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(CASE REPORT)

Mirtazapine in Primary Insomnia: Case report and Literature review

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Abstract

Introduction: Insomnia is a prevalent sleep disorder characterized by difficulty in falling asleep, maintaining sleep, or achieving restorative sleep, despite adequate opportunities. This condition often results in significant daytime impairments, including fatigue, concentration difficulties, and irritability. Insomnia can be primary or comorbid with other disorders such as anxiety or depression.

Case Presentation: A 27-year-old woman presented with severe and chronic insomnia, persisting for 14 years with recent exacerbation. Her symptoms included significant difficulty in initiating and maintaining sleep, resulting in an average of only 3-4 hours of sleep per night and complete sleep deprivation for periods exceeding half an hour over the past 5 days. This sleep deficit led to pronounced emotional instability, physical discomfort, and reduced appetite, although suicidal ideation was absent. She had a past history of drug use for different psychiatric illnesses. She was started on mirtazipine 30mg and showed abrupt improvement in her symptoms. She was discharged afterwards.

Discussion: The patient's chronic insomnia and its secondary effects necessitate a comprehensive treatment approach. Mirtazapine, an antidepressant with potent histamine receptor antagonism, has shown efficacy in improving sleep quality across diverse patient profiles. However, side effects like weight gain and sedation require careful monitoring. Combining mirtazapine with prolonged-release melatonin has demonstrated enhanced outcomes, particularly in perimenopausal women. Cognitive Behavioral Therapy for Insomnia (CBT-I) remains the first-line treatment due to its efficacy and long-term benefits.

Conclusion: Mirtazapine can be a valuable option in the therapeutic arsenal for primary insomnia, but ongoing research is needed to refine treatment strategies. Personalized treatment plans considering patient history and response are crucial for effectively managing primary insomnia and improving patient outcomes.

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Keywords: Insomnia; Sleep disorder; Mirtazapine; Sleep quality; Cognitive Behavioral Therapy for Insomnia (CBT-I); Prolonged-release melatonin; Emotional instability; Antidepressant; Histamine receptor antagonism**.**

1. Introduction

Insomnia is a type of sleep disorder that is typically marked by difficulty in falling asleep, staying asleep, or achieving nonrestorative sleep, despite having ample opportunity to do so. This condition often leads to adverse consequences during the day, such as fatigue, inability to concentrate, and irritability.[1] It is the most common sleep disturbance and can be primary, occurring independently, or comorbid, associated with another disorder, such as anxiety or depression.[2]

Symptoms of this sleep disturbance include difficulty falling asleep, staying asleep, or waking up too early in the morning. It can significantly impact a person's daily functioning and overall well-being. Treatment options may include lifestyle changes, therapy, or medication, depending on the underlying cause and severity of the condition. Seeking help from a healthcare professional is crucial in managing this common sleep disorder effectively. Insomnia is not merely a nighttime issue but also involves subjective feelings and experiences, which can be understood from a phenomenological perspective, integrating mind and body.[3]

Interestingly, while insomnia is often associated with psychological or psychiatric causes, it can also be secondary to medical or circadian rhythm disorders.[4] The condition has been historically medicalized, with its perception shifting from a normal state of wakefulness to a pathological issue, influenced by sociocultural and professional factors [5]. Moreover, the medical management of insomnia reflects a complex interplay between medicalization and pharmaceuticalization, with implications for treatment approaches.[6]

2. Case Report

A 27-year-old woman presented with a constellation of symptoms indicative of severe and chronic insomnia, compounded by recent exacerbation. She has struggled with insomnia for a staggering 14 years, with recent nights characterized by significant difficulty initiating and maintaining sleep, resulting in an average of only 3-4 hours of sleep per night. In the past 5 days, she experienced complete sleep deprivation for periods exceeding half an hour, highlighting the severity of her sleep disturbances. These sleep deficits have precipitated pronounced emotional instability, marked by increased irritability, frequent tearfulness, and episodes of uncontrollable anger outbursts.

