Original Article

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Comparative Evaluation of Oral Melatonin versus Oral Alprazolam as Premedication in Patients Undergoing Tympanoplasty: A Randomised Control Study

Anaesthesia Section

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ABSTRACT

Introduction: Preoperative anxiety is commonly experienced by patients who are admitted to hospital for any surgery and the role of premedication becomes important from an anaesthetist's point of view, to relieve anxiety, provide sedation and ensure adequate analgesia.

Aim: To compare the effects of oral melatonin versus oral alprazolam as premedication and their impact on postoperative recovery characteristics in patients undergoing tympanoplasty.

Materials and Methods: In this randomised controlled study which was conducted from August 2022 to March 2024 at the Department of Anaesthesiology, School of Medical Sciences and Research, Sharda University, Greater Noida, Uttar Pradesh, India, a total of 70 adult patients were randomly allocated into two groups. Group M (n=35) received oral melatonin 6 mg and group A (n=35) received oral alprazolam 0.50 mg 120 minutes before surgery. The objectives of the study were to compare anxiety, sedation, cognition and pain using the Visual Analogue Scale (VAS), Ramsay Sedation Score (RSS), Digit Symbol Substitution Test (DSST) score and Numerical Rating Scale (NRS), respectively. The Shapiro-Wilk test, Independent t-test, Chi-square test and Fisher's-exact test were used for statistical analysis.

Results: The age distribution, gender, body mass index, American Society of Anaesthesiologists (ASA) status and mean duration of surgery were comparable between the two groups. Mean VAS scores were significantly lower in group M at 60 minutes (3.03±1.29 vs 3.77±1.21) and at 120 minutes (2.17±1.12 vs 2.91±1.12). Even in the postoperative period, compared to group A, the VAS score was lower in group M after extubation at various time intervals. RSS scores were lower in group M compared to group A at 60 minutes and at 120 minutes of drug administration. In the postoperative period, compared to group A, group M had lower sedation scores after extubation at 30 minutes, 60 minutes, 90 minutes and 120 minutes (p-value <0.0001). Compared to group A, group M had statistically significantly higher DSST scores at various time intervals in both the preoperative and postoperative periods (p-value <0.0001). group M had significantly lower NRS scores after extubation at various time intervals (p-value <0.0001) compared to group A, indicating that pain was significantly lower in the postoperative period with the use of melatonin.

Conclusion: Oral melatonin (6 mg) is shown to be an effective alternative to alprazolam (0.5 mg) as a premedication. Oral melatonin offered superior anxiolysis while inducing less sedation compared to alprazolam. In addition, there was better preservation of cognitive function with melatonin compared to alprazolam.

Keywords: Anxiety, Cognition, Pain, Sedation, Visual analogue scale

INTRODUCTION

Tympanoplasty, as a surgical procedure, involves the repair and reconstruction of perforations in the tympanic membrane, with or without ossiculoplasty. It can be performed under local anaesthesia, general anaesthesia, or monitored anaesthesia care. Like any surgery, patients undergoing tympanoplasty may experience discomfort due to pain, suction noise, instrument manipulation and head and neck positioning, which can cause stress and result in psychological distress for the patients [1].

Psychological distress is defined as a collective term for levels of anxiety and depression. Among these, preoperative anxiety is commonly experienced by patients admitted to hospital for any surgery. This anxiety can be described as an unpleasant state of tension or uneasiness that arises from a patient's doubts or fears relating to the surgery and anaesthesia. It increases the patient's catecholamine secretion, which may lead to hypertension, tachycardia and arrhythmias. Furthermore, it hinders patients' adjustment in hospitals and is associated with adverse outcomes and unexpected results [2,3].

Due to this psychological distress preceding any surgery, the role of premedication becomes important from an anaesthetist's perspective. The key goals include relieving anxiety, providing sedation and ensuring adequate analgesia [4].

