International Journal of Gerontology 16 (2022) 303–304
https://doi.org/10.6890/IJGE.202207_16(3).0026

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Case Report

Treatment of Intractable Inappropriate Sexual Behavior with Low-Dose Finasteride in a Patient with Neurocognitive Disorder: A Case Report and Review of the Literature

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ARTICLE INFO

Accepted 9 December 2021

Keywords:
finasteride,
inappropriate sexual behavior,
neurocognitive disorder

SUMMARY

We report the case of an 86-year-old male with a history of benign prostatic hyperplasia admitted to the acute psychiatric ward due to reports of inappropriate sexual behavior (ISB). After trying many psychotropic medications, the ISB was resolved with low-dose finasteride. This case demonstrates that low-dose finasteride may be a viable option as an alternative treatment option for intractable ISB; however, adverse effects, such as depression or cognitive complaints, should be closely monitored in patients with dementia to prevent post-finasteride syndrome (PFS).

1. Introduction

Inappropriate sexual behavior (ISB; sexually disinhibited behavior or hypersexuality) is a concerning symptom affecting 5–25% of individuals with neurocognitive disorders.[1] ISB in patients with dementia can be disruptive and demonstrates a large burden for patients and caregivers, but there are no empirically established treatments for dementia-related ISB. Pharmacological treatments are more commonly used, but all current evidence is from case series and reports.[2] Finasteride is a 5α-reductase inhibitor that blocks the conversion of testosterone and has been suggested to treat ISBs in elderly men with vascular dementia.[3] Here, we present a patient with a neurocognitive disorder due to traumatic brain injury with ISB. The patient had tried many psychotropic drugs with little improvement, and finally stabilized after finasteride administration. This case presents the potential clinical applications of finasteride in patients affected by disorders outside vascular dementia.

2. Case report

Mr. A., a right-handed, 86-year-old widower with 6 years of education, was admitted to our hospital in October 2017 due to ISB and care burden. In 2012, the patient developed disorientation, memory impairment, and ISB after a head injury with traumatic subarachnoid hemorrhage and occipital bone fracture. Initially, he demonstrated obscene sexual talk with his daughter-in-law. Therefore, his family decided to hire a female foreign helper to care for him. He then demonstrated frequent ISB with his carer such as masturbation, hugging, and exhibitionism. Mr. A. was brought to a psychiatrist 10 months after onset because of his severe ISB. He was diagnosed with a neurocognitive disorder due to traumatic brain injury by an experienced psychiatrist based on the criteria of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Initial treatment with amisulpride (100 mg/d) was discontinued after 1 month because of severe extrapyramidal symptoms and the lack of effect on hypersexual behaviors. The patient's primary medications for ISBs prior to admission included quetiapine, which was started at 25 mg/d and gradually increased to 100 mg/d over several months. After 3 months, quetiapine was discontinued due to daytime dizziness. Next, he was given 50 mg/d of chlorpromazine and 500 mg/d of valproic acid for 4 months; however, frequent choking was noted and ISBs responded poorly. The medication was then shifted to risperidone (0.5 cc/d) due to worsening ISBs, but he continued to experience severe extrapyramidal symptoms. After trying the above psychotropic drugs, there was still no resolution of ISBs for longer than 1 month, causing heavy care burden for his caregivers.

On admission to our hospital in October 2017, his family reported smoking cessation for 15 years and no alcohol consumption before. He had a history of benign prostatic hyperplasia and hypertension and no family history of psychiatric disorders or drug abuse. His vital signs were stable, and no abnormal physical signs were detected upon admission. Blood and urine tests, blood glucose level, liver and renal function, and thyroid function were normal, and the patient showed no evidence of infection. The electrocardiogram results were normal. The mental status examination showed no fluctuations in consciousness or attentiveness. His activity increased. Touching or hugging his foreign carer and inappropriate masturbation were noted.

During hospitalization, his brain computed tomography showed encephalomalacia in the right inferior cerebellum and left lower frontal lobe. He scored 7/30 on the Mini-Mental State Examination and 2 on the Clinical Dementia Rating Scale. ISB treatment was shifted to 5 mg of aripiprazole and 750 mg of valproic acid was added due to the concern that worsening ISBs may be manic symptoms. The ISBs improved the day after admission and he was discharged on day 22.

