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Original Article

Perioperative Administration of Oral Melatonin for Hemodynamic and Analgesic Control during Dental Implant Placement: A Clinical Study

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ABSTRACT

Background: Despite melatonin's established pharmacologic profile as an anxiolytic and antioxidant agent, its perioperative use in implant dentistry remains underexplored. As patient anxiety and hemodynamic fluctuations during oral surgical procedures can impact outcomes, investigating safe and effective premedication strategies is of clinical relevance. **Aim:** To evaluate the efficacy of oral melatonin in maintaining hemodynamic stability, and minimizing postoperative pain in patients undergoing implant placement. **Materials and Methods:** This clinical study included 80 systemically healthy participants aged 25-60 years, scheduled for single-tooth implant placement in the molar region. Participants were randomly assigned to receive either 6 mg oral melatonin or a placebo 30 min prior to surgery. Hemodynamic parameters-Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and Heart Rate (HR)-were recorded at baseline (T0), 20 min into surgery (T1), and immediately postoperatively (T2). Postoperative pain was assessed using a visual analog scale (VAS). Statistical analysis included independent *t*-tests and repeated measures ANOVA ($p<0.05$ considered significant). **Results:** Melatonin significantly reduced postoperative pain (VAS: 3.54±0.19) compared to placebo (VAS: 6.89±0.25; $p=0.000$). Significant reductions in SBP, DBP, and HR were observed in the melatonin group across all time points ($p<0.05$), with significant intergroup differences at T1 and T2. No adverse effects were reported. **Conclusion:** Oral melatonin is a safe, effective, and well-tolerated premedication that stabilizes hemodynamic responses, and alleviates postoperative pain in implant patients.

Keywords: Hemodynamic Stability, Implant Dentistry, Melatonin, Premedication.

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INTRODUCTION

Dental implant therapy has become a cornerstone of restorative dentistry, offering predictable functional and aesthetic outcomes for the replacement of missing teeth.[1-3] However, despite the procedural advancements and high success rates, undergoing implant surgery can provoke significant preoperative anxiety in patients. This anticipatory stress is frequently triggered by the fear of pain, unfamiliar clinical environments, and invasive procedures, and may manifest as physiological alterations, including elevated heart rate, increased blood pressure, and other stress-related responses. These physiological fluctuations can complicate surgical procedures and negatively influence patient cooperation and healing outcomes.[4]

Traditionally, pharmacological agents such as benzodiazepines and sedatives have been employed to alleviate preoperative anxiety. While effective, their use is limited by undesirable side effects such as excessive sedation, cognitive impairment, dependency potential, and interference with intraoperative monitoring.[5] As a result, there is growing interest in identifying safer, non-sedating alternatives that can mitigate anxiety without compromising patient alertness or procedural safety.[6]

Melatonin, an indoleamine synthesized primarily by the pineal gland, has garnered considerable attention for its anxiolytic, antioxidant, and anti-inflammatory properties.[7] Best known for its role in circadian rhythm regulation, melatonin also modulates gamma-aminobutyric acid receptors, contributing to its calming effect on the central nervous system.[8] Unlike conventional anxiolytics, melatonin is associated with minimal side effects

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and does not impair psychomotor performance, making it particularly suitable for short, outpatient surgical interventions like dental implant placement. In addition to its anxiolytic profile, melatonin has been shown to enhance bone metabolism by promoting osteoblast activity, collagen production, and mineral deposition-processes essential for implant osseointegration.[9] These pleiotropic properties present melatonin as a potentially valuable adjunct in implant dentistry, with the added advantage of enhancing the biological environment for implant success.

Despite its well-established pharmacologic profile, clinical evidence supporting the perioperative use of melatonin in implant dentistry remains scarce. The present study was designed to evaluate the efficacy of oral melatonin in maintaining hemodynamic stability and reducing postoperative pain in patients undergoing implant placement. By comparing melatonin with placebo, this study seeks to explore its potential integration into implant protocols as a well-tolerated and effective anxiolytic agent, thereby improving patient comfort and surgical outcomes in a minimally invasive manner.

MATERIALS AND METHODS

Study Design

This clinical study was conducted in the Department of Implantology at Saveetha Dental College and Hospitals, Chennai, India. A total of 80 participants, aged between 25 and 60 years, who required single-tooth implant placement in either the maxillary or mandibular molar region, were enrolled. Inclusion criteria comprise systemically healthy individuals aged 25-60 years with a single missing molar tooth suitable for implant-supported prosthetic restoration. Exclusion criteria included individuals with a history of tobacco use or smoking, pregnant or lactating women, patients with systemic conditions, recent antibiotic use, or any pharmacologic therapy within the past six months, subjects with current or previous periodontitis, patients taking mood stabilizers or sedatives, and individuals with known drug allergies.

Prior to the commencement of the study, ethical clearance was obtained from the Institutional Review Board of Saveetha University, and informed written consent was secured from all participants. The required sample size was determined using G*Power software (version 3.1.9.4), based on previously published data regarding mean and standard deviation.[10]

Intervention

Participants were randomly allocated into two groups:

Group 1 - Test (n=40): Received 6 mg of oral melatonin 30 min before the start of implant surgery.

