mitigate perioperative complications. The practice of premedication has significantly evolved over time[1]. With advancements in surgical techniques and anaesthetic practices, it has become apparent that patients awaiting surgery often experience anxiety, fear, and sleep disturbances[2]. Modern anaesthesia prioritizes rapid recovery, early ambulation, and same-day discharge, especially in minimally invasive and laparoscopic procedures. Therefore, the ideal premedicant should provide anxiolysis and sedation without prolonging recovery or impairing cognitive function. Melatonin, an endogenous hormone primarily secreted by the pineal gland, has emerged as a promising alternative treatment. Besides regulating circadian rhythms, melatonin plays significant roles in reproductive physiology regulation, antioxidant defense, and modulation of biological functions[3-6]. Melatonin possesses several pharmacological properties that make it an attractive preoperative premedicant. It induces sedation, anxiolysis, mild analgesia, amnesia, and antihypertensive effects while preserving psychomotor and

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cognitive functions. Unlike benzodiazepines, melatonin induces natural sleep without causing residual sedation, hangovers, or dependence. These characteristics make it particularly suitable for patients undergoing elective surgical procedures requiring early postoperative recovery. Oral melatonin has been extensively used for managing jet lag, insomnia, circadian rhythm disorders, and delayed sleep phase syndrome, demonstrating an excellent safety profile[7-10].

Given the increasing demand for safe and effective premedication in modern anaesthetic practice, oral melatonin may serve as a viable alternative to conventional sedative agents. However, evidence regarding its perioperative effects remains limited. Consequently, the present study was conducted to evaluate the clinical effects of oral melatonin 10 mg administered two hours before elective surgery. The primary objective was to assess its sedative, anxiolytic, and amnestic effects, while the secondary objective was to observe changes in perioperative vital parameters following its administration.

METHODOLOGY

This prospective clinical observational study was conducted in the Department of Anaesthesiology at R.D. Gardi Medical College, Ujjain, and its associated hospitals after obtaining approval from the Institutional Ethics Committee and Research Guidance Committee. A total of 30 adult patients undergoing elective surgical procedures under general, regional, or local anaesthesia during routine operating hours were included in the study. Written informed consent was obtained from all participants, and observations were recorded using a pre-designed case record proforma. Preoperative demographic details, including age, sex, height, weight, and educational status, were documented. All patients underwent detailed pre-anaesthetic evaluation, including clinical examination and routine laboratory investigations comprising complete blood count, haemoglobin estimation, urine analysis, random blood glucose, serum creatinine, electrocardiography, and chest radiography where indicated. Only patients belonging to the American Society of Anesthesiologists (ASA) physical status I and II, aged 18–75 years, and educated up to at least matriculation level were included. Patients undergoing emergency surgery, pregnant or lactating women, individuals with a known allergy to melatonin, history of psychiatric illness or drug abuse, chronic uncontrolled systemic diseases, significant cardiovascular, renal, hepatic, or neurological disorders, epilepsy, ASA physical status III or IV, and patients with education below matriculation were excluded from the study. All participants were kept nil per oral after midnight and received oral mouth-dissolving melatonin 10 mg approximately 120 minutes before surgery. Baseline vital parameters, including pulse rate, blood pressure, respiratory rate, and oxygen saturation, were recorded before drug administration and subsequently at predetermined intervals. Anxiety, sedation, and orientation were assessed using predefined scoring systems by an independent observer who was not involved in the study. Postoperatively, patients were monitored for orientation and adverse events, including nausea, vomiting, dizziness, headache, irritability, respiratory depression, and haemodynamic instability. Anxiety was assessed using a 10-point numerical scale, where scores of 1–3, 4–6, and 7–10 represented mild, moderate, and severe anxiety, respectively. Sedation was evaluated on a five-point scale ranging from 0 (alert) to 4 (unresponsive). Postoperative orientation was assessed using a three-point scale based on orientation to time and place. The primary outcome measures were changes in anxiety, sedation, and postoperative orientation following oral melatonin administration. Secondary outcome measures included changes in haemodynamic and respiratory parameters and the incidence of adverse effects. Data were entered into Microsoft Excel and analysed using appropriate statistical methods. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Continuous variables were analysed using the paired Student's t-test, whereas categorical variables were compared using the Chi-square test. A p-value <0.05 was considered statistically significant.

Results

The study included predominantly males (76.7%), with the highest proportion in the 26–35 years age group (33.3%). Most participants had matriculation-level education (43.3%) and underwent regional anesthesia (90.0%), mainly central neuraxial block (83.3%) as shown in Table 1.

The pulse rate, SBP, DBP, and respiratory rate decreased progressively during the perioperative period, whereas the SpO_2 remained stable. The observed changes were statistically significant ($p < 0.001$) as shown in Table 2.

The mean anxiety score decreased progressively from 2.24 ± 1.39 at baseline to 0.00, after surgery. The proportion of patients with no anxiety increased from 13.3% pre-treatment to 100% postoperatively, while that of patients with mild anxiety decreased from 86.7% to 0%. No patient had moderate or severe anxiety at any time point.

