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A Case Report of Melatonin-Induced Parasomnia

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ABSTRACT

Background and Objective: Parasomnia occurs due to various hereditary reasons, psychiatric or medical diseases, as well as substance or medication use. The occurrence of medication-induced parasomnia not only causes concern for the patient and family, but also causes the patient to refuse to continue the treatment. The aim of this case report is to consider melatonin as one of the causes of medication-induced parasomnia.

Case Report: The patient is a 17-year-old woman who referred to the Sleep Disorders Clinic of a university center due to delayed sleep phase disorder. After ruling out medical causes and diagnosing delayed sleep-wake phase disorder, she was treated with 1.5 mg melatonin by a psychiatrist. The patient experienced visual hallucinations, sleep paralysis and nightmares that night. A month and a half later, similar symptoms appeared after re-taking melatonin. After discontinuing the medication, there were no symptoms in the 6-month follow-up.

Conclusion: According to the results of this study, melatonin can cause parasomnia. In the above patient, due to the possibility of parasomnia-related risks and low acceptance of treatment, it is necessary to give the necessary warnings to the patient and family and seek help from non-pharmacological treatments.

Keywords: *Melatonin, Delayed Sleep-Wake Phase Disorder, Parasomnia, Sleep Disorders*.

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Introduction

Parasomnia is characterized by unusual behavior, perception or excitement in sleep. In The International Classification of Sleep Disorders-Third Edition, parasomnias are divided into three categories: Non-REM, REM and other parasomnias. The characteristic of NREM parasomnia, unlike REM parasomnia, is the lack of awareness of what happened. Sleepwalking and confusional arousal are examples of NREM, and nightmares, sleep paralysis, and hallucinations are examples of REM parasomnia (1). Parasomnia can cause danger to the patient or others. One of the causes of parasomnias is consumption or discontinuation of substances (such as alcohol) and medications (such as zolpidem) (1, 2).

Along with the necessary measures to maintain the patient's safety, benzodiazepines have traditionally been used in the treatment of NREM parasomnia, and tricyclic antidepressants and melatonin have been used for REM parasomnia, especially REM sleep behavior disorder (3). Melatonin is made from serotonin precursor in the pineal gland. Melatonin is the most important known chemical mediator in the regulation of sleep-wake rhythm and timing of body activities (4). Circadian rhythm disorders are characterized by changes in the timing of sleep-wake. One of these disorders is delayed sleep-wake phase disorder in which a person falls asleep later than expected despite the right conditions. As a result of lack of accordance between an individual's sleeping and wake time and other people and society's programs, the individual suffers from dysfunction. Melatonin is one of the important drugs in the treatment of circadian rhythm disorder. This drug is prescribed for the treatment of delayed sleep-wake phase disorder in the evening to regulate the mentioned rhythm (5). Melatonin is introduced as a drug with minimal complications (6). However, in the reported case, the patient suffered from severe symptoms of parasomnia after taking melatonin. The aim of this case report is to consider melatonin as one of the causes of medication-induced parasomnia so that psychiatrists and other sleep therapists take necessary precautions in prescribing this drug.

Case Report

A case report of melatonin-induced parasomnia was investigated at Mazandaran University of Medical Sciences and approved with the code of ethics IR.MAZUMS.REC.1400.492. The patient is a 17-year-old woman who came to the hospital with complaints regarding trouble falling asleep, which has worsened since at least three years ago. Despite having a room with suitable physical conditions, she did not feel sleepy until 3-4 AM. This problem caused sleepiness during the day and led to studies-related problems for the patient. However, on the days when she was able to sleep in the morning, she slept for at least 8 hours and after waking up, she had a good feeling and took care of her work quite well. No evidence of parasomnia and other sleep disorders, depression, other major psychiatric disorders, and substance or medication use was found in the patient's history. In the family history, the patient's father also had a similar sleep pattern with less intensity in his youth, but none of the family members had other psychiatric disorders. No specific medical problem was discovered in the physical examinations and tests. A psychiatric interview was conducted by an experienced psychiatrist to investigate other psychiatric disorders, and no problems were recorded. A Sleep Log was filled for two weeks. It indicated a 3-hour delay in sleep onset (considering 00:00 as the usual moment for sleep onset). In cases where the sleep duration was at least 8 hours if there was enough time, the patient woke up with a feeling of satisfaction. According to patient history, the Sleep