Group 2 - Control (n=40): Received a placebo identical in size and appearance 30 min before the start of implant surgery.

Surgical Protocol

All implant surgeries were performed by a single operator (PJ) following a standardized surgical protocol. Participants rinsed with 2% chlorhexidine mouthwash for 1 min before the procedure. Local anaesthesia was administered using 2% lidocaine with 1:100,000 epinephrine, not exceeding a total dose of 6 mL. SLA implants (SLA®, Straumann, Basel, Switzerland) were placed using a sequential drilling technique. The total surgical duration was limited to 45 min.

Melatonin (6 mg; Healthvit Supplements, West-Coast Pharmaceutical Works Ltd., India) or matching placebo tablets were administered 30 min before surgery. The placebo was manufactured to match melatonin in both shape and color to ensure blinding.

Outcome Assessment

Pain perception was assessed using a Visual Analog Scale (VAS) ranging from 0 (no pain) to 10 (severe pain), immediately after surgery. Hemodynamic parameters-Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and Heart Rate (HR)-were recorded at three time points: baseline (T0), 20 min into the procedure (T1), and immediately post-procedure (T2). A single calibrated examiner (AR) performed all assessments to ensure consistency. Following the assessments, postoperative instructions were provided, and appropriate antibiotics and analgesics were prescribed.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, Version 23.0; SPSS Inc., Chicago, IL, USA). The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Inter-group comparisons of continuous variables (age, postoperative pain scores, SBP, DBP, and HR) were conducted using the independent t-test. Gender distribution between the groups was compared using the Chi-square test. Intra-group comparisons of SBP, DBP, and HR across the three time points were analyzed using one-way repeated measures ANOVA. A p-value <0.05 was considered statistically significant.

RESULTS

The baseline demographic profile between the Melatonin (Group 1) and Placebo (Group 2) cohorts revealed no significant differences. Group 1 included 22 males (55%) and 18 females (45%), while Group 2 comprised 21 males (52.5%) and 19 females (47.5%), with a p-value of 0.815. The mean age of participants was 40.13±3.7 years in the Melatonin group and 41.35±4.5 years in the Placebo group, showing no significant difference (p=0.873) (Table 1).

Table 1: Characteristics of study groups in relation to gender and age.

Variables	Group 1 (Melatonin) (*n*=40)	Group 2 (Placebo) (*n*=40)	*p* value
Male	22 (55%)	21 (52.5%)	0.815[a]
Female	18 (45%)	19 (47.5%)	
Age (years; Mean±SD)	40.13±3.7	41.35±4.5	0.873[b]

[a]Chi-square test, [b]Independent *t*-test.

Table 2: Comparison of postoperative pain scores of study groups.

Group	VAS Score (Mean±Standard Deviation)	*p* value (intergroup comparison) [a]
Melatonin	3.54±0.19	0.000*
Placebo	6.89±0.25	

[a] Independent *t* test; * Statistically significant.

There were no adverse effects reported by participants in either group. A statistically significant reduction in postoperative pain was observed in the Melatonin group compared to the Placebo group. The mean VAS score in the Melatonin group was 3.54±0.19, whereas the Placebo group reported a significantly higher score of 6.89±0.25. The intergroup comparison yielded a *p*-value of 0.000, indicating a highly significant analgesic effect of melatonin administration in the postoperative period (Table 2).

SBP, DBP, and HR showed significant reductions in the Melatonin group across all time intervals. For SBP, values declined from 126.5±2.2 mmHg at baseline to 120.6±2.1 at 20 min and 118.2±2.1 postoperatively (p=0.002), while the Placebo group showed non-significant changes (p=0.065). Intergroup comparisons at T1 and T2 were significant (p=0.014 and 0.005, respectively). Similarly, DBP in the Melatonin group dropped from 84.4±1.6 to 78.2±2.8 mmHg (p=0.001), whereas the Placebo group showed no significant intragroup change (p=0.059), but intergroup comparisons at T1 and T2 were significant (p=0.032 and 0.027). HR followed a comparable trend, decreasing significantly in the Melatonin group (82.5±3.1 to 72.8±3.2 bpm, p=0.001), with non-significant variation in the Placebo group (p=0.187), and significant intergroup differences at both T1 and T2 (p=0.041 and 0.012, respectively) (Table 3).

DISCUSSION

With the rapid advancements and growing interest in oral implantology, current research is increasingly focused on optimizing patient outcomes during implant procedures.[11-13] The present study evaluated the perioperative efficacy of oral melatonin in patients undergoing implant surgery, with a particular focus on hemodynamic stability and postoperative pain control. Although no previous studies have assessed melatonin in the context of implant placement, our findings are supported by related literature in oral surgery and dental anaesthesia. In our study, melatonin significantly reduced systolic and diastolic blood pressure, heart rate, and postoperative pain scores compared to placebo, indicating a beneficial anxiolytic and analgesic profile. These results suggest that melatonin has the potential to modulate perioperative stress responses and improve patient comfort during implant procedures.

Several previous studies provide indirect but relevant evidence supporting our findings. Torun *et al.*,[14] conducted a double-blinded randomized controlled trial comparing oral melatonin with oral midazolam and placebo in patients undergoing third molar extraction. They found that melatonin significantly reduced anxiety without impairing cognitive or psychomotor function, suggesting it as a safe alternative to traditional sedatives. Similarly, Mukherjee *et al.*,[15] compared the anxiolytic effects of oral melatonin and music therapy in patients undergoing mandibular third molar surgery and reported that melatonin significantly reduced blood pressure and pulse rate, with a concurrent decrease in salivary cortisol levels-highlighting its physiological and endocrine effects on stress reduction. In a randomized trial by Seet *et al.*,[16] melatonin was administered 90 min before the extraction of all four wisdom teeth under general anaesthesia. Their analysis revealed that female patients had a significantly faster reduction in both pain and anxiety scores compared to placebo, reinforcing melatonin's role in modulating surgical stress, with a possible gender-related variation in response.

Pediatric studies have shown similar findings; Isik *et al.*,[17] reported that melatonin did not achieve the sedation success rates of midazolam but performed better than placebo, suggesting a mild sedative effect. Ansari *et al.*,[18] and Faghihian *et al.*,[19] also documented the effectiveness of oral melatonin as premedication for intravenous sedation and general anaesthesia in children, highlighting its safety and utility across age groups. In the domain of major oral surgeries, Lee *et al.*,[20] demonstrated the neuroprotective and antioxidant benefits of melatonin following orthognathic surgery. Over 21 days of oral melatonin intake, patients showed faster nerve healing, reduced pain, and improved antioxidant profiles. Their findings not only highlighted melatonin's capacity to alleviate postoperative discomfort, but also its role in modulating oxidative stress and enhancing neurosensory recovery-mechanisms that may underlie the reduced pain and stabilized vitals observed in our study. Also, topical melatonin gel in patients undergoing fixed appliance therapy showed a positive effect in terms of gingival and oral health and a reduction in salivary nickel and chromium levels.[21] Moreover, numerous studies[22-24] have documented that the adjunctive use of topical or

Table 3: Comparison of hemodynamic parameters.

Variables	Group	Baseline (T0)	20 min (T1)	Post-op (T2)	*p* value (intragroup comparison) [a]
SBP (mmHg)	Melatonin	126.5±2.2	120.6±2.1	118.2±2.1	0.002*
	Placebo	125.1±2.4	124.1±2.2	120.6±2.3	0.065
p value (intergroup comparison)[b]		0.341	0.014*	0.005*	
DBP (mmHg)	Melatonin	84.4±1.6	81.8±1.5	78.2±2.8	0.001*
	Placebo	84.0±1.9	83.5±1.7	81.1±2.1	0.059
p value (intergroup comparison)[b]		0.573	0.032*	0.027*	
Heart Rate (bpm)	Melatonin	82.5±3.1	78.5±2.8	72.8±3.2	0.001*
	Placebo	83.2±3.4	82.3±2.9	80.5±3.6	0.187
p value (intergroup comparison)[b]		0.658	0.041*	0.012*	

[a] ANOVA; [b] Independent *t* test; * Statistically significant.

systemic melatonin in periodontal therapy results in significant improvement in key clinical parameters, including gingival index scores, probing pocket depth, periodontal index, and bleeding on probing. Furthermore, studies by Hazzaa *et al*.,[25] and El-Gammal *et al*.,[26] have shown that local application of melatonin on implant surfaces significantly enhanced bone density, implant stability, and marginal bone preservation, reinforcing melatonin's dual role as a modulator of inflammation and a promoter of peri-implant tissue regeneration.

The strength of the present study lies in its novel focus on oral melatonin as a premedication strategy specifically for implant surgery-a clinical scenario in which its application remains underexplored. The study design, strict inclusion criteria, and homogeneity of the study groups enhanced the internal validity of the results. Furthermore, the combined use of subjective measures (pain via VAS) and objective physiological parameters (SBP, DBP, and HR) provided a comprehensive assessment of melatonin's perioperative effects. However, this study was confined to immediate postoperative outcomes, without evaluation of long-term parameters such as healing progression, implant osseointegration, or patient-reported quality of life. Despite these constraints, the findings suggest that oral melatonin is a safe, well-tolerated, and cost-effective premedication with significant hemodynamic, and analgesic benefits. Further multicenter trials are warranted to validate these findings and explore the potential integration of melatonin into standardized implantology protocols.

CONCLUSION

This study demonstrated that oral melatonin, when administered prior to implant placement, effectively stabilizes hemodynamic parameters including systolic and diastolic blood pressure and heart rate and significantly lowers postoperative pain levels. Its superior anxiolytic and analgesic effects, observed without any adverse events, support its use as a safe and effective premedication in implant dentistry.

ABBREVIATIONS

SBP: Systolic blood pressure; **DBP:** Diastolic blood pressure; **HR:** Heart rate; **VAS:** Visual analog scale.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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