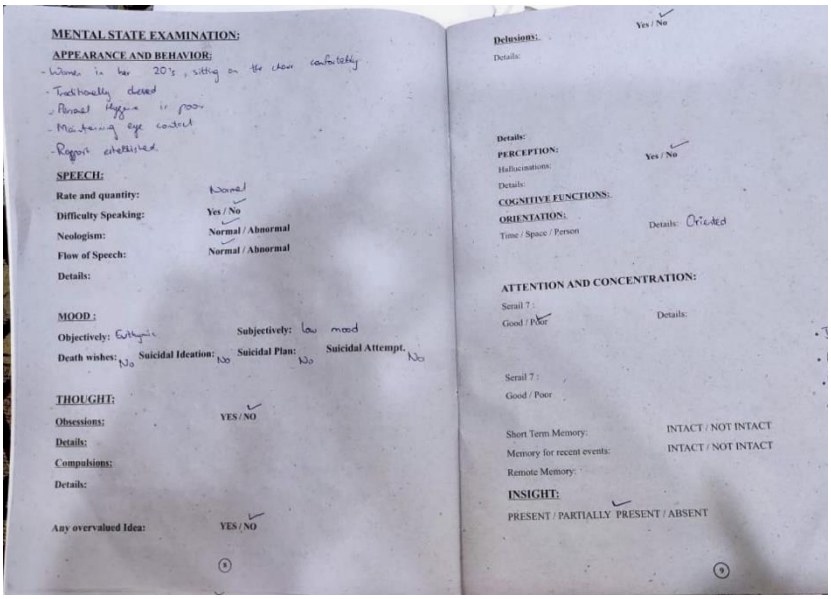

Figure 1 Mental State Examination (MSE) report of the patient at admission.

In addition to emotional distress, the patient reported substantial physical discomfort, including severe body aches and pervasive daytime lethargy. Her diminished appetite, leading to the consumption of just one meal daily, underscores the systemic impact of chronic sleep deprivation on her nutritional intake and overall physical health. Despite these

challenges, the absence of suicidal ideation or negative thoughts suggests a resilient mental state amidst profound sleep-related dysfunction.

During examination, the patient appeared physically comfortable in bed but displayed poor hygiene and a palpable sense of low mood, indicative of the toll her insomnia has taken on her daily life and self-care routines. Notably, her cognitive function remained intact, as evidenced by a flawless performance on memory recall tests (3/3), reassuring against any cognitive impairment that could suggest an alternative diagnosis.

Laboratory investigations, including liver function tests and thyroid function tests, yielded normal results, ruling out underlying medical conditions that could mimic or exacerbate her symptoms. This confirms that her presentation primarily stems from chronic insomnia and its secondary effects rather than organic pathology.

Her past drug history included Escitalopram, Quitiapine and Propanalol. The patient was started on mirtazipine 30mg once daily and after few days she started to show improvements. She reported better sleep duration, depth, and consistency. Along with that, experiencing increased energy level and reduced fatigue.

3. Literature Review

Table 1 Case Studies on the Use of Mirtazapine for Insomnia Treatment

Case	Study Title	Age/Gender	Treatment Method	Findings	Reference
Case 1	Therapeutic Uses of Mirtazapine in Psychiatric Patients	Not specified	Mirtazapine	Effective in improving sleep quality	Alam A, Voronovich Z, Carley JA. A review of therapeutic uses of mirtazapine in psychiatric and medical conditions. Prim Care Companion CNS Disord. 2013;15(5):PCC.13r01525. doi: 10.4088/PCC.13r01525. Epub 2013 Oct 10. PMID: 24511451; PMCID: PMC3907331.
Case 2	Case Series of Perimenopausal Women with Insomnia Treated with Mirtazapine	Perimenopausal Women	Mirtazapine	Improved sleep outcomes with mirtazapine	Dolev, Zipora. (2011). Case series of perimenopausal women with insomnia treated with mirtazapine followed by prolonged-release melatonin add-on and monotherapy. Archives of women's mental health. 14. 269-73. 10.1007/s00737-011-0205-7.
Case 3	Case Report of Nightmares with Mirtazapine	52-year-old Man	Mirtazapine	Side effects observed with mirtazapine	Kavoor AR, Mitra S. Nightmares with mirtazapine - A case report. Indian J Psychiatry. 2020 Nov-Dec;62(6):734-735. doi: 10.4103/psychiatry.IndianJPsychiatry_609_19. Epub 2020 Dec 12. PMID: 33896984; PMCID: PMC8052893.
Case 4	Insomnia in Postmenopausal Women: Approaches	Postmenopausal Women	Prolonged-release Melatonin	Effective adjunct to mirtazapine in managing insomnia	Jeon G-H. Insomnia in Postmenopausal Women: How to Approach and Treat It? *Journal of Clinical Medicine*. 2024; 13(2):428. https://doi.org/10.3390/jcm13020428

Based on the given case presentations and comparative table on treatment studies, there are several discussions that can be drawn from them.