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Log for the diagnosis of delayed sleep-wake phase disorder was provided by a sleep fellowship psychiatrist as well as a pulmonary & sleep specialist. Melatonin 0.75 mg was started at 9 pm for the patient. The patient fell asleep after taking melatonin at 12:00 PM. At 1 o'clock, she woke up for a short time and fell asleep again. At 3 o'clock in the morning, the patient woke up and heard her father's voice telling her to get up (illusion), but at the same time, the patient realized that the voice was not real. After a few minutes, the patient fell asleep again. At 4 o'clock in the morning, she saw her father standing in front of her and addressing her. In her description, the patient said: "My father called me. He was standing in front of me. I was awake, but it was as if I was stuck to the bed and no matter what I did, I couldn't move. I was so scared. I could finally scream and then jump. I fell asleep after a few minutes. At 6 in the morning, I woke up again with my father's voice and ran to him, but he said that he did not call me."

Due to the presence of nightmares, hallucinations when waking up, paralysis during sleep, frequent awakenings, melatonin was discontinued for the patient the next night, and no problems occurred during sleep until melatonin was restarted. 45 nights later, the patient again took 0.75 mg of melatonin at 9:00 PM, and again frequent awakenings with nightmares, visual and auditory hallucinations, and feeling of limb paralysis occurred in sleep. The patient's medication was discontinued and no symptoms of parasomnia were observed in the 6-month follow-up. By changing the hours of activity, nutrition and light therapy, the patient's bedtime was changed to around 00:30 and the patient's performance improved.

Discussion

The most important finding that led to the report of the above case was the use of a low dose of melatonin and the absence of any medical or psychiatric disease in the patient. In the reported case, without a history of other psychiatric disorders or other sleep disorders and medical problems, REM parasomnia symptoms included sleep paralysis and nightmares after melatonin administration. The symptoms had no previous history and appeared on the same night of taking the drug, so the drug was discontinued. The same symptoms were seen with the second use of the drug. The score calculated based on drug side effect scale evaluation by Naranjo et al. was equal to 8, which is equivalent to "Probable" drug side effect (7).

The scope of parasomnia varies from sleep talking to non-REM sleep walking and hallucinations or certain behaviors during REM sleep (1). The occurrence of parasomnias can be after the use or discontinuation of some medications. Nightmares have been reported with antidepressants such as fluoxetine and sleepwalking and even sleep-driving with medications such as zolpidem. These side effects usually end by stopping the drug (8). In the review of the sources, not only was there no article related to melatonin-induced parasomnia, but the evidence indicated the effect of melatonin on the parasomnia of REM sleep behavior. This effect is probably exerted through melatonin type 1 receptor (9).

Visual hallucinations, excitement more than usual, paralysis of limbs and remembering events show the existence of REM Parasomnia. The melatonin receptor consists of two types of G protein type 1 (MT1) and type 2 (MT2). These two types of melatonin receptors have effects on sleep timing, memory and many other known functions, but their effects on sleep structure are opposite (10). MT1 receptors are located in the locus coeruleus and lateral hypothalamus, and their destruction causes an increase in NREM. The locus coeruleus and lateral hypothalamus are active in REM sleep. It seems that the effect on melatonin type 1 receptor increases REM sleep. The activity of some lateral hypothalamus neurons causes paralysis during

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sleep by affecting the gigantocellular reticular nucleus (11). In this patient, the intensified response of the MT1 receptor can be considered to be involved in the occurrence of symptoms.

Melatonin-induced parasomnia has not been reported so far; therefore, this report is unique in this respect. When the drug causes parasomnia, it is not only recommended to discontinue it, but the patients themselves do not continue it, which of course can cause the continuation of the underlying disease in some cases (12). Melatonin is a drug that is generally well tolerated. According to the complication mentioned in this report, melatonin cannot be considered completely without complications. As a result, in the above patient, the use of other non-pharmacological treatments, including light therapy, should be considered as an alternative treatment.

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