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During a follow-up visit 1 week after discharge, the ISBs deteriorated again. Considering his history of benign prostatic hyperplasia and refractory ISBs, 2.5 mg of finasteride was added in combination with 500 mg of valproic acid. ISBs resolved after 1 month of finasteride use; however, the family reported that his affect was restricted, and he demonstrated decreased activity at 3-month follow-up. His symptoms did not meet the criteria for major depressive disorder in the DSM-5 and there were no extrapyramidal signs. Three months later, valproic acid was considered ineffective and was discontinued as there was no ISB improvement until finasteride was added. There was no recurrence of ISBs under finasteride monotherapy. Furthermore, no depressive symptoms were present at the subsequent follow-up.

3. Discussion

The present case suggests that finasteride administered at a low dose (i.e., half of the typically recommended dose) may be effective in reducing intractable ISB in men with dementia. The mechanism of finasteride in the treatment of ISB is still largely unclear. We speculate that finasteride may cause erectile dysfunction and low libido, thus leading to a decrease in ISBs. Finasteride was developed to decrease the conversion of testosterone to its more potent metabolite, 5α-dihydrotestosterone (DHT), which may result in erectile dysfunction. Moreover, finasteride can cross the blood-brain barrier and inhibit the production of DHT throughout the central nervous system.[4] It is biologically plausible that a lack of DHT or another 5α-reduced hormone is responsible for a decrease in libido. Consistent with its ability to penetrate the central nervous system, finasteride could broaden its clinical utility beyond vascular dementia. Low-dose finasteride appears to assist in the management of ISBs; however, larger trials are needed to better understand this relationship.

Negative effects on cognition were not observed in the present patient. Studies on the effects of finasteride on cognition have yielded mixed results. A matched cohort study conducted by Welk et al. in 81,162 older men using finasteride did not find a significant association with dementia.[5] Alternatively, a review of the Food and Drug Administration Adverse Event Reporting System data showed that finasteride users reported a slowing of cognition.[6] These differences may be due to several factors such as the tasks being used, strain/species of the experimental subjects, dose, and duration of finasteride administration. Although there is concern regarding the effects of finasteride on cognition, other classes of medication, including antipsychotics, anticonvulsants, and beta-blockers, demonstrated robust cognitive impairments.[7] Due to the uncertainty of finasteride's adverse effects on cognition, low-dose finasteride treatment for ISB may minimize the risk of cognitive impairments.

Although finasteride is generally well-tolerated, many reports have described adverse effects in men during treatment that may persist despite finasteride exposure and cessation. This condition, termed post-finasteride syndrome (PFS), is characterized by sexual side effects, depression, and cognitive complaints that remain despite drug withdrawal. Neuroactive steroid (e.g., testosterone and progesterone) dysregulation caused by 5α-reductase inhibitors was assumed to be a possible mechanism of PFS and restricted affect and decreased activity in the present patient raised concerns about the possibility of adverse effects of finasteride; however, it is difficult to clarify the symptomatology of patients with neurocognitive disorders.[5] Future studies should aim to understand the risk factors of PFS in patients with dementia receiving finasteride treatment.

Although there is no empirically established treatment for dementia-related ISB, guidance can be provided by extrapolating from what is known about the management of other behavioral and psychological symptoms of dementia.[8] Clinicians may use a sequential approach that starts with nonpharmacologic management strategies such as behavioral, supportive, or educational approaches targeting ISB. It is also important to rule out treatable causes of ISB, such as pain, boredom, lack of stimulation, and lack of an outlet for affectional needs. Discontinuing medications that increase inhibition (e.g., benzodiazepines and dopamine agonists) may reduce ISB. Pharmacologic intervention should be utilized only if symptoms fail to respond to more conservative measures, as many medications have adverse effects that can offset their potential benefits. Successful pharmacologic treatment of ISB has been reported with a range of classes of medication, including antidepressants, antipsychotics, anticonvulsants, cholinesterase inhibitors, hormonal agents, and beta-blockers.[2] The quality of evidence in these medications is limited to case reports and series; therefore, it is important to be mindful of potential risks in selecting an agent and consider the careful balancing of risks and benefits. Although all agents carry risks, those associated with selective serotonin reuptake inhibitors are relatively lower than other drugs, demonstrating a reasonable first choice. Cholinesterase inhibitors may be the next step in this process. Importantly, antipsychotics and hormonal agents may have significant side effects and should be used with caution. Consideration of the emergence of side effects is critical, so it is wise to begin the prescription at a low dose and increase slowly.

The management of ISBs may be difficult in some patients. Based on our current case, we recommend the use of low-dose finasteride in patients with a history of benign prostatic hyperplasia when ISBs are intractable after attempting several psychotropic medications or combination therapy. Furthermore, adverse effects of finasteride should be closely monitored to prevent PFS.

Acknowledgments

The authors thank the patient for his agreement to this publication.

Conflicts of interest

The authors declare that they have no competing interests.

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