Effective Use of Mirtazapine in Insomnia Treatment: The first case is about a 27-year-old woman who has presented with severe insomnia mood disturbances as well as physical symptoms. In this regard, Mirtazapine which has been

discussed in Case 1 and Case 2 is considered to be an effective treatment option. According to both papers, it is efficacious in improving sleep quality which aligns with chronic insomnia and recent exacerbation for the patient. Another thing that indicates achievement of this therapy in respect to emotional symptoms like irritability or tearfulness shows us that it could form a part of an all-embracing approach including mirtazapine.

Mirtazapine's Side Effects Consideration: On the other hand, it causes nightmares according to Case 3 involving a male patient aged 52 years. This underlines importance of individualized treatment approaches combined with close monitoring for side effects especially for younger patients such as a 27 year old female patient. When prescribing mirtazapine, medical experts need to balance its benefits against any potential side effects just like personalized medicine does in psychiatry.

Role of Prolonged-Release Melatonin as an Adjunct: Further, this case talks about the adjunct therapy for insomnia in postmenopausal women called prolonged-release melatonin (Case 4). This is a way to make mirtazapine sleep better without increasing any bad effects. In this context, other treatments such as prolonged-release melatonin could have additional advantages in maintaining long-term sleep patterns and enhancing overall life quality when considering the age and sex of the patient.

Clinical Implications and Treatment Decision-Making: These cases underline the significance of individualized care plans. Regarding a twenty-seven-year-old female with severe insomnia accompanied by emotional and physical symptoms; however, initiation treatment using mirtazapine would address multifaceted aspects of her state. However, careful consideration of potential side effects and the incorporation of adjunct therapies like prolonged-release melatonin may optimize treatment outcomes while minimizing risks. When formulating therapeutic plan, clinicians should consider patient-specific factors and symptomatology to ensure holistic management and patient well-being.

In summary, while mirtazapine shows promise in managing insomnia and related symptoms, careful monitoring and consideration of adjunct therapies are crucial in optimizing treatment efficacy and minimizing adverse effects, particularly in younger patients like the 27-year-old woman described.

4. Discussion

Primary insomnia, also known as chronic insomnia, is typically treated with Cognitive Behavioral Therapy for Insomnia (CBT-I), which is considered the first-line treatment due to its efficacy and long-term benefits (7). CBT-I is a multi-component treatment that includes Sleep Restriction Therapy (SRT), Stimulus Control Therapy (SCT), Cognitive Therapy (CT), and Sleep Hygiene (SH).[8]

Stimulus Control Therapy is particularly well validated and often regarded as a core component of CBT-IIt focuses on re-associating the bed with sleep by limiting time awake in bed and establishing a consistent wake-up time. These behavioral interventions help strengthen the association between the bed and sleep, promoting more restful nights naturally.[9] While CBT-I is effective on its own, it can also be combined with pharmacological treatments, although CBT-I has been shown to have more durable effects than medication in the long term.[10]

It is important to note that while sleep hygiene education is commonly included in CBT-I, it should be considered an adjunct rather than a primary intervention.Therefore, the focus of CBT-I remains on addressing the underlying thoughts and behaviors that contribute to insomnia, such as excessive worrying about sleep or poor sleep habits. By targeting these root causes directly, CBT-I can bring about lasting improvements in sleep quality and duration. Sleep hygiene education, while beneficial, serves as a supplement to these core therapeutic strategies.

Mirtazapine, an antidepressant with potent histamine receptor antagonism, has shown consistent efficacy in improving sleep quality across diverse patient profiles. Case reports, such as those reviewed, highlight its role in alleviating insomnia symptoms [11], particularly in individuals unresponsive to traditional therapies. For instance, a middle-aged woman with no prior mood symptoms or stressors experienced significant improvement with mirtazapine 30mg, underscoring its utility in managing insomnia when other treatments fail.[12]

The variability in treatment response necessitates personalized approaches. While mirtazapine generally improves sleep onset and maintenance, its side effects, such as weight gain and sedation, should be carefully monitored.[11] Combining mirtazapine with prolonged-release melatonin has shown enhanced outcomes in perimenopausal women, emphasizing the benefit of adjunct therapies tailored to patient demographics and clinical presentation.[13]

The major concern was about considering the individual characteristics of patients such as age, comorbidity and prior treatment response that should be used when selecting treatments for insomnia. This will require further studies to find out what optimal dosing regimens are, how well the drug works over a long period of time, and how its efficacy compares with other pharmacological drugs or non-pharmacological interventions. Additionally, this would help in refining treatment algorithms through investigating possible predictors of treatment response towards improving outcomes in primary insomnia.

