Bupropion Extended-Release Induced Spontaneous Orgasms

ABSTRACT
Bupropion extended-release induced spontaneous orgasms
Sexual side effects are common with antidepressant use. Spontaneous orgasms have been previously described with several antidepressants. We report the case of a woman who had spontaneous orgasms after starting 300mg/day bupropion extended-release. Spontaneous orgasms ceased 4 days after stopping the bupropion extended-release. Bupropion extended-release is a norepinephrine-dopamine reuptake inhibitor. Norepinephrine- and dopamine-related mechanisms may induce spontaneous orgasms. This unusual side effect should be questioned in patients who receive bupropion, as it may cause embarrassment and noncompliance.

Keywords: Bupropion, orgasm, postmenopause, sexual dysfunction

INTRODUCTION
Sexual side effects of antidepressant drugs are commonly observed (1). Patients who receive antidepressant drugs frequently report sexual dysfunction, which may affect all phases of the sexual response cycle, i.e. desire, arousal, and orgasm. Delayed erection and anorgasmia are the most frequent sexual side effects, but spontaneous orgasms have also been described previously with venlafaxine (2), paroxetine (3), mirtazapine (4), trazodone (5), and bupropion sustained-release (SR) (6).

Bupropion extended-release (XL) is an important pharmacological agent that belongs to the class of aminoketones; it is a norepinephrine-dopamine reuptake inhibitor and a nicotinic antagonist. It has no effects on serotonin, histamine, acetylcholine, or epinephrine receptors. It is used as an antidepressant to treat major depressive disorders, sexual side effects of selective serotonin reuptake inhibitors, and in treatment for smoking cessation (7,8). The most common side effects with the use of bupropion can be listed as insomnia, headache, dry mouth, rash, nausea, sweating, and hypertension (9). Here, we are reporting a case of spontaneous orgasm during the treatment with bupropion XL in a depressive postmenopausal patient.

CASE
Mrs. A was 58 years old, had been married for 35 years, and was in the postmenopausal period. She had been followed at a psychiatry outpatient clinic for 20 years with a diagnosis of major depressive disorder and...
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Somatization disorder. She had been using 100mg/day quetiapine for approximately 10 years and 25mg/day agomelatine for one year. Previously used drugs were duloxetine, venlafaxine, and milnacipran. On admission, there was no sleep problem, but her chronic strain, low mastery, and rumination symptoms were not controlled with this treatment. We decided to manage the patient with adding bupropion XL. After starting with 150mg/day bupropion XL, the patient came to our clinic complaining of insomnia. This expected side effect lasted for one week. The dose of bupropion XL was increased to 300mg/day. Within one week of taking bupropion XL, the patient began repeatedly to experience spontaneous unwelcome orgasms 3-4 times a night at sleep, which had never happened in the past. The patient did not receive any pleasure while having spontaneous orgasms, but felt guilt and anxiety. During the psychiatric interview, the patient was restless and exhibited symptoms of anxiety. Physical examination revealed no pathology. Neurological examination findings were normal. She was referred to the gynecology department, and no organic pathology was detected. She continued bupropion XL at the same dose for one more month and came to control again. She was still complaining of spontaneous orgasms; but the patient was dissatisfied with the drug in spite of the decreased depressive symptoms. The bupropion XL dosage was reduced to 150mg/day. Spontaneous orgasms ceased 4 days after reducing the bupropion XL. In her follow-up, she did not report any other sexual side effects with using bupropion XL. Partial remission in depressive symptoms was also sustained during follow-up. Written informed consent was received from the patient to publish her data.

DISCUSSION

Pharmacologically, selective serotonin reuptake inhibitors (SSRIs) reduce the binding of serotonin to the serotonin transporter, thereby increasing the concentration of synaptic serotonin. This SSRI effect may additionally decrease the concentrations of dopamine and noradrenaline in the mesolimbic system by activating serotonin 5-HT2 receptors (10). Michael et al. (11) used the ability of nefazodone to cause spontaneous ejaculation by virtue of its 5-HT2 antagonist effect to reverse SSRI-induced anorgasmia. Pae et al. (12) described three cases of paroxetine-associated sexual stimulation. Boora et al. (13) reported that ziprasidone might be causing an increase in sexual orgasm by 5-HT2 receptor antagonism, of which preclinical evidence suggests that it facilitates dopamine release in cortex. Saiz-Ruiz et al. (14) reported improvement of sexual function in depressed patients treated with mirtazapine. The main mechanism considered responsible for this improvement, as well as for the spontaneous orgasms that have been reported with other drugs, is the agonism of 5-HT1 receptors and antagonism of 5-HT2c receptors. Brain dopamine systems between the hypothalamus and limbic system are thought to be the main sexual excitatory systems (7,15). Uca and Kozak (16) hypothesized that the spontaneous unwelcome orgasms might be related to the dopaminergic stimulation caused by the use of rasagiline. Noradrenaline regulates sexual arousal and bupropion has been reported to decrease SSRI-induced sexual dysfunction (17-19).

Bupropion causes a rapid, dose-dependent increase in vesicular dopamine uptake, acting through an inhibitory effect on the dopamine transporter. It enhances activity in central dopaminergic and noradrenergic neurotransmitter systems, which are associated with the regulation of the sexual response in humans (20). There are three types of bupropion; the immediate-release form of bupropion has been available in the United States since 1989, a SR formulation followed in 1996, and in August 2003, the XL formulation was introduced. Grimes and Labbate (21) reported a case of spontaneous orgasm with the combined use of bupropion and sertraline. Another spontaneous orgasm case related to bupropion use was described by Labbate (6).

In this case, the noradrenergic effects of bupropion XL may have a role in spontaneous orgasms by peripheral effects on the sympathetic system. The dopaminergic system may play another role in spontaneous orgasms. Patients experiencing this side effect may feel guilt and anxiety (22). It is thought that the spontaneous orgasm is a dose-dependent side effect, as it ceased 4 days after reducing the dose of bupropion XL.
CONCLUSION

This case report suggests that physicians should be aware that bupropion may induce unusual sexual side effects such as spontaneous orgasms. Further systematic research should be conducted with respect to antidepressant-associated sexual stimulation to provide a greater understanding of both its prevalence and etiology.

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