Use of Modafinil in Co-existing Major Depression and Erectile Dysfunction: A Case Report

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SUMMARY

Erectile dysfunction is a sexual dysfunction which is commonly comorbid with major depression. Antidepressant treatment does not always improve comorbid sexual dysfunctions in major depression. In fact, sexual dysfunction may worsen or get complicated following the introduction of antidepressants. Modafinil is a drug with stimulant effect on the central nervous system by binding to norepinephrine and dopamine transporters and consequently increasing synaptic norepinephrine and dopamine levels. Modafinil is primarily used in the treatment of narcolepsy and chronic fatigue syndrome. In addition, it is known for its effectiveness in attention deficit hyperactivity disorder and as an add-on option for major depression. In this paper, we report the case of a 39-year-old man with major depression whose comorbid erectile dysfunction improved after addition of modafinil to antidepressant treatment. Fluoxetine 20mg/day was initiated and despite the improvement of most of the depressive symptoms and the sexual desire, his complaints of fatigue, weakness and erectile dysfunction continued. With the addition of modafinil (200 mg /day), improvement was observed not only in psychomotor symptoms but also in erectile dysfunction of the patient.

Keywords: Modafinil, depression, sexual dysfunction, erectile dysfunction, treatment

INTRODUCTION

Sexual dysfunctions are common in patients with major depressive disorder. One of the most common complaints of sexual dysfunction comorbid with depression in middle aged men is erectile dysfunction (Thase et al. 1988, Araujo et al. 1998). Selective serotonin reuptake inhibitors (SSRIs) which are widely used in the treatment of depression do not improve sexual dysfunction comorbidity. On the contrary, one of the most common side effects of SSRIs is sexual dysfunction (Masand and Gupta 2002, Williams et al. 2006). Modafinil is a drug with stimulant properties used primarily for treatment of narcolepsy and chronic fatigue syndrome. However, it showed efficacy in attention deficit and hyperactivity disorder and as an add-on medication in depression (Ballon and Feifel 2006, Goss et al. 2013). In this report, we present the case of a 39-year old male patient on antidepressant therapy for major depression, who showed improvement in comorbid erectile dysfunction after adding modafinil to his treatment.

CASE

A.R., a 39-year-old male patient, married and living with his family and working as a mechanical engineer, presented to psychiatry outpatient clinic with complaints of breakdown, unwillingness, fatigue, sleepiness, headache and difficulties with consentration. He had the depressive symptoms for the last four months. Shortly after the onset of symptoms, he had complaints of loss of sexual desire and also erection difficulties when feeling sexual desire. His psychiatric history included a previous episode of depression lasting for three months and

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dating back five years. He had been treated with fluoxetine (20 mg/day) for one year and his depressive symptoms had resolved completely. At the time his only sexual problems was loss of sexual desire which improved after the treatment. There was no other history of any other mental disorder. At his psychiatric assessment, he was alert, cooperative and fully oriented. His self-care seemed to be appropriate and he was low in mood with appropriate affect. His speech speed was slightly slow, associations were appropriate and goal oriented. There was no evidence of delusions or hallucinations. His thought content included expressions of hopelessness and unworthiness. He denied suicidal or homicidal thoughts. He had insight about his complaints. He had a score of 27 on the Hamilton Rating Scale for Depression (HAM-D 17). His laboratory tests including full blood count, vitamin B12, folate and electrolyte levels, and the liver, kidney and thyroid function tests were all in the normal range. On the basis of these findings and his symptoms, he was diagnosed with major depressive disorder with atypical features.