Table 1: Baseline characteristics of the study participants (N = 30)

Characteristic	*Category*	*n (%) / Mean ± SD*
Age (years)	Mean age	40.44 ± 13.10
	18–25	6 (20.0)
	26–35	10 (33.3)
	36–45	5 (16.7)
	46–55	5 (16.7)
	56–65	3 (10.0)
	66–75	1 (3.3)
Sex	Male	23 (76.7)
	Female	7 (23.3)
Educational status	Up to matriculation (10th standard)	13 (43.3)
	Higher secondary (12th standard)	11 (36.7)
	Graduate	6 (20.0)
Weight (kg)	Mean weight	60.76 ± 11.82
	≤45	5 (16.7)
	46–55	7 (23.3)
	56–65	5 (16.7)
	66–75	7 (23.3)
	≥76	6 (20.0)
Height (cm)	Mean height	173.13 ± 8.7 cm
	≤152	1 (3.3)
	155–167	7 (23.3)
	170–182	18 (60.0)
	≥185	4 (13.3)
Type of anaesthesia	Central neuraxial block	25 (83.3)
	Brachial plexus block	2 (6.7)
	General anaesthesia	3 (10.0)
	Local anaesthesia	0 (0.0)

The reduction in anxiety was statistically significant from 60 min onwards ($p < 0.001$) as shown in Table 3.

The mean sedation score increased progressively from 0.00 ± 0.00 at baseline to 1.32 ± 0.56, after surgery. The proportion of alert patients decreased from 100% pre-treatment to 3.3% postoperatively, while the proportion of patients arousable to voice increased to 60.0% and those arousable to tactile stimulation to 36.7%. No patient had a sedation score of 3 or 4. The increase in sedation score was statistically significant from 60 min onwards ($p \leq 0.001$) as shown in Table 4.

Postoperative orientation and recovery profile

All 30 patients achieved complete postoperative orientation, and no episodes of delayed recovery, confusion or disorientation were observed.

Adverse events following oral melatonin administration

ANo treatment-related adverse events were observed in any of the 30 study participants during the perioperative period. No episodes of respiratory depression, hemodynamic instability, excessive sedation, or gastrointestinal complications were observed.

Discussion

The present study assessed the clinical effects of administering 10 mg of oral melatonin two hours prior to elective surgery in 30 ASA I–II adult patients undergoing various surgical procedures under general, regional, or local anaesthesia. Throughout the perioperative period, the pulse rate, blood pressure, respiratory rate, and oxygen saturation remained clinically stable, despite a gradual reduction in pulse rate and systolic blood pressure following melatonin administration. Similar findings were reported by Priyamvada Gupta et al. (2016), who observed no significant haemodynamic changes after administering 6 mg of oral melatonin[11]. Ismail (2009) also demonstrated that oral melatonin, administered 90 minutes before cataract surgery, did not significantly alter heart rate, blood pressure, respiratory rate, or oxygen saturation[12]. Likewise, Naguib and Samarkandi (1998) reported stable haemodynamic parameters following melatonin premedication compared with midazolam and placebo[13]. Daniel Lee (2009) similarly found no significant changes in cardiovascular or respiratory variables after oral melatonin administration before dental procedures[14].These findings suggest that oral melatonin provides anxiolysis without compromising cardiovascular or respiratory stability. A significant reduction in anxiety scores was observed from 60 minutes onward, with nearly all patients becoming anxiety-free by 120 minutes post-administration of melatonin. Sedation

Table 2: Changes in pulse rate and vital parameters during the perioperative period following oral melatonin administration (N = 30)

Time point	*Pulse (beats/min) Mean ± SD*	*SBP (mmHg) Mean ± SD*	*DBP (mmHg) Mean ± SD*	*SpO_2 (%) Mean ± SD*	*Respiratory rate (breaths/min) Mean ± SD*
Pre-treatment	82.84 ± 11.55	130.16 ±11.72	83.60±6.455	98.76±0.436	17.04 ±1.37
30 min	81.80 ±12.11	125.84 ±11.78	78.44±8.766	98.16±0.850	16.04 ±1.37
60 min	78.56 ±10.22	122.92 ±11.37	74.84±7.186	98.48±0.823	16.08 ±1.50
90 min	77.72 ±10.39	121.80 ±11.75	75.16±8.050	98.40±0.764	15.84 ±1.57
120 min	77.64 ±10.02	121.92±10.778	76.32±7.846	98.52±0.770	16.12 ±1.30
120 min after surgery	77.20 ±10.63	124.40±11.489	78.00±7.000	98.68±0.627	15.84 ±1.03
Overall P value	<0.001	<0.001	<0.001	<0.001	<0.001

Table 3: Changes in anxiety level following oral melatonin administration (N = 30)

