Development of Modafinil Dependence Following Self-medication for Sexual Dysfunction: A Case Series

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Modafinil has been widely used for its cognition-enhancing properties and shown to increase alertness and productivity and reduce fatigue.[1] The mechanism by which modafinil affects sexual function is likely by influencing the dopaminergic and norepinephrine pathways in the brain, which play a crucial role in sexual function.[2,3] Though it is not included in the list of substances in substance use disorders, a few case reports have demonstrated its addictive potential.[4] According to the International Classification of Diseases 11th version (ICD-11, two out of the three criteria groups and one criteria among each group are 1) strong desire/craving and impaired control; 2) neglect of other activities and use despite harmful consequences; and 3) withdrawal and evidence of tolerance need to be present for at least one month for a "dependence syndrome" for a particular substance.[5] To the best of our knowledge, no cases have been described in the past where patients developed modafinil dependence following self-medication to improve their sexual functioning. We describe three such cases diagnosed with modafinil dependence and current use, with ICD-11 criteria with comorbid sexual dysfunction.

Case 1

A 28-year-old married male graduate, from a high socio-economic status and urban background who premorbidly had dependent personality traits had a family history of bipolar disorder and cannabis dependence in his father. In the past, a neurologist had diagnosed him with major depression, which had onset two years ago, with reduced sexual desire as one of the complaints. He had a partial response on sertraline 100 mg; however, on increasing the dose to 200 mg, though his depressive symptoms improved considerably, his sexual desire decreased further. His complete hemogram (CH), liver function test (LFT), renal function test (RFT), fasting blood glucose (FBG), postprandial blood glucose (PPBG), fasting lipid profile (FLP), and thyroid function test (TFT) were within normal limits (WNL) when his sexual problems were evaluated 1.5 years ago. One year ago, he started taking modafinil 100 mg during the evening for 1–2 days weekly, which improved his sexual desire. However, he gradually started taking modafinil every morning to reduce fatigue, myalgia, and inattention. He would mostly think about when to take a dose of modafinil and keep a stock of it with him. He would feel considerably anxious and irritable if he missed taking modafinil. Almost six months before the presentation, he increased the daily dose of modafinil and had to take it TID, for a total dose of 800 mg. Concurrently, he consumed Lorazepam (2 mg daily) to mitigate modafinil-induced difficulty in initiating sleep. On the mental status examination (MSE), his affect was dysphoric, and he was in the pre-contemplation stage of motivation. Serum prolactin and testosterone levels and the X-ray spine were WNL. Modafinil was tapered to 100 mg every two days and stopped after two weeks. Vortioxetine was started at 5 mg OD and increased to 20 mg OD over two weeks. Sertraline was tapered and stopped. Lorazepam was stopped after two weeks. At every two months of follow-up for six months, no relapse to modafinil use was observed.

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No recurrence of depressive symptoms was observed with vortioxetine 20 mg.

Case 2

A 34-year-old married female graduate from middle socio-economic status with an urban background premorbidly had anxious personality traits. There was a family history of nicotine and alcohol dependence in her father and dementia in her mother. She had received escitalopram 10 mg from a psychiatrist for generalized anxiety disorder of three years duration, with partial response. Later, the dose was increased to 20 mg, and pregabalin 75 mg was added. Since then, for the past year, she has had difficulty with orgasm during sexual activity and subsequent vaginal dryness. Her anxiety symptoms were significantly better, and CH, LFT, RFT, FBG, PPBG, FLP, TFT, and X-ray spine were WNL. One year ago, as commercial lubricating agents improved the vaginal dryness but the difficulty in orgasm persisted, she started using modafinil 100 mg a few hours before sexual activity. She gradually increased the dose to 400 mg to get the desired effect but started feeling low in the forenoon, with fatigue and decreased interest in doing office work. She would keep a surplus of modafinil with her. She then started taking it in the morning and would be irritable and less involved in family activities if she missed a dose. When she presented, she had been taking a total dose of 1000 mg per day for the previous eight months. She also regularly consumed melatonin (5 mg) to maintain her sleep quality. On MSE, her mood was anxious, and she was in the pre-contemplation stage of motivation. Serum follicle-stimulating hormone, luteinizing hormone, and prolactin levels were WNL. Modafinil was tapered to 100 mg every two days and stopped after three weeks. Vortioxetine was started at 5 mg OD and increased to 15 mg OD over two weeks. Escitalopram and pregabalin were tapered and stopped. Melatonin (5 mg) was continued. At three months of follow-up, no relapse to Modafinil use was observed. No recurrence of anxiety symptoms was observed with vortioxetine 15 mg. Melatonin 5 mg was stopped after three months of follow-up.