We recommended fluoxetine (20 mg/day) considering his positive response to the same medication in the past. The patient showed improvement in the depressive symptoms by the second week of his treatment. At the fifth week of the treatment most of the depressive symptoms had improved and he scored 8 points on HAM-D. His sexual desire also showed a significant improvement. However, despite the improvement of other depressive symptoms, his complaints of fatigue, exhaustion and erectile dysfunction persisted. At this stage, consultative urological investigations did not yield any results to explain the erectile dysfunction. In the sixth week of fluoxetine treatment, modafinil (100 mg/day) was added to the treatment to improve the complaints of fatigue and exhaustion. After one week, modafinil dose was increased to 200 mg/day for optimal efficiency and on the basis or the patient's weight. He reported significant improvement in erectile dysfunction after modafinil treatment. The HAM-D score of the patient was found to be 5 at that stage.

DISCUSSION

Despite the common complaint of comorbid erectile dysfunction in major depression, the causal relationship between these two disorders is not clear. Erectile dysfunction can be observed as part of depression, and erectile dysfunction by itself can induce a 'secondary' depressive episode (Araujo et al.1998). Other factors such as alcohol misuse, cardiovascular problems, and hipogonadism can trigger either condition or both (Seidman and Roose 2000). In the reported case, the erectile dysfunction complaint had followed the onset of depressive symptoms, suggesting it to be a result of or 'secondary' to depression. The first line treatment with fluoxetine was based on the patients response to the agent in his previous depressive episode, but, unlike in the past, this time the psychomotor retardation did not respond to fluoxetine treatment. The patient was suffering from marked erection difficulty even after his sexual desire showed improvement and he reported erection difficulty for most of his sexual activities. At that stage, the patient's sexual problem was defined as an arousal disorder and diagnosed as erectile dysfunction. One possible reason for the continuation of erectile dysfunction after depression in our patient might be due to performance anxiety leading to persistance of erection difficulty (Langer et al.2017). One other cause of persistent erectile dysfunction might be the side effect of fluoxetine.Modafinil is used as an additive treatment in both unipolar and bipolar depression patients and shows therapeutic efficacy on depression symptoms. The treatment enhancing effect of modafinil is observed more particularly on psychomotor symptoms such as fatigue and exhaustion (Goss et al. 2013). In the case discussed here, with the addition of modafinil to the treatment, not only the psychomotor symptoms and other depression symptoms, but also the complaint of erection difficulty improved. Modafinil shows its mechanism by binding to norepinephrine and dopamine transporters, resulting in increased levels of norepinephrine and dopamine in the synaptic cleft. Modafinil has also been shown to increase serotonin and glutamate levels and decrease GABA levels (Minzenberg and Carter 2008). These neurotransmitter changes are mostly seen in neocortical areas, but also in subcortical areas. Subcortical changes are associated with vigilance and its effectiveness in narcolepsy, fibromyalgia and idiopathic hypersomnia has been linked to these mechanisms. Cortical changes were thought to be associated with the positive effect of modafinil on cognitive functions (Ballon and Feifel 2006).

It has been reported that methylphenidate, one of the stimulant drugs, has effect on sexual desire and increases sexual arousal in response to sexual stimulation (Volkow et al. 2007, Schmid et al. 2015). It is also used for the treatment of sexual dysfunction caused by antidepressants (Francois et al. 2017). There are not any reports in the literature on the positive effect of modafinil as a stimulant drug on erectile dysfunction or depression related sexual dysfunction. There are case reports on the role of modafinil in spontaneous orgasm or hypersexuality (Uca and Altaş 2014, Bulut et al. 2015, Swapnajeet et al. 2016). It has been reported In a preclinical study that modafinil induced ejaculation delay in rats (Marson et al. 2010). It has been suggested that modafinil may cause dopaminergic activity in the medial preoptic area of the hypothalamus and may cause stimulating effects on male sexual function (Dominguez and Hull 2005, Qu et al. 2008). In this context, it was thought that improvement of erectile dysfunction after the addition of modafinil to treatment may be associated with dopaminergic stimulation

in the medial preoptic area. Although, in the case reported here, the symptoms of depression were significantly reduced prior to the addition of modafinil to treatment, it is difficult to conclude that modafinil has a direct effect on sexual arousal. Although a definite cause-effect relationship could not be established on the case we have discussed, it may be useful for clinicians to take into account changes in the