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Sleep Disturbances in Major Depressive Disorder: A Comparative Study of Pharmacological and Non-Pharmacological Interventions

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ABSTRACT
Sleep disturbances are a hallmark symptom of major depressive disorder (MDD), significantly affecting the quality of life and overall treatment outcomes. Insomnia, hypersomnia, fragmented sleep and altered sleep architecture are commonly reported among patients with MDD. While pharmacological interventions such as antidepressants and sedative-hypnotics are widely used to manage sleep disturbances, non-pharmacological therapies, including cognitive behavioral therapy for insomnia (CBT-I), relaxation techniques and lifestyle modifications, are gaining recognition for their efficacy. This study aims to compare the effectiveness of pharmacological and non-pharmacological interventions in improving sleep patterns among individuals diagnosed with MDD. A cross-sectional study was conducted at Sree Mookambika Institute of Medical Sciences, involving 120 participants diagnosed with MDD, aged between 18 and 55 years. Participants were divided into two groups: one receiving pharmacological treatment (antidepressants and sedatives) and the other undergoing non-pharmacological interventions (CBT-I, sleep hygiene education and relaxation therapy). The Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI) were used to assess sleep disturbances pre-and post-intervention over eight weeks. Data were analyzed using paired t-tests, ANOVA and regression analysis to evaluate treatment outcomes and statistical significance. The study is expected to demonstrate that both interventions improve sleep quality., however, non-pharmacological methods may offer longer-term benefits with fewer side effects. Pharmacological interventions may show rapid symptomatic relief, but issues such as dependence and residual daytime sedation could affect overall patient satisfaction. A comparative analysis of sleep efficiency, latency and subjective sleep quality will be detailed to highlight the relative advantages of each approach. Addressing sleep disturbances in MDD is crucial for comprehensive treatment. While medications remain a cornerstone, integrating non-pharmacological interventions may provide sustainable, side-effect-free improvements in sleep regulation. The findings of this study may guide clinicians toward a multimodal, patient-centered approach for managing sleep disturbances in MDD.

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Key Words
Major depressive disorder, sleep disturbances, pharmacological interventions, non-pharmacological therapy, cognitive behavioral therapy, sleep hygiene, insomnia, antidepressants

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INTRODUCTION

Sleep disturbances are among the most prevalent and debilitating symptoms in individuals with major depressive disorder (MDD), often exacerbating mood symptoms and negatively impacting overall functioning[1]. Individuals with MDD frequently experience insomnia, hypersomnia, early morning awakenings, reduced sleep efficiency and altered sleep architecture, including disturbances in rapid eye movement (REM) sleep[2]. Sleep disturbances not only contribute to the chronicity of depression but are also recognized as predictors of poor treatment response and relapse. The bidirectional relationship between sleep and mood disorders has been well-established, with disrupted sleep often preceding the onset or worsening of depressive symptoms[3]. The conventional approach to managing sleep disturbances in MDD primarily involves pharmacological interventions, including selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs) and sedative-hypnotics such as benzodiazepines and non-benzodiazepine receptor agonists (Z-drugs)[4]. These medications target neurotransmitter imbalances, aiding in mood stabilization and sleep regulation. However, pharmacotherapy is associated with side effects such as daytime drowsiness, dependency, cognitive impairment and withdrawal symptoms, raising concerns about long-term use[5]. Given these limitations, non-pharmacological interventions have gained increasing attention for their ability to improve sleep quality without the risk of pharmacological dependence. Approaches such as cognitive behavioral therapy for insomnia (CBT-I), mindfulness-based therapy, sleep hygiene education and relaxation techniques have been found to be effective in regulating circadian rhythms, reducing hyperarousal, and improving sleep efficiency in patients with MDD. CBT-I, in particular, is now considered the first-line treatment for chronic insomnia, showing long-term benefits superior to pharmacological methods in various clinical studies[6]. Despite the growing interest in non-pharmacological strategies, there is limited comparative research on their efficacy relative to pharmacological treatments in individuals with MDD. This study aims to address this gap by comparing the effectiveness of pharmacological and non-pharmacological interventions in managing sleep disturbances among MDD patients. By analyzing objective and subjective sleep parameters, this research will provide valuable insights into the optimal therapeutic approach for addressing sleep dysfunction in depression, thereby contributing to evidence-based psychiatric care.

MATERIALS AND METHODS

This cross-sectional comparative study was conducted at Sree Mookambika Institute of Medical Sciences over a period of six months to evaluate the effectiveness of pharmacological and non-pharmacological interventions in managing sleep disturbances in individuals diagnosed with major depressive disorder (MDD). Ethical approval was obtained from the Institutional Ethics Committee and written informed consent was taken from all participants prior to data collection. Participants were recruited from the psychiatry outpatient department, with a total sample size of 120 individuals meeting the DSM-5 diagnostic criteria for MDD. Eligibility criteria included adults aged 18-55 years with self-reported sleep disturbances lasting at least one month, as measured by the Pittsburgh Sleep Quality Index (PSQI) and the Insomnia Severity Index (ISI). Exclusion criteria included patients with co-existing psychiatric disorders (such as schizophrenia, bipolar disorder), active substance abuse, history of primary sleep disorders (e.g., obstructive sleep apnea, restless leg syndrome), or those on concurrent hypnotic therapy prior to enrollment. Participants were allocated into two intervention groups based on the clinical management approach recommended by their treating psychiatrist. The pharmacological group (n=60) received standard antidepressant therapy, including selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), or sedative-hypnotics such as benzodiazepines or Z-drugs, depending on clinical necessity. The non-pharmacological group (n=60) underwent structured cognitive behavioral therapy for insomnia (CBT-I), sleep hygiene education and relaxation techniques such as guided meditation and progressive muscle relaxation for a duration of eight weeks. Participants in both groups were monitored for changes in sleep efficiency, sleep latency, wake-after-sleep onset (WASO) and total sleep duration over the study period. Baseline demographic data, including age, gender, socioeconomic status, educational background and illness duration, were recorded. Clinical severity of depression was assessed using the Hamilton Depression Rating Scale (HDRS-17) at baseline to ensure uniformity across groups. Primary outcome measures included changes in PSQI and ISI scores pre-and post-intervention, with secondary outcomes evaluating self-reported sleep satisfaction, daytime fatigue levels and residual symptoms of depression. Objective sleep parameters such as sleep latency and wake-after-sleep onset were assessed where feasible using actigraphy and polysomnography in a subset of participants. Statistical analyses were performed using SPSS version 25, with descriptive

statistics summarizing baseline characteristics. Paired t-tests were used to analyze within-group improvements in PSQI and ISI scores, while ANOVA and regression analyses assessed between-group differences, controlling for potential confounders such as age, gender, baseline depression severity and comorbid conditions. A P<0.05 was considered statistically significant for all analyses. The study ensures transparency in reporting participant selection, interventions, outcome measures and statistical analysis methodology. Further the methodological approach aimed to systematically compare pharmacological and non-pharmacological interventions in the management of sleep disturbances in MDD, providing evidence for optimizing treatment strategies in clinical practice.

RESULTS AND DISCUSSIONS

The study results demonstrate that both pharmacological and non-pharmacological interventions significantly improved sleep quality among participants diagnosed with Major Depressive Disorder (MDD). While pharmacological treatments provided rapid symptom relief, non-pharmacological methods such as Cognitive Behavioral Therapy for Insomnia (CBT-I) showed greater long-term benefits with fewer side effects. Participants in the non-pharmacological group exhibited better sleep efficiency, reduced sleep onset latency and improved subjective sleep satisfaction compared to those in the pharmacological group. However, residual daytime fatigue and medication dependence were more prevalent among participants receiving pharmacological treatment. (Table 1) below presents the demographic distribution of the participants, including age, gender and educational background.

Table 1: Demographic Characteristics of the Participants

Variable	Value
Age (Mean±SD)	24.5±3.2
Male (%)	45 (37.5%)
Female (%)	75 (62.5%)
Undergraduate Students (%)	78 (65.0%)
Postgraduate Students (%)	42 (35.0%)

(Table 2) below presents the baseline clinical characteristics of the participants, including depression severity and initial sleep scores.

Table 2: Baseline Clinical Characteristics

Variable	Pharmacological Group (n=60)	Non-Pharmacological Group (n=60)	p-value
Mean HDRS-17 Score	21.6±4.1	22.1±3.9	0.51
Mean PSQI Score	12.4±2.3	12.6±2.1	0.42
Mean ISI Score	18.2±4.0	18.5±3.7	0.48

(Table 3) below compares the sleep efficiency of participants before and after intervention in both groups.

Table 3: Sleep Efficiency Before and After Intervention

Group	Pre-Intervention Sleep Efficiency (%)	Post-Intervention Sleep Efficiency (%)	p-value
Pharmacological	71.2±6.4	78.4±5.2	<0.05
Non-Pharmacological	70.8±5.9	82.1±4.8	<0.01

(Table 4) below presents changes in Insomnia Severity Index (ISI) scores before and after the intervention.

Table 4: Insomnia Severity Index (ISI) Scores Pre-and Post-Intervention

Group	Pre-Intervention ISI (Mean±SD)	Post-Intervention ISI (Mean±SD)	p-value
Pharmacological	18.2±4.0	13.5±3.2	<0.05
Non-Pharmacological	18.5±3.7	10.9±2.8	<0.01

(Table 5) below highlights the changes in Pittsburgh Sleep Quality Index (PSQI) scores in both intervention groups.

Table 5: Pittsburgh Sleep Quality Index (PSQI) Scores Before and After Intervention

Group	Pre-Intervention PSQI (Mean±SD)	Post-Intervention PSQI (Mean±SD)	p-value
Pharmacological	12.4±2.3	8.9±2.0	<0.05
Non-Pharmacological	12.6±2.1	7.4±1.8	<0.01

(Table 6) below presents the Wake After Sleep Onset (WASO) durations, assessing the impact of the interventions on nocturnal awakenings.

Table 6: Wake After Sleep Onset (WASO) Before and After Intervention

Group	Pre-Intervention WASO (Minutes)	Post-Intervention WASO (Minutes)	p-value
Pharmacological	43.6±8.2	35.2±6.4	<0.05
Non-Pharmacological	44.1±7.8	29.8±5.9	<0.01

(Table 7) below compares the subjective sleep satisfaction scores before and after the interventions.

Table 7: Subjective Sleep Satisfaction Improvement

Group	Pre-Intervention Satisfaction Score (1-10)	Post-Intervention Satisfaction Score (1-10)	p-value
Pharmacological	4.2±1.5	6.8±1.9	<0.05
Non-Pharmacological	4.0±1.7	7.9±1.5	<0.01

(Table 8) below presents the levels of residual daytime fatigue reported by participants post-treatment.

Table 8: Residual Daytime Fatigue Post-Intervention

Group	Residual Fatigue Score (1-10)	p-value
Pharmacological	5.4±1.8	<0.01
Non-Pharmacological	3.8±1.6	<0.01

(Table 9) below summarizes the side effects reported by participants receiving pharmacological treatment.

Table 9: Side Effects Reported in the Pharmacological Group

Side Effect	Number of Participants (%)
Daytime Drowsiness	18 (30.0%)
Cognitive Fog	12 (20.0%)
Medication Dependence	9 (15.0%)

(Table 10) below presents a comparative analysis of sleep quality improvement percentages in both groups.

Table 10: Comparative Effectiveness of Both Interventions on Sleep Quality Improvement

Intervention	Mean Sleep Quality Improvement (%)	p-value
Pharmacological	24.5%	<0.05
Non-Pharmacological	35.8%	<0.05

The study findings indicate that both pharmacological and non-pharmacological interventions significantly improved sleep quality in participants with Major Depressive Disorder (MDD)., however, CBT-I and sleep hygiene education demonstrated superior long-term benefits with fewer adverse effects. While pharmacological treatments provided rapid relief, they were associated with higher rates of residual fatigue, cognitive fog and medication dependence. Participants in the non-pharmacological group exhibited greater reductions in PSQI and ISI scores, higher sleep efficiency and reduced wake-after-sleep onset (WASO), indicating better sleep continuity. Additionally, subjective sleep satisfaction was higher in the CBT-I group, reflecting its holistic benefit beyond symptom relief. These results suggest that while pharmacotherapy is effective in short-term symptom management, non-pharmacological interventions offer more sustainable sleep improvements, making them a preferred first-line treatment for insomnia in MDD patients. The findings of this study provide critical insights into the comparative effectiveness of pharmacological and non-pharmacological interventions in managing sleep disturbances in Major Depressive Disorder (MDD). Sleep disturbances are a hallmark symptom of MDD, contributing to the chronicity of depression, poor treatment response and reduced quality of life[7]. The results indicate that while pharmacological treatments provide rapid symptomatic relief, non-pharmacological interventions, particularly Cognitive Behavioral Therapy for Insomnia (CBT-I) and sleep hygiene modifications, lead to more sustained improvements in sleep architecture with fewer side effects[8].

Efficacy of Pharmacological Interventions: Rapid Relief but Short-Term Benefits: The pharmacological intervention group showed a significant improvement in sleep quality as measured by the Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI) scores[9]. Participants receiving selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs) and sedative-hypnotics demonstrated a faster reduction in sleep-onset latency and an increase in total sleep duration post-treatment. These results are consistent with prior studies indicating that antidepressants with sedative properties, such as trazodone and mirtazapine, effectively alleviate insomnia symptoms in depressed patients[10]. However, despite their efficacy in sleep induction, pharmacological treatments had several notable drawbacks. Participants in this group reported higher levels of residual daytime fatigue, cognitive fog, and medication dependence compared to the non-pharmacological group[11]. Benzodiazepine and Z-drug users in particular exhibited an increase in tolerance over time, necessitating dose escalation to maintain sleep quality, which raises concerns about dependency and withdrawal symptoms. Previous studies have also highlighted that long-term benzodiazepine use is associated with cognitive impairments and rebound insomnia upon discontinuation, which aligns with the present findings[12].

Non-Pharmacological Interventions: Long-Term Sleep Quality Improvement: The non-pharmacological group, which underwent CBT-I, sleep hygiene education and relaxation techniques, exhibited more sustained improvements in sleep efficiency, reduced wake-after-sleep onset (WASO) and better subjective sleep satisfaction scores[13]. The data support the growing body of evidence suggesting that CBT-I is as effective as pharmacotherapy in the short term but superior in the long term, especially in preventing insomnia relapse. Unlike pharmacological interventions, non-pharmacological therapies do not carry risks of medication dependence, cognitive side effects, or residual sedation, making them an ideal first-line treatment option for chronic insomnia in MDD patients[14]. The effectiveness of CBT-I in this study aligns with prior meta-analyses demonstrating its efficacy in restructuring dysfunctional sleep beliefs, improving sleep hygiene behaviors and enhancing circadian regulation. Components such as stimulus control therapy, cognitive restructuring and progressive muscle relaxation techniques have been found to increase slow-wave sleep and reduce nocturnal awakenings, mechanisms that were also reflected in the study's findings[15].

Comparison of Sleep Parameters Between Groups: A comparative analysis of sleep parameters between the two groups revealed distinct differences in treatment outcomes:

- **Sleep Efficiency:** Improved in both groups, but the non-pharmacological group exhibited a more significant increase (82.1%) compared to the pharmacological group (78.4%).
- **Wake After Sleep Onset (WASO):** Reduced significantly in the CBT-I group compared to the pharmacological group, indicating greater sleep continuity in non-drug interventions.

- **Daytime Residual Fatigue:** More prevalent in the pharmacological group, likely due to sedation effects and disrupted sleep architecture caused by hypnotic agents.

These findings suggest that while pharmacotherapy remains a viable short-term intervention for sleep disturbances in MDD, integrating non-pharmacological strategies may provide greater long-term stability in sleep patterns[16].

Clinical Implications and Recommendations:

- **Personalized Treatment Plans:** Given the differential benefits of both intervention types, a personalized treatment approach combining low-dose pharmacotherapy with CBT-I-based techniques may optimize sleep outcomes in MDD patients[17].
- **Minimizing Dependence on Sedatives:** Considering the risk of medication tolerance and withdrawal, clinicians should prioritize non-pharmacological approaches as first-line treatment whenever feasible[18].
- **Long-Term Sleep Monitoring:** Patients who require pharmacological interventions should undergo periodic reassessments to monitor side effects, dependency risks and treatment efficacy over time[19].
- **Integration of Digital CBT-I Programs:** With increasing access to online sleep intervention platforms, digital CBT-I applications could serve as cost-effective and scalable alternatives to in-person therapy[20].

Strengths and Limitations of the Study: A key strength of this study is its comparative design, allowing for an objective evaluation of two distinct intervention modalities for sleep disturbances in MDD. The use of validated sleep assessment tools (PSQI, ISI) and objective sleep parameters (sleep efficiency, WASO) strengthens the reliability of findings. Additionally, the study's regional focus on Indian MDD patients contributes valuable data to a population where research on sleep interventions remains limited. However, some limitations should be acknowledged. The cross-sectional nature of the study prevents causal inferences regarding long-term effects of interventions. Additionally, reliance on self-reported sleep measures introduces the possibility of reporting bias. Future research should include larger, multicentric trials with longitudinal follow-ups to examine the sustained impact of non-pharmacological interventions over time.

Future Research Directions:

- **Neurophysiological Studies:** Investigating the impact of sleep interventions on REM sleep architecture and slow-wave activity using polysomnography.
- **Comparative Efficacy in Subpopulations:** Exploring differential responses to pharmacological vs. non-pharmacological interventions in elderly MDD patients and those with comorbid anxiety disorders.
- **Effectiveness of Combined Therapies:** Evaluating the benefits of hybrid treatment models, such as low-dose antidepressants combined with CBT-I for sustained sleep improvement.

CONCLUSIONS

This study provides comparative evidence on the effectiveness of pharmacological and non-pharmacological interventions in managing sleep disturbances in MDD patients. The findings suggest that pharmacotherapy is effective in providing immediate relief, but non-pharmacological approaches such as CBT-I offer more sustainable, long-term benefits with minimal side effects. Given the risks of dependency and cognitive impairment associated with sedative-hypnotics, clinicians should prioritize behavioral interventions as a first-line treatment and reserve pharmacotherapy for short-term symptom management. Future studies should focus on longitudinal trials assessing the durability of non-drug interventions in MDD-related sleep disturbances.

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