

# Modafinil Induced Spontaneous Ejaculation Without Orgasm: A Case Report

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**Abstract:** Modafinil is used for the treatment of narcolepsy and obstructive sleep apnea syndrome, and as add-on therapy for psychiatric diseases such as attention-deficit/hyperactivity disorder, schizophrenia, depression, cocaine addiction. The exact mechanism of action is unknown. Modafinil may be helpful for the treatment of erectile dysfunction and premature ejaculation. The addition of modafinil to antidepressant treatment may provide positive effects on sexual dysfunction. However, side effects such as hypersexuality and unwanted orgasm have been reported with modafinil treatment. In this article, a patient who had developed spontaneous ejaculations after the addition of modafinil for the treatment of depression with venlafaxine is discussed. Although venlafaxine treatment continued after the discontinuation of modafinil, spontaneous ejaculation did not continue. It should be kept in mind that agents with dopaminergic and noradrenergic effects, such as modafinil, can cause undesirable sexual side effects.

**Key Words:** modafinil, spontaneous ejaculation, side effects

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Modafinil was approved by the Food and Drug Administration for the treatment of narcolepsy in 1998.<sup>1</sup> The exact mechanism of action is not yet fully known. Modafinil plays a role in the modulation of orexin, a hypothalamic neuropeptide that regulates wakefulness and appetite,<sup>2</sup> and increases alertness similar to methamphetamine.<sup>3</sup> It can also block the dopamine transporter by increasing brain dopamine levels. Modafinil is used in the treatment of daytime sleepiness such as obstructive sleep apnea syndrome and narcolepsy. In addition, many studies are showing that it is effective as an addiction therapy in psychiatric diseases such as attention-deficit/hyperactivity disorder, schizophrenia, depression, and cocaine addiction.<sup>1,4</sup>

Cases with hypersexuality and unwelcome orgasm have been reported with modafinil treatment. In this article, a patient who developed spontaneous ejaculation after adding modafinil to venlafaxine for the treatment of depression is discussed.

## CASE REPORT

A 41-year-old, married, male patient without any health problems applied to the psychiatric outpatient clinic with a complaint of daytime sleepiness. He was admitted for a psychiatric assessment 1 year ago, and anxiety, anhedonia, weakness-fatigue, decreased interest and desire, and anergy were detected. He was diagnosed as having major depressive disorder according to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* and prescribed venlafaxine 75 mg/d. Depressive complaints subsided after drug therapy, but daytime sleepiness continued

despite the regular drug therapy for 1 year without affecting his daily life. Recently, with the increase in his workload, his functionality decreased because of daytime sleepiness. No abnormalities were detected in thyroid function tests and blood biochemistry. Modafinil 100 mg/d was added to venlafaxine therapy. Daytime sleepiness was detected, which significantly declined during the outpatient control 1 month later. However, he described spontaneous ejaculation that began 15 days after modafinil treatment. Unwelcome spontaneous ejaculation has been occurring nearly every day, without any sexual stimulation and orgasm. He had a regular sexual life, 2 to 3 times a week. He did not report any problems in his sexual desire and sexual function. No pathology was detected with laboratory tests and urology consultation. Modafinil treatment was stopped. He stated that following 3 days after the cessation of modafinil, involuntary ejaculation disappeared completely. Venlafaxine dosage was increased to 112.5 mg/d. Daytime sleepiness decreased significantly, and his functionality returned to normal.

## DISCUSSION

Ejaculation is expelling the ejaculate in 3 stages: emission, ejection, and ejaculation/orgasm. The seminal fluid accumulates in the posterior urethra through the sympathetic system during the emission phase. Rhythmic muscle contractions are provided with parasympathetic system reflexes, the bladder neck closes, and the external urethral sphincter relaxes during the ejection phase. Ejaculate comes out of the urethra with pressure in the ejaculation/orgasm phase. Sensorial stimulation reaches the central nervous system through the pudendal nerve in the last phase of sexual intercourse, and an orgasmic feeling is experienced simultaneously with the ejaculate being expelled.<sup>5</sup>

Ejaculatory anhedonia, which is one of the ejaculation disorders, is defined as having physiological ejaculation but not being able to enjoy or have an orgasm. This can be seen as a side effect of antidepressants from each group, besides organic reasons.<sup>6</sup>

The medial preoptic area (MPOA) in the hypothalamus, the nucleus paragigantocellularis, the posteromedial nucleus of the stria terminalis, the posterodorsal medial amygdala, and the medial parvisellular suprafascicular nucleus of the thalamus are the areas that control ejaculation. The MPOA stimulates ejaculation through 5-HT<sub>1A</sub> receptors; serotonergic pathways descending into the lumbosacral motor nuclei from the nucleus paragigantocellularis inhibit ejaculation via 5-HT<sub>1B</sub> and 5-HT<sub>2C</sub> receptors.<sup>5</sup>

Modafinil causes the increase in extracellular dopamine, noradrenaline, serotonin, glutamate, histamine, and hypocretin levels, and a decrease in GABA level.<sup>1,4</sup> Dopamine can increase sensorimotor integration by acting on the MPOA. It can also coordinate autonomic effects on genital reflexes. Small increases in dopamine levels in MPOA can inhibit genital reflexes through D<sub>2</sub>-like receptors. Slightly larger increases may initiate parasympathetically mediated erection and mating stages through D<sub>1</sub>-like receptors. A larger amount of dopamine or D<sub>2</sub> agonists in MPOA can shift the autonomic balance to the favor of seminal emission and discharge.<sup>7</sup> There are some case reports and studies that modafinil is useful for the treatment of erectile dysfunction and premature ejaculation.<sup>8–10</sup>

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In addition, cases of hypersexuality and spontaneous orgasm related to modafinil have been reported.<sup>2,11,12</sup> In our case, spontaneous ejaculation after the addition of modafinil to venlafaxine 75 mg/d treatment may be associated with increased dopamine stimulation in MPOA.

Some cases of spontaneous ejaculation with noradrenergic antidepressants have been reported.<sup>6,13–17</sup> Spontaneous ejaculations that occur without sexual stimulation are generally seen after mixing and defecation.<sup>14</sup> Venlafaxine is an antidepressant that inhibits serotonin, noradrenaline, and dopamine reuptake and is used for treating major depression, generalized anxiety disorder, panic disorder, and social phobia. Venlafaxine has selective serotonin reuptake inhibitor similar effects at low doses, and noradrenergic and dopaminergic effects occur at high doses.<sup>18</sup> Some sexual side effects could occur such as decreased libido, abnormal ejaculation, delayed orgasm, anorgasmia, and erectile dysfunction.<sup>15</sup> In our case, the dosage of venlafaxine was low, no sexual side effects were reported with the treatment he used before, and when modafinil was stopped, spontaneous ejaculation disappeared completely. Therefore, it was thought that the current situation was not related to venlafaxine. However, concomitant use of venlafaxine and modafinil may have increased the dopaminergic effect.

To the best of our knowledge, this is the first case related to involuntary ejaculation during the use of modafinil. Although this phenomenon is rare, our case shows modafinil may cause some sexual side effects. Modafinil may be helpful for the treatment of erectile dysfunction and premature ejaculation. Positive effects on sexual dysfunction can be achieved with the addition of modafinil to antidepressant treatment. In addition, it should be considered that agents with dopaminergic and noradrenergic effects may cause some unwanted sexual side effects.

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