Case 3

A 32-year-old married male graduate from a high socio-economic status and urban background premorbidly had anxious personality traits. There was a family history of nicotine and alcohol dependence in his father. He was diagnosed with hypothyroidism a year ago and was on levothyroxine 100 mcg. His CH, LFT, RFT, FBG, PPBG, C-Reactive Protein, and FLP were WNL at the time hypothyroidism was diagnosed. He started taking modafinil 100 mg OD to improve his decrease in sexual desire and difficulty in erection, and he increased the dose to 400 mg over six months to obtain the same response. Subsequently, after not taking modafinil, he started getting anxiety, fatigue, and decreased attention and concentration the following day, for which he started taking it in the morning also. He also used to keep modafinil tablets with him even if he was not consuming them. He would often remain absent during office hours if modafinil was not consumed. He also became irritable and aggressive towards his wife if he did not take modafinil regularly, and he eventually increased it over six months to 900 mg/day. He consumed clonazepam 1 mg after sexual activity as he had difficulty with sleep onset after starting modafinil. On MSE, he was in the pre-contemplation stage of motivation. The serum thyroid stimulating hormone level was 18.2 mIU/ml. Anti-thyroid peroxidase, anti-thyroglobulin, and anti-thyroid-stimulating hormone receptor antibodies were negative, and serum prolactin and testosterone levels (suggested by an endocrinologist) were WNL. The X-ray spine was WNL. The urologist's opinion was taken, and no further investigations were suggested. Modafinil was tapered to 100 mg every two days and stopped after three weeks. Tadalafil 20 mg was advised to be used one hour before sexual activity for 2–3 days per week, with a minimum gap of one day. Clonazepam was tapered and stopped over two weeks, and melatonin 3 mg was prescribed. He was referred to an endocrinologist, and the levothyroxine dose was increased to 150 mcg. At every two months of follow-up for six months, no relapse to modafinil use was observed. Tadalafil and melatonin were stopped after two months of follow-up. His TFT was normal at three months of follow-up with the endocrinologist, and levothyroxine was continued at 150 mcg.

The subjects obtained modafinil over-the-counter following information from friends and the internet about modafinil increasing sexual functioning. None of them met the criteria for any psychotic disorder, and Case 3 did not meet the diagnostic criteria for any anxiety or mood disorder. Their general and systemic examinations were within normal limits. All the cases were screened to rule out any possible medical causes of the sexual dysfunction.[6] The patients were managed in outpatient settings and referred to a clinical psychologist for motivation enhancement therapy. Sexual functioning was reported to be satisfactory at the end of therapeutic intervention and follow-up. The diagnosis at the end of follow-up was kept as modafinil dependence, early full remission (ICD-11). Written informed consent was obtained from the subjects to include their clinical data.

Discussion

All the cases fulfilled the ICD-11[5] criteria for dependence on modafinil. They had cravings, where they were preoccupied throughout the day with obtaining and consuming modafinil; difficulty in controlling its consumption; a withdrawal state characterized by anxiety, fatigability, and decreased attention and concentration impairing daily function; tolerance, where they had to increase the modafinil dose to get the desired effect in sexual and daily functioning; neglect of daily and occupational activities with an increased amount of time spent thinking about modafinil consumption and procuring it; and harmful consequences in the form of decreased sleep. The initiation of modafinil in our subjects can be clearly linked to their sexual dysfunction.

The use of psychotropic agents and various medical conditions can both lead to sexual dysfunctions.[6] As seen in cases 1 and 2, selective serotonin reuptake inhibitor (SSRI) drugs like sertraline and escitalopram can be clearly linked to sexual dysfunction. Though the exact mechanism is unknown, a possible mechanism of SSRI-induced sexual dysfunction is their inhibitory effects on dopamine and nitrous oxide synthase.[7] Pregabalin has also been linked to sexual dysfunction, as seen in case 2.[8] A possible mechanism involves the inhibition of calcium channels in both the central and peripheral nervous systems, leading to a decrease in excitatory neurotransmission and sexual dysfunction.[8] Hypothyroidism, in a similar way, has an inhibitory effect on the neurotransmitters that have a positive effect on sexual func-

tioning and increases prolactin production, causing sexual dysfunction.[9]

Modafinil dependence has been previously described in four case reports, despite being reported to have lower abuse potential.[4] In one patient with bipolar disorder, an increase in modafinil dose was associated with hypersexuality, indicating that modafinil can enhance sexual functioning.[4] In the other three cases, one male patient with schizoaffective disorder developed modafinil dependence when it was initiated for mood and sleep disturbances associated with shift work,[10] one male patient with schizoaffective disorder developed dependence when it was initiated for mood fluctuations,[11] and another male patient developed modafinil dependence when it was used to treat cannabis dependence.[12] The common withdrawal symptoms were malaise, feeling low, anxiety, fatigue, boredom, and decreased attention and concentration. Our cases differ from those above, where the subjects started modafinil due to sexual dysfunction.

