Persistent Insomnia in an Elderly Man With HIV Receiving Dolutegravir-Based Antiretroviral Therapy

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Sleep disorders are more common in people with HIV than in the general population.[1,2] While multiple factors such as HIV-related pathophysiology, psychosocial conditions, and comorbidities can contribute, integrase strand transfer inhibitors (INSTIs) in antiretroviral therapy (ART) have been linked to neuropsychiatric side effects, especially sleep disturbances.[3,4] This case highlights the reversibility of an INSTI-induced sleep disorder in a heavily treatment-experienced patient with HIV.

Case Report

We present the case of an 80-year-old white unmarried homosexual man diagnosed with HIV in the mid-1980s, continuously receiving ART since the mid-1990s. Due to multiple resistances to protease inhibitors and nucleoside reverse transcriptase inhibitors (NRTIs), his therapy was progressively intensified. In 2008, raltegravir (an INSTI) was added, later switched to dolutegravir in 2021 due to persistent low-level viremia. The patient also had a history of moderate-to-severe depression and HIV-associated mild cognitive impairment. Since 2018, he reported episodic insomnia, initially triggered by family conflicts or external stressors. Over time, insomnia worsened, becoming chronic and requiring various psychotropics (zolpidem, zopiclone, dipiperon, mirtazapine, trazodone, trimipramine, melatonin, relaxane) as well as cognitive-behavioral therapy for insomnia, but with only partial relief. Between 2019 and 2024, he was repeatedly hospitalized at the University Hospital of Old Age Psychiatry and Psychotherapy in Bern for severe chronic insomnia and recurrent depressive episodes, significantly impairing his daily life. During his latest voluntary admission in June 2024, despite zolpidem and escitalopram, he reported complete inability to sleep, leading to psychological distress and suicidal ideation. He expressed that, if physically able, he would end his life by drowning.

A thorough review of comedications and contributing factors revealed no alternative cause for his treatment-resistant insomnia. However, analysis of his medical history highlighted the potential role of his ART. Diagnosed with HIV in the mid-1980s, the patient has a history of HIV-associated opportunistic infections, though none appeared directly related to the sleep issues. By June 2024, his regimen included NRTIs (tenofovir alafenamide, emtricitabine), a protease inhibitor (darunavir/cobicistat), a nonnucleoside reverse transcriptase inhibitor (doravirine), and INSTI (dolutegravir). Given the known link between INSTIs and neuropsychiatric symptoms, treatment simplification was discussed with the infectiology department at the University Hospital in Bern. Dolutegravir was discontinued while maintaining the remaining ART, with viral load remaining <50 copies/mL.

After discontinuing dolutegravir and initiating lorazepam, the patient's sleep and depressive symptoms gradually improved. Lorazepam was later tapered off without symptom recurrence. He was discharged to a retirement home due to physical frailty and repeated falls, which made independent living unsafe. The move also aligned with his wish for more social interaction and companionship. In the last 6 months, the patient reported a sustained improvement in his sleep.

Discussion

Sleep and mood disorders, like insomnia and depression, are common but often under-recognized in patients with HIV,[2,6] significantly affecting quality of life, treatment adherence, and the risk of further neuropsychiatric comorbidities.[7] This case highlights the importance of evaluating neuropsychiatric side effects, especially with INSTI-based ART regimens, which are widely used for their high resistance barrier and generally low side effect risk.[8] The Swiss HIV Cohort Study found neuropsychiatric symptoms to be the most frequent side effects of integrase inhibitors, though still uncommon and rarely leading to treatment discontinuation.[5] Given the multifactorial nature of sleep disorders, other causes like depression should always be considered. In this case, the patient's persistent insomnia and depressive symptoms resolved after stopping the INSTI-based regimen and initiating short-term lorazepam use, which was later discontinued without symptom recurrence—suggesting dolutegravir as the likely trigger. Notably, the patient had previously tolerated raltegravir (another INSTI) without issues, highlighting safety differences within the drug class and the need for ongoing evaluation even after ART modifications. This case emphasizes the value of early identification and management of ART-related

psychiatric symptoms and the benefits of multidisciplinary care in complex cases.

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