5. Conclusion

In conclusion, based on clinical evidence and case reports mirtazapine can be considered as a valuable option in the armory of therapeutics for primary insomnia. However, there is need for ongoing research to understand it better so as to come up with comprehensive management strategies that meet specific patient needs. Personalized treatment plans considering patient history and response remain crucial in managing primary insomnia effectively.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from the patient included in the study.

References:

[1] Lipton, J., Kothare, S. V., & Becker, R. E. (2008). Insomnia of childhood. Current Opinion in Pediatrics, 20(6), 641–649. https://doi.org/10.1097/mop.0b013e32831897cb

[2] Manber, R., Ong, J., & Carlyle, E. (2008). Diagnostic Tools for Insomnia (pp. 41–53). crc. https://doi.org/10.3109/9781420019926-6

[3] Aviram, O., & Bar-Yoseph, T. L. (1995). Phenomenology of Sleep: Gestalt Therapy and Insomnia. British Gestalt Journal, 4(1), 23–30. https://doi.org/10.53667/romm5638

[4] Park, H. S., Hong, S. B., & Joo, E. Y. (2009). Sleep onset Insomnia. Journal of Korean Sleep Research Society, 6(2), 74–85. https://doi.org/10.13078/jksrs09015

[5] Aebischer, G., & Rieder, P. A. (2019). Awaking insomnia: sleeplessness in the 19th century through medical literature. Medical Humanities, 18(13), 340–347. https://doi.org/10.1136/medhum-2019-011683

[6] Coveney, C., Williams, S. J., & Gabe, J. (2018). Medicalisation, pharmaceuticalisation, or both? Exploring the medical management of sleeplessness as insomnia. Sociology of Health &Amp; Illness, 41(2), 266–284. https://doi.org/10.1111/1467-9566.12820

[7] Perlis, M. L., Soeffing, J., Orff, H., Smith, M. T., Nowakowski, S., & Jungquist, C. (2010). Cognitive-Behavioral Therapy for Insomnia (Vol. 56, Issue 10, pp. 281–296). humana. https://doi.org/10.1007/978-1-60327-042-7_22

[8] Muench, A., Vargas, I., Posner, D., Perlis, M. L., Perlis, M. L., & Perlis, M. L. (2021). Chapter 1 - Standard cognitive behavioral therapy for insomnia (CBT-I): When is the adaptation of CBT-I warranted? In Adapting Cognitive Behavioral Therapy for Insomnia (pp. 3–24). elsevier. https://doi.org/10.1016/b978-0-12-822872-2.00012-8

[9] Walker, J., Muench, A., Perlis, M. L., & Vargas, I. (2022). Cognitive Behavioral Therapy for Insomnia (CBT-I): A Primer. Clinical Psychology and Special Education, 11(2), 123–137. https://doi.org/10.17759/cpse.2022110208

[10] Findley, J. C., & Perlis, M. L. (2014). Cognitive Behavioral Treatment of Chronic Insomnia (pp. 67–82). springer new york. https://doi.org/10.1007/978-1-4939-1185-1_7

[11] Kavoor AR, Mitra S. Nightmares with mirtazapine - A case report. Indian J Psychiatry. 2020 Nov-Dec;62(6):734-735. doi: 10.4103/psychiatry.IndianJPsychiatry_609_19. Epub 2020 Dec 12. PMID: 33896984; PMCID: PMC8052893.

[12] Alam A, Voronovich Z, Carley JA. A review of therapeutic uses of mirtazapine in psychiatric and medical conditions. Prim Care Companion CNS Disord. 2013;15(5):PCC.13r01525. doi: 10.4088/PCC.13r01525. Epub 2013 Oct 10. PMID: 24511451; PMCID: PMC3907331.

[13] Dolev, Zipora. (2011). Case series of perimenopausal women with insomnia treated with mirtazapine followed by prolonged-release melatonin add-on and monotherapy. Archives of women's mental health. 14. 269-73. 10.1007/s00737-011-0205-7.