Benzodiazepines (BZDs) are widely used as preoperative medications to induce anxiolysis, amnesia and sedation in patients undergoing surgery. Various drugs belong to the class of BZDs, including midazolam, alprazolam, lorazepam and diazepam. Although they are effective in inducing sedation and anxiolysis, they are associated with side-effects such as increased episodes of arousal during sleep, restlessness and hangover effects. Among benzodiazepines, alprazolam, which is classified as a triazolobenzodiazepine, is noted to be more selective for anxiolysis compared to other members of the group, such as midazolam, lorazepam, or diazepam [5]. Alprazolam is a short-acting drug that exhibits anxiolytic, sedative, hypnotic, anticonvulsant and amnesic effects, albeit with the drawback of causing psychomotor impairment and cognitive dysfunction. Furthermore, alprazolam has also been reported to induce episodes of arousal [6].

Melatonin (N-acetyl-5-methoxytryptamine) is an endogenous pineal hormone produced in the body [7,8]. Its use as a premedication has demonstrated efficacy in providing preoperative sedation and anxiolysis without causing impairment in psychomotor functions,

cognition, or recovery characteristics. From the anaesthetist's perspective, melatonin exhibits good anxiolytic, hypnotic, sedative, anti-inflammatory and antioxidant properties, thereby being classified as an efficacious and safe alternative for premedication during surgeries [9]. Moreover, melatonin addresses restlessness and arousal caused by BZDs through the suppression of endogenous melatonin, since melatonin itself is an endogenous pineal hormone that is administered during premedication. The overall mechanism of melatonin administration may also promote sound sleep, thereby alleviating preoperative stress levels and reducing anxiety [5,6].

Not many studies have been conducted to compare the effects of oral melatonin and alprazolam as premedication for elective surgeries, such as tympanoplasty, in terms of anxiety, sedation, cognition and analgesia [6].

The present study was conducted to compare the two drugs regarding safety and efficacy for anxiety, cognition and postoperative analgesia. The results of this study may facilitate better usage of either drug for providing premedication in surgical procedures.

MATERIALS AND METHODS

The present randomised controlled study was conducted from August 2022 to March 2024 at the Department of Anaesthesiology, School of Medical Sciences and Research, Sharda University, Greater Noida, Uttar Pradesh, India. Ethical approval was obtained from the Institutional Ethical Committee under reference number SU/SMS&R/76-A/2022/88, dated 04/07/2022. The trial was registered with the Central Trials Registry-India under the registration number CTRI/2022/08/044912, dated 25/08/2022. Both the patient and the data collector were blinded to the group to which the patient belonged. Written informed consent was obtained from all participants, ensuring they understood the nature of the study and were willing to allow the use of their data for research.

Sample size calculation: The study conducted by Patel T and Kurdi MS observed that the post-medication sedation score and Digit Symbol Substitution Test (DSST) score were 0.5±0.5 and 27.22±11.05 in the melatonin group, compared to 1.3±0.7 and 18.75±5.75 in the midazolam group [10].

Taking these values as a reference, the sample size was calculated as follows:

The formula for calculation of sample size based on pooled Standard Deviation (SD):

$N \geq 2\ (\text{pooled SD})^2 \times (Z\alpha + Z\beta)^2 / (\text{mean difference})^2$

Where N=sample size

$\text{pooled SD} = \sqrt{(S1^2 + S2^2)/2}$

S1=SD of the melatonin group

S2=SD of the midazolam group

Zα=value of Z at two-sided alpha error of 5%

Zβ=value of Z at power of 95%

mean difference=difference in mean of the two groups.

Calculations were as follows:

1) For post medication sedation score

S1=SD of the melatonin group=0.5

S2=SD of the midazolam group=0.7

$\text{Pooled SD} = \sqrt{0.5^2 + 0.7^2}/2$

$= 0.61$

$N >= 2\ (0.61)^2 \times (1.96 + 1.645)^2 / (0.8)^2$

$>= 15.03$

Sample size=16 (approx.)

2) For post medication DSST score

S1=SD of the melatonin group=11.05

S2=SD of the midazolam group=5.75

$\text{Pooled SD} = \sqrt{11.05^2 + 5.75^2}/2$

$= 8.81$

$N >= 2\ (8.81)^2 \times (1.96 + 1.645)^2 / (8.47)2$

$>= 28.11$

Sample size=29 (approx.)

The minimum required sample size, with 95% power for the study and a 5% level of significance, was determined to be 29 patients in each study group. Considering that case availability was not a constraint during the study period, a larger sample size of 70 patients (35 in each group) was selected to minimise the margin of error.