Modafinil increases dopamine, norepinephrine, serotonin, glutamate, and orexin and decreases serotonin and gamma-aminobutyric acid (GABA).[2,3] Increasing dopamine inhibits dopamine transporters by increasing dopaminergic activity in the medial preoptic area, thus causing sexual arousal and increasing sexual drive.[3] Improvement in orgasm can also be related to increases in norepinephrine and glutamate levels.[2,3] The decrease in GABA levels caused by modafinil can also improve sexual functioning, as GABA has a negative effect on it.[2,3] Modafinil has positive effects on cognitive functions like attention, memory, executive function, and processing speed.[2] This property of modafinil may be a possible reason for improving premature ejaculation, as it helps to have better cognitive control over sexual activity and, specifically, ejaculation time.[2] In the past, multiple reports (mostly case reports and series) have shown that modafinil, used in the dose range of 100 to 200 mg, improved sexual functioning.[2,3] The side effects were self-limited. Hence, it may be hypothesized that modafinil positively affects sexual desire, orgasm, erection, and ejaculation time.

Vortioxetine, a novel antidepressant that is a 5-HT1A receptor agonist, is a potential option for individuals with SSRI-induced sexual dysfunction.[13,14] This is highlighted in cases 1 and 2. Discontinuation of pregabalin and correction of euthyroid status can quickly improve the sexual dysfunction secondary to pregabalin use and hypothyroidism, as seen in cases 2 and 3, respectively.[8,9] Tadalafil, a phosphodiesterase 5 inhibitor, is an option for erectile dysfunction at a dose of 20 mg.[6] In case 3, tadalafil was effective, and the patient had satisfactory sexual functioning after attaining an euthyroid state, even after tadalafil was discontinued.

Conclusion

At therapeutic dosages, modafinil can be a useful agent to treat sexual dysfunction. However, it is potentially addictive, which is a disadvantage compared to other traditional drugs used for sexual dysfunction. Further studies need to be carried out regarding the same and to explore the possibilities of including modafinil in the list of substances included in stimulant dependence.

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Declaration Regarding the Use of Generative AI

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References

1. Greenblatt K and Adams N. *Modafinil*. Treasure Island (FL): StatPearls Publishing, 2023 [cited 2023 May 10]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK531476/
2. Haghighi M, Jahangard L, Meybodi AM, et al. Influence of modafinil on early ejaculation—Results from a double-blind randomized clinical trial. *J Psychiatr Res* 2022; 146: 264–71. Available from: https://www.sciencedirect.com/science/article/pii/S0022395621006646
3. Yilbaş B. Could modafinil be an option in the treatment of sexual dysfunctions due to antidepressant use in women? Two case reports. *Turk Psikiyatri Derg* 2022; 33(3): 206–210.
4. Swapnajeet S, Subodh B and Gourav G. Modafinil dependence and hypersexuality: A case report and review of the evidence. *Clin Psychopharmacol Neurosci*. 2016; 14(4): 402–404. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5083941/
5. International Classification of Diseases, Eleventh Revision (ICD-11), World Health Organization (WHO) 2019/2021, https://icd.who.int/browse11.
6. Avasthi A, Grover S and Rao TSS. Clinical practice guidelines for management of sexual dysfunction. *Indian J Psychiatry* 2017; 59(Suppl 1): S91–115. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5310110/
7. Atmaca M. Selective serotonin reuptake inhibitor-induced sexual dysfunction: Current management perspectives. *Neuropsychiatr Dis Treat* 2020; 16: 1043–1050. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7182464/
8. Hamed SA. Sexual dysfunctions induced by pregabalin. *Clin Neuropharmacol* 2018; 41(4): 116–122.
9. Gabrielson AT, Sartor RA and Hellstrom WJG. The impact of thyroid disease on sexual dysfunction in men and women. *Sex Med Rev* 2019; 7(1): 57–70.
10. Krishnan R and Chary KV. A rare case modafinil dependence. *J Pharmacol Pharmacother* 2015; 6(1): 49–50. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4319252/
11. Kate N, Grover S and Ghormode D. Dependence on supratherapeutic doses of modafinil: A case report. *Prim Care Companion CNS Disord* 2012; 14(5): PCC.11l01333. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3583757/
12. Ozturk A and Deveci E. Drug abuse of modafinil by a cannabis user. *Klinik Psikofarmakoloji Bülteni-Bulletin of Clin Psychopharmacol* 2014; 24(4): 405–407. Available from: https://doi.org/10.5455/bcp.20130624013303
13. Jing E and Straw-Wilson K. Sexual dysfunction in selective serotonin reuptake inhibitors (SSRIs) and potential solutions: A narrative literature review. *Ment Health Clin* 2016; 6(4): 191–196. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6007725/
14. Rao TSS and Andrade C. Antidepressants and sexual dysfunction: Is vortioxetine among the exceptions? J Psychosexual Health 2022; 4(3): 155–6. Available from: https://doi.org/10.1177/26318318221116038