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A Case Report on Metoprolol Induced Nightmares and Hallucinations

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ABSTRACT
Metoprolol is a cardioselective beta-1-adrenergic blocker. It is frequently prescribed for cardiovascular conditions but is associated with potential central nervous system adverse effects, including hallucinations and nightmares. We discuss the case of an 84-year-old female with mixed aortic valve disease who experienced hallucinations and nightmares after starting metoprolol medication. Her symptoms improved after she stopped using metoprolol, indicating a likely causative link. This example emphasizes the significance of rapidly diagnosing and addressing adverse medication reactions, especially in elderly patients who may have underreported symptoms. Understanding the pharmacological properties of lipophilic beta-blockers and their effects on neurological function is critical for improving patient care and reducing negative outcomes.

Keywords: Metoprolol, Nightmares, Hallucinations

INTRODUCTION
Beta-blockers are widely used for the treatment of cardiovascular and non-cardiovascular conditions. Metoprolol is an essential drug in cardiovascular pharmacology, acting as a cardioselective beta-1-adrenergic blocker and a widely used β-adrenergic antagonist.[1]
Bradycardia, visual impairment, dizziness, headache, rash and pruritus are common adverse effects of metoprolol. Among the reported adverse effects linked to metoprolol, there were approximately 58,247 cases, with 576 cases specifically reporting nightmares and 446 cases reporting hallucinations.[2] Here, we report the case of an 84-year-old female who experienced hallucinations and nightmares during metoprolol treatment.

CASE STUDY
An 84-year-old female patient was admitted with mixed aortic valve disease and complained of hallucinations and nightmares. A detailed history revealed that these symptoms began after starting oral metoprolol 25 mg once daily three years ago, in April 2021, for hypertension. The hallucinations and nightmares, unnoticed by her family and presumed to be age-related, started two months after initiating

metoprolol. However, discussions during this hospitalization suggested a potential link between the timing of her medication and these symptoms, prompting suspicion of metoprolol as the cause. After a cardiology consultation, metoprolol was discontinued. The patient, who was hemodynamically stable and showed symptom improvement, was discharged. She demonstrated positive changes with reduced hallucinations and nightmares within one week of metoprolol withdrawal.

DISCUSSION

Liposolubility refers to a substance's physicochemical attribute that establishes the basic features of a medicinal preparation, influencing its metabolic, pharmacokinetic, pharmacodynamic, and toxicological profiles.[3] Certain beta-blockers can permeate through the blood-brain barrier due to their lipophilic properties. Metoprolol and propranolol are examples of first-class beta-blockers that are metabolized by the liver, almost entirely absorbed in the small intestine, and highly soluble in lipids.[3] The most frequent adverse effects caused by inhibiting beta-adrenergic receptors are fatigue and cold extremities. The use of beta-blockers has been linked over time to a variety of adverse effects on the central nervous system, including delirium or psychosis, Parkinson's disease, visual hallucinations, depression, lethargy, sleep disturbances and nightmares, and an increased risk of falling.[3] Beta-blockers inhibit rapid eye movement (REM) sleep by inhibiting serotonergic and beta-adrenergic receptors, which can result in an array of problems, including insomnia.[4] Melatonin helps regulate our sleep patterns, but beta-blockers can reduce melatonin levels, leading to nightmares and sleep disorders.

[5] In these individuals, the administration of melatonin significantly increased the amount of time they slept overall, increased their efficiency, and reduced the time needed to attain Stage 2 sleep. [5] The concept of "binding," which refers to the fusion of separate cell activity to form cohesive brain networks, is closely related to bizarre dreams. The term "bizarreness" may be reinterpreted to include a range of unusual pairings of traits that successfully combine dream illustrations.[6]

Multiple studies have indicated that lipophilic beta-blockers may play a causative role in the occurrence of visual hallucinations, with symptoms often resolving upon discontinuation of treatment. Goldner et al. established a correlation between metoprolol usage and visual hallucinations, a side effect frequently mistaken for dreams or nightmares, leading to underdiagnosis. Compounding the issue, patients often hesitate to report such symptoms, making it challenging to accurately estimate the true incidence of hallucinations.[7] Sirois et al. noted that hallucinations can manifest as an isolated symptom in patients receiving metoprolol, but in elderly individuals or those with preexisting cognitive impairments, they may progress to delirium.[8] Notably, hallucinations induced by metoprolol typically subside within a few days following the cessation of treatment.[7]

Pathological nightmares arise when they occur with high frequency and substantial impairment, impacting the individual's social, occupational, and emotional spheres.[9] A systematic review revealed that one-third of individuals experiencing symptomatic nightmares were undergoing beta-blocker therapy.[10]

Lipophilic beta-blockers and those with higher serotonin 5HT1A receptor affinity, shorter half-lives, and a lack of alpha-blockade are more likely to cause nightmares; thus, nightmares are more common with propranolol, metoprolol, and pindolol and least common with sotalol, carvedilol, and labetalol.[11] If there is a temporal correlation between the development of nightmares and a potentially causative medication, stopping the medication or gradually reducing its dosage will typically resolve the nightmares.

Upon evaluation at our ADR monitoring center, the causality was determined to be “probable” using the WHO-UMC causality assessment scale. The type of ADR was classified as “type C” according to the

Rawlins- Thompson classification, and the ADR was assessed as "level 2, moderate" in terms of severity based on the modified Hartwig's scale. As per the WHO criteria, the seriousness of the reaction was categorized as "other medically important," and the outcome of the reaction was "recovering". Additionally, according to the Schumock and Thornton scale, the ADR was deemed "not preventable". The assessment of causality and other attributes of the ADR was conducted using established scales and criteria to ensure a comprehensive and standardized evaluation.[12]

CONCLUSION

Lipophilic beta-blockers have the ability to cross the blood-brain barrier, leading to potential adverse effects that may go unnoticed by clinicians. This report highlights the need for prompt and proper identification and management of these ADRs.

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DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for all clinical information to be reported in the journal. The patient understands that her name and initials will not be published and that due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Nil

CONFLICTS OF INTEREST

There are no conflicts of interest.

ABBREVIATIONS

FDA - Food and Drug Administration
REM - Rapid Eye Movement
USG - UltraSonography
OD - Once daily
5-HT1A - 5-Hydroxytryptamine 1 A receptor
ADR- Adverse drug reaction
WHO-UMC- World Health Organisation-Uppsala monitoring Centre
PvPI- Pharmacovigilance Program Of India

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