Inclusion and Exclusion criteria: Patients aged 18 to 60 years of both genders, classified as American Society of Anaesthesiologists (ASA) Grade I/II, who were undergoing tympanoplasty surgery under general anaesthesia, were included in the study. Patients who refused to participate in the study, those receiving steroids, analgesics, anti-epileptics, sedatives, or antipsychotics and individuals with a history of endocrine, cardiovascular, renal, or Central Nervous System (CNS) diseases, chronic pain, mental illness, or allergy to the study drugs were excluded. Pregnant patients, those with a BMI greater than 30 kg/m^2 and individuals who were unable to read and write basic letters and numbers were also excluded from the study.

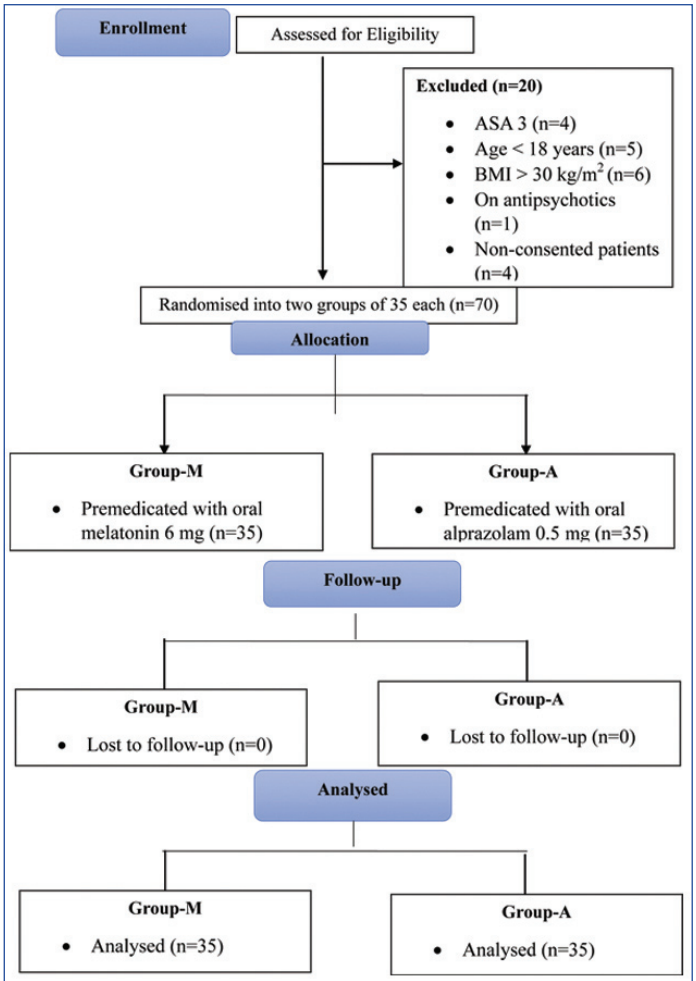
Study Procedure

Before surgery, all patients underwent a pre-anaesthetic check-up. They were informed about the anaesthesia technique and the perioperative course and all were instructed to remain nil per oral for a minimum of eight hours before surgery.

Anxiety levels were assessed using a 10 cm linear VAS, where the extremes of the scale were marked as "no anxiety" at the 0 cm end and "anxiety as bad as it can be" at the 10 cm end [11]. Sedation was assessed using the Ramsay Sedation Scale (RSS) [12]. The Digit Symbol Substitution Test (DSST) was employed to assess the cognition of patients, who were provided with a pencil and paper featuring a key grid of numbers and matching symbols, along with a test section containing numbers and empty boxes [13]. There were five rows of 25 randomly distributed numbers, with their corresponding symbols represented by empty boxes. After 90 seconds, the number of empty boxes filled in by the patient from left to right was counted and a score was given based on the number of correct symbols inserted. Decreased cognitive dysfunction was indicated by lower DSST scores. Pain was assessed using the Numeric Rating Scale (NRS), an 11-point scale where 0 represented 'no pain' and 10 signified 'worst imaginable pain' [14].