Time point	*Mean anxiety score ± SD*	*No anxiety n (%)*	*Mild anxiety n (%)*	*Moderate anxiety n (%)*	*Severe anxiety n (%)*	*Comparison with baseline*
Pre-treatment	2.24 ±1.39	4 (13.3)	26 (86.7)	0	0	—
30 min	2.00 ±1.58	7 (23.3)	23 (76.7)	0	0	0.083
60 min	0.72 ±0.98	19 (63.3)	11 (36.7)	0	0	<0.001
90 min	0.32 ±0.75	25 (83.3)	5 (16.7)	0	0	<0.001
120 min	0.08 ±0.40	29 (96.7)	1 (3.3)	0	0	<0.001
120 min after surgery	0.00 ±0.00	30 (100)	0	0	0	<0.001

Table 4: Changes in sedation score following oral melatonin administration (N = 30)

Time point	*Mean sedation score ± SD*	*Alert n (%)*	*Arousable to voice n (%)*	*Arousable to tactile stimulation n (%)*	*Score 3–4 n (%)*	*p-value*
Pre-treatment	0.00 ±0.00	30 (100)	0	0	0	—
30 min	0.12 ±0.33	26 (86.7)	4 (13.3)	0	0	0.083
60 min	0.36 ±0.49	19 (63.3)	11 (36.7)	0	0	0.001
90 min	0.76 ±0.44	7 (23.3)	23 (76.7)	0	0	<0.001
120 min	1.08 ±0.40	1 (3.3)	25 (83.3)	4 (13.3)	0	<0.001
120 min after surgery	1.32 ±0.56	1 (3.3)	18 (60.0)	11 (36.7)	0	<0.001

scores also increased progressively while preserving patient responsiveness and cooperation. These observations align with those of Naguib and Samarkandi (1998), who demonstrated superior anxiolysis with melatonin compared with placebo and effects comparable to midazolam[13]. Similar results were reported by Patel and Kurdi (2015) [15] and Kurdi and Muthukalai (2014)[16], who observed effective preoperative anxiolysis without impairment of cognitive or psychomotor performance. Caumo et al. (2007) further demonstrated reduced postoperative analgesic requirements and improved recovery following melatonin administration[17]. Ismail (2009) reported effective anxiolysis and prolonged postoperative analgesia in elderly patients undergoing cataract surgery[12]. Naguib (2006) found that melatonin reduced the induction doses of intravenous anaesthetic agents while providing satisfactory sedation and anxiolysis without affecting orientation[18]. A systematic review by Hansen et al. (2013), which included 12 randomized controlled trials involving 774 patients, concluded that melatonin effectively reduces preoperative anxiety and offers efficacy comparable to benzodiazepines without causing dependence or residual sedation[19,20]. However, some investigators have reported conflicting findings. Capuzzo et al. (2006) found no significant anxiolytic benefit in elderly patients, suggesting that the effect of melatonin may diminish with advancing age[21]. Similarly, Isik et al. (2008)[22], Sury and Fairweather (2006)[23], and Daniel Lee (2009)[14] reported limited

sedative or anxiolytic effects in paediatric or dental populations. A review by Andersen et al. (2014) concluded that although melatonin shows considerable promise, further well-designed clinical studies are required before routine perioperative use can be universally recommended[24].

ll patients in the present study regained complete postoperative orientation, and no episodes of respiratory depression, hemodynamic instability, nausea, vomiting, dizziness, headache, or irritability were observed. These findings agree with those of Yousaf et al. (2010), who described melatonin as a remarkably safe drug with excellent tolerability, even at doses much higher than those used clinically[25,26].Lemoine et al. (2011) demonstrated the long-term safety of prolonged-release melatonin without withdrawal symptoms or suppression of endogenous melatonin production[27,28]. Dollins et al. (1993) also reported minimal adverse effects following oral melatonin administration[29]. Schmidt et al. (2007) observed safe sedation without respiratory depression in children undergoing auditory brainstem response testing[30]. Priyamvada Gupta et al. (2016) similarly reported minimal postoperative adverse events in patients receiving melatonin premedication[11].

Overall, the findings of the present study are consistent with previous studies and suggest that oral melatonin 10 mg administered two hours before surgery is an effective premedicant that provides significant anxiolysis and mild sedation while maintaining hemodynamic stability, preserving postoperative orientation, and demonstrating an excellent safety profile.

Conclusion

Preoperative administration oforal melatonin 10 mg, two hours before elective surgery, provided effective anxiolysis and mild sedation in the patients without causing clinically significant hemodynamic or respiratory changes. All patients remained well-oriented postoperatively, and no drug-related adverse effects were observed. These findings suggest that oral melatonin is a safe andeffective premedicant that reduces preoperative anxiety, provides satisfactory sedation, preserves cognitive recovery, and may serve as a useful alternative to conventional benzodiazepine premedication in patients undergoing elective surgery.

Declaration of patient consent -Written informed consent has been obtained from all the participants .The manuscript has been read and approved by all the authors, the requirements for authorship as stated earlier in this document have been met and each author believes that the manuscript represents honest work.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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