

Cinacalcet-Induced Insomnia in Two Patients with End-Stage Renal Disease: A Case Report

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Abstract: *Background: insomnia is defined as a lack of satisfaction with sleep quality or quantity and is related to difficulty starting or sustaining sleep and early-morning wake up with disability returning to sleep[1]. Insomnia is more prevalent between women and the elderly and can begin separately or induced by another disease[2],[3]. There are three major types of insomnia, according to The International Classification of Sleep Disorders, 3rd edition[4]: Short-term insomnia, has also been named transient insomnia. Signs of short-term insomnia are present for less than three months' duration, but they conducted by notable concern. Chronic insomnia has also been named secondary insomnia and comorbid insomnia. Symptoms appeared a minimum three times weekly for three months or longer and are unrelated to insufficient time for sleep (unrelated to sleep limitation) or unsuitable sleep conditions, or different sleep disorder. Other insomnia is a term used for subjects who reported difficulty beginning or sustaining sleep but do not fit all of the criteria for either short-term or chronic insomnia.*

Keywords: Sleep disorders, adverse effects, renal medicine, pharmacology, and therapeutics

1. Case Presentation

Patient 1: in January 2019, 59-years old woman with end-stage renal disease (ESRD) and hemodialysis dependent for ten months presented to the nephrology outpatient clinic complained of difficulty initiating sleep in spite of the availability of enough environments. Recently she has started intake cinacalcet 30 mg tablet once daily, which is titrated after two weeks to 60 mg daily for her secondary hyperparathyroidism according to the nephrologist's prescription. After three weeks of commencing her new medication, she presented with insomnia. Which is unresolved by itself for several days. She didn't report any psychological illness and had no family history of any sleep-related disorders. Her ongoing treatments, including insulin for diabetes, amlodipine a calcium channel blocker for hypertension, alfacalcidol a vitamin D derivative, calcium supplementations, and sevelamer a phosphate binding agent.

Patient 2: in February 2019, 55-years old man with ESRD and hemodialysis dependent for two years presented to the nephrology outpatient clinic complained of difficulty falling asleep without an apparent reason. Recently he has begun consumption cinacalcet 30 mg tablet once daily, which is titrated after two weeks to 60 mg daily for his secondary hyperparathyroidism according to the nephrologist's direction. After one month of commencing his new pill, he suffered insomnia, which is described by the patient as bothersome and wearying. He didn't display any psychological illness and had no family history of any sleep-related disorders. Home treatments include candesartan an angiotensin receptors blockers for hypertension, and alfacalcidol a vitamin D derivative.

Differential diagnosis: Circadian rhythm disorders, Short duration sleep, Chronic sleep restriction (insufficient sleep syndrome), Central sleep apnea, or Sleep-disruptive environmental circumstances.

2. Treatment

Because almost of hypnotic medicines undergo renal excretion, which may be limited in patients who have kidney disease, that's lead to an increased blood level of these medications and extreme sedation, so the behavioral therapies for insomnia are suggested in both cases including relaxation, cognitive therapy, sleep hygiene education, and cognitive behavioral therapy. At the same time, the nephrologist in charge recommended continuing the course of management of hyperparathyroidism with cinacalcet with close monitoring of the insomnia development.

Follow up and outcomes:

After two months of starting the treatment with cinacalcet for secondary hyperparathyroidism and after achieving the therapeutic goal, cinacalcet has stopped while a complete resolution of insomnia symptoms didn't reach a satisfactory level for the patients with behavioral therapies offered for them. And after discontinuing the offending agent, the circadian rhythm returned to normal spontaneously within a few days.

3. Discussion

Insomnia is considered the most prevalent sleep disorder, with an estimated prevalence of 10 to 15%, relying on the applied diagnostic criteria[5]. Insomnia patients are anxious that their inadequate sleep has negative impacts on their productivities of everyday tasks and significantly report individual effectiveness shortage[6]. Several medications used in the management of chronic illness can produce sleepiness and wakefulness as adverse events. Medicines with greater fat-solubility more readily cross the blood-brain barrier[7]. Usually, managing secondary hyperthyroidism with cinacalcet was well tolerated and effectively reduced parathyroid hormone levels[8]. However, in our two patients, they reported unfamiliar adverse effects manifested by sleep-related disorders, insomnia specifically which

concurrently started with the use of cinacalcet. This adverse event appears quite distant to the primary adverse effect with cinacalcet, which is hypocalcemia. And completely unrelated to the mechanism of action which involve the stimulatory action of calcium on the calcium-sensing receptor to inhibit parathyroid hormone secretion by the parathyroid glands[9]. To our knowledge and up to date, this is the first case report regarding this issue.

4. Recommendation

- 1) Further reevaluation of cinacalcet dose in patients with ESRD.
- 2) More attention should be focused on the neurological and psychological adverse effects profile of cinacalcet.
- 3) Behavioral therapies for insomnia induced by cinacalcet may not be sufficient, and pharmacological intervention should be considered.
- 4) Thorough follow up should be made periodically to chronic kidney disease patients with polypharmacy.
- 5) Slower dosing titration regimen of cinacalcet is advised in patients with secondary hyperparathyroidism due to chronic kidney disease.
- 6) When the patients didn't get health care providers consultations, they may follow a self-medication strategy and fall in substance abuse.

5. Patient's Perspective

Patient (1): Insomnia brought me a stressful feeling, had a negative impact on my quality of life, my daily performance significantly deteriorated, I thought I had to stop the medication despite the Consequences.

Patient (2): I compelled to leave my work some days. My activity is much lower than the previous period due to lack of sleep hours.

6. Conflict of interest

The authors had no conflict of interest.

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