A total of 20 patients were excluded from the study based on the exclusion criteria [Table/Fig-1]. All consecutive eligible patients were enrolled. Random allocation was performed using computer-generated random numbers and allocation concealment was ensured by using sequentially numbered opaque sealed envelopes [Table/Fig-1]. On the day of surgery, patients were brought to the preoperative area two hours before the procedure. Baseline assessments were conducted for sedation, anxiety and cognitive function and scores were recorded. The study medications, either oral melatonin 6 mg (group M) or oral alprazolam 0.5 mg (group A/Control group), were administered 120 minutes before anaesthesia induction according to the randomisation [5,15].

Patients were reassessed for anxiety, sedation and cognition at 30, 60, 90 and 120 minutes after taking the medication, both before and after surgery. Intraoperatively, patients were monitored using Electrocardiography (ECG), Pulse Oximetry (SpO_2), Non Invasive Blood Pressure (NIBP) and End-tidal CO_2 ($EtCO_2$). Induction was achieved with injection fentanyl (2 µg/kg), injection propofol (2 mg/kg) and injection vecuronium (0.1 mg/kg). After intubation, anaesthesia was maintained with a mixture of O_2:N_2O in a ratio of 40:60, isoflurane and neuromuscular blockade was sustained by intermittent doses



[Table/Fig-1]: Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

of vecuronium (1 mg every 30 minutes). Nitrous oxide (N_2O) was replaced with air at the time of graft placement. Postoperatively, neuromuscular blockade was reversed with neostigmine and glycopyrrolate and patients were extubated after complete recovery of neuromuscular function, which was ascertained clinically.

STATISTICAL ANALYSIS

The presentation of categorical variables was done in the form of numbers and percentages (%), while quantitative data were presented as mean±Standard Deviation (SD). The normality of the data was assessed using the Shapiro-Wilk test. For statistical analysis, comparisons of quantitative variables were performed using the independent t-test. For qualitative variables, comparisons were analysed using the Chi-square test; if any cell had an expected value of less than 5, Fisher's-exact test was applied. Data entry was conducted in Microsoft Excel and the final analysis was performed using the Statistical Package for Social Sciences (SPSS) software, version 25.0 (IBM, Chicago, USA). A p-value of less than 0.05 was considered statistically significant for all tests.

RESULTS

The demographic characteristics of the study participants indicate that there were no significant differences between group M and group A across various parameters. The age distribution, gender, body mass index, ASA status and mean duration of surgery were comparable between the two groups [Table/Fig-2].

During the preoperative period, group M exhibited significantly lower anxiety levels at 60 and 120 minutes post-administration of the drug (p-value=0.016 and p-value=0.007, respectively). Sedation levels were comparable initially but became significantly higher in group A at 60, 90 and 120 minutes. Cognition scores were significantly better in group M at 60, 90 and 120 minutes post-administration. These findings suggest that group M experienced lower anxiety, less sedation and maintained higher cognitive function compared to group A during the preoperative period [Table/Fig-3].

Demographic profile		Group M (n=35)	Group A (n=35)	p-value
Age (years)		28.51±8.88	27.94±6.66	0.762
Gender	Female	21 (60%)	19 (54.29%)	0.629
	Male	14 (40%)	16 (45.71%)	
ASA Class	I	27 (77.14%)	26 (74.29%)	0.78
	II	8 (22.86%)	9 (25.71%)	
Body mass index (kg/m²)		23.22±2.57	24.28±3.05	0.122
Duration of surgery (min)		111.14±19.06	104.86±22.77	0.215

[Table/Fig-2]: Comparison of demographic characteristics among the study participants.

Variables	Group M (n=35)	Group A (n=35)	p-value
VAS Score for anxiety			
Before administration of drug	4.11±1.55	3.83±1.2	0.391
After 30 minutes	3.97±1.46	3.83±1.2	0.657
After 60 minutes	3.03±1.29	3.77±1.21	0.016
After 90 minutes	2.6±1.38	3.17±1.01	0.052
After 120 minutes	2.17±1.12	2.91±1.12	0.007
RSS for sedation			
Before administration of drug	1.97±0.17	2±0	0.324
After 30 minutes	2.03±0.17	2.03±0.17	1
After 60 minutes	2.03±0.17	2.23±0.43	0.013
After 90 minutes	2.03±0.17	2.83±0.45	<0.0001
After 120 minutes	2.03±0.17	3.03±0.17	<0.0001
DSST for cognition			
Before administration of drug	15.14±7.5	16.63±5.77	0.356
After 30 minutes	21.6±11.21	19.69±6.41	0.384
After 60 minutes	24.83±12.61	19.14±5.64	0.019
After 90 minutes	26.11±13.27	16.31±5	0.0002
After 120 minutes	25.97±13.01	14.83±5.21	<0.0001

[Table/Fig-3]: Comparison of preoperative anxiety, sedation and cognition scores between Group M and A.

The NRS scores for pain were significantly lower in group M than in group A after extubation at 30, 60, 90 and 120 minutes. In the postoperative period, it was observed that VAS scores for anxiety were significantly lower in group M than in group A at 30, 60, 90 and 120 minutes after extubation (p-value <0.0001). group M also had lower sedation scores than group A at 30, 60, 90 and 120 minutes post-extubation (p-value <0.0001). In the postoperative period, when compared to group A, group M had higher DSST scores after extubation at 30, 60, 90 and 120 minutes [Table/Fig-4]. Both drugs had minimal effects on haemodynamics at all time intervals.

Variables	Group M (n=35)	Group A (n=35)	p-value
Postoperative NRS for pain			
After extubation 30 minutes	1.69±0.9	3.66±1.08	<0.0001
After extubation 60 minutes	1.63±0.84	3.49±0.85	<0.0001
After extubation 90 minutes	1.37±0.69	3.2±0.87	<0.0001
After extubation 120 minutes	1.29±0.67	3.14±0.91	<0.0001
Postoperative VAS for anxiety			
After extubation 30 minutes	1.6±0.74	2.71±0.99	<0.0001
After extubation 60 minutes	1.51±0.7	2.63±0.94	<0.0001
After extubation 90 minutes	1.29±0.62	2.51±0.85	<0.0001
After extubation 120 minutes	1.17±0.45	2.4±0.77	<0.0001
Postoperative RSS for sedation			
After extubation 30 minutes	3.14±0.73	3.74±0.44	0.0001
After extubation 60 minutes	2.49±0.56	3.31±0.47	<0.0001

After extubation 90 minutes	2.17±0.38	2.86±0.36	<0.0001
After extubation 120 minutes	2.11±0.32	2.77±0.43	<0.0001
Postoperative DSST for cognition			
After extubation 30 minutes	5.49±5.27	1.17±2.51	<0.0001
After extubation 60 minutes	13.86±7.97	5.03±4.21	<0.0001
After extubation 90 minutes	18.66±9.73	9.17±3.61	<0.0001
After extubation 120 minutes	21.49±11.15	11.03±4.32	<0.0001

[Table/Fig-4]: Comparison of postoperative pain, anxiety, sedation and cognition between Groups M and A.

DISCUSSION

In the present study, anxiety was assessed using the VAS score. Before the administration of the drug, patients in both group M and group A had comparable VAS scores, with a median value of four. Subsequently, after the administration of the drug, the VAS scores were comparable at 30 minutes. Statistically significant differences were found at 60 minutes, where group M fared better in controlling anxiety, exhibiting a lower VAS score at both 60 and 120 minutes. This indicates that melatonin was more effective at providing preoperative anxiolysis compared to alprazolam.

Even in the postoperative period, we observed that the VAS scores were significantly lower in group M when compared with group A at 30, 60, 90 and 120 minutes after extubation. This finding aligns with a similar study by Khare A et al., which compared oral melatonin and oral alprazolam; in group M, there was a significant reduction in the mean VAS score after 120 minutes of administration compared to baseline. In group A, there was also a significant reduction in the mean VAS score after 120 minutes of administration compared to baseline. However, in an intergroup comparison, the mean VAS score was statistically significantly lower in group M than in group A at 120 minutes after the administration of the study drug. Thus, the reduction in anxiety was significantly greater in the melatonin group than in the alprazolam group [6].

Pokharel K et al., reported that VAS anxiety scores were significantly reduced from their baseline scores at various time intervals in both the alprazolam and melatonin groups; however, the difference was not statistically significant between the groups [5]. Among other studies, the efficacy of melatonin has been demonstrated by Ionescu D et al., who compared melatonin and midazolam as premedication in laparoscopic cholecystectomies. They found that oral melatonin resulted in significant anxiolysis postoperatively, with the melatonin group showcasing significantly lower postoperative anxiety scores at 60 minutes and 24 hours postoperatively [16]. This finding was also supported by Ismail SA and Mowafi HA, who reported that melatonin resulted in anxiolysis during cataract surgery under topical anaesthesia, as it led to a significant reduction in the median anxiety scores from five to three after premedication and to three during surgery [17].

Overall, when administered orally, melatonin has been reported to produce significant anxiolysis and sedation within 60-120 minutes after premedication, resulting in calm and tranquil patients with stable haemodynamics and minimal side-effects. In comparison to alprazolam, melatonin appears to be superior in reducing anxiety.

In the present study, sedation was assessed using the Ramsay Sedation Scale (RSS) score, with comparable mean values in group M and group A before the administration of the drug. Statistically significant differences were found in the RSS scores after 60 minutes of drug administration. It was observed that group M achieved lower sedation values compared to group A at 60, 90 and 120 minutes post-administration. The effect on sedation was also highlighted in the postoperative period, wherein group M displayed a lower sedation score compared to group A after extubation at 30, 60, 90 and 120 minutes. This indicates that melatonin caused less sedation than alprazolam.

These findings align with those reported by Khare A et al., who noted that melatonin resulted in less sedation compared to alprazolam. The mean RSS scores were similar in both group M and group A at baseline; however, in group M, there was a significant increase in the mean RSS score after 120 minutes of administration compared to baseline. Similarly, in group A, there was a significant increase in the mean RSS score after 120 minutes of administration compared to baseline. Nonetheless, in an intergroup comparison at 120 minutes after the administration of the drug, the mean RSS score was significantly higher in group A than in group M [6].

The study conducted by Pokharel K et al., also found a significant increase in sedation scores compared to baseline at various time points for both alprazolam and melatonin; however, intergroup comparisons showed that the differences did not reach statistical significance [5]. Similarly, De Witte JL et al., reported that oral alprazolam (0.5 mg) resulted in more sedation compared to placebo within a time frame of 60 to 90 minutes after premedication on the day of surgery [18]. Overall, these findings indicate that melatonin provided adequate sedation while allowing patients to remain arousable, in contrast to alprazolam, which induced relatively more sedation.

In the present study, cognitive functions were assessed using the Digit Symbol Substitution Test (DSST), which revealed comparable DSST scores at baseline between the two groups. However, DSST scores were found to be higher in group M compared to group A at subsequent time intervals after the administration of the drug. Specifically, group M demonstrated statistically significant higher values at 60 minutes, 90 minutes and 120 minutes after drug administration. This finding was also evident in the postoperative period, where group M had higher DSST scores than group A after extubation at 30 minutes, 60 minutes, 90 minutes and 120 minutes. This suggests that melatonin had fewer side-effects on the cognitive functions of the patients.

Similar results were reported in other studies, including one by Khare A et al., with comparable mean DSST scores in both group M and group A at baseline, group M exhibited a significant increase in mean DSST scores after 120 minutes of administration compared to baseline, while group A showed a significant decrease in mean DSST scores after 120 minutes. In an intergroup comparison at 120 minutes post-administration, the mean DSST score was statistically higher in group M compared to group A. Overall, melatonin proved to be more effective in maintaining cognitive function than alprazolam [6].

These findings align with the study conducted by Patel T and Kurdi MS, which examined the effects of oral melatonin and oral midazolam on cognitive and psychomotor functions. They observed an increase in DSST scores in the melatonin group. The mean DSST scores, both before and after premedication in the melatonin group, indicated that scores improved and patients performed better on the test 60-90 minutes after the administration of premedication. This supports the use of melatonin as an effective alternative to midazolam, as it preserves patients' cognitive and psychomotor skills [10].

Similarly, in the study by Naguib M and Samarkandi AH, patients who received melatonin did not exhibit any impairment in cognitive functions, which further favours the use of melatonin. The melatonin group had significantly better DSST scores at 15, 30 and 90 minutes compared to the midazolam group. The study suggested that melatonin can be effectively used as premedication in scenarios where impairment of cognitive and psychomotor functions could negatively impact the patient's wellbeing [7]. Overall, melatonin has demonstrated greater efficacy in preserving cognitive function compared to alprazolam.

The authors also assessed postoperative pain levels using the Numerical Rating Scale (NRS), where they found that, compared to group A, group M had significantly lower NRS scores after extubation at 30 minutes, 60 minutes, 90 minutes and 120 minutes. This indicates that pain was significantly lower in the postoperative stage with the use of melatonin. In line with this, Javaherforooshzadeh F et al., compared melatonin with a placebo and found that administering 6 mg of melatonin was more effective in reducing pain after lumbar surgery, as significantly more patients reported less pain in the recovery room postsurgery [19].

Ismail SA and Mowafi HA also observed that, compared to the placebo group, the melatonin group had significantly lower median perioperative verbal pain scores and a reduced intraoperative need for fentanyl (p=0.007) [17]. In comparison, the study by Haddadi S et al., found that administering 6 mg of melatonin one hour before cataract surgery significantly reduced pain experienced under a retrobulbar block and the requirement for additional doses of fentanyl was also lower [20]. Overall, the administration of melatonin can decrease anxiety and improve sleep, which may contribute to a reduction in the intensity of pain.

From the anaesthesiologist's perspective, it is crucial to manage the haemodynamic changes that occur following anaesthesia induction. In the present study, the authors found that both drugs had minimal effects on haemodynamics. Regarding heart rate, values were comparable between group M and group A at baseline before drug administration, remaining within the normal range and both groups demonstrated similar values at 30, 60, 90 and 120 minutes after drug administration.

Even in the postoperative stage, group A displayed a comparable heart rate to group M, with a p-value of more than 0.05. Similarly, blood pressure was maintained in both the preoperative and postoperative stages, with Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP) exhibiting mild fluctuations while remaining within the normal range, without any significant hypotension or oxygen desaturation.

Among other studies, Haddadi S et al., found that melatonin did not affect the haemodynamic parameters during the retrobulbar block, nor during any of the operative or postoperative stages [20]. Ismail SA and Mowafi HA also reported that there was no significant difference in heart rate between the two groups at any time point, although a mild decrease in MAP was noted following melatonin administration [17]. These findings are consistent with those of Pokharel K et al., and Khare A et al., where both melatonin and alprazolam did not induce adverse haemodynamic disturbances such as hypotension, bradycardia, or tachycardia. Overall, the anxiolytic effects of either drug may potentially contribute to the haemodynamic stability observed following their administration [5,6].

In addition to various pharmacological agents, several non pharmacological methods have also been employed to alleviate preoperative anxiety. These include cognitive-behavioural therapy, spiritual/religious interventions, music therapy, preoperative preparation videos, aromatherapy, massage, meditation, guided imagery relaxation therapy, hypnosis and acupuncture. Due to the side-effects associated with pharmacological interventions for preoperative anxiety, non pharmacological approaches are increasingly suggested as alternatives. Overall, few side-effects have been reported concerning non pharmacological interventions, making them suitable for patients of different ages and with various types of diseases and surgeries. However, due to ongoing controversies regarding the efficacy of these interventions for preoperative anxiety, more randomised clinical trials with larger sample sizes are required to evaluate their effectiveness [21]. Additionally, various other drugs such as gabapentin, pregabalin and flupirtine have also been used to alleviate preoperative anxiety [22,23].

Limitation(s)

The study has several limitations, as it was a single-centre study without any long-term follow-up. Secondly, among benzodiazepines, only alprazolam was compared. Thirdly, recovery time, the incidence of postoperative nausea and vomiting and patient satisfaction were not evaluated. Lastly, the dosages of either drug were not varied or compared.

CONCLUSION(S)

The analysis of the results and observations from the present study revealed that oral melatonin, at a dose of 6 mg administered 120 minutes prior to induction, is more effective in controlling anxiety and pain, both before and after surgery, when compared to oral alprazolam (0.5 mg). Unlike oral alprazolam, oral melatonin does not cause excessive sedation or impairment in cognitive function. Both drugs demonstrate comparable haemodynamic stability. Thus, it is concluded that oral melatonin (6 mg) may be used effectively for patients where anxiolysis, along with the maintenance of cognitive function, effective pain management and reduced sedation in the postoperative period, are priorities. These results can assist in improving anaesthetic practices and patient care strategies, providing evidence-based guidance to clinicians regarding the use of melatonin and alprazolam as premedication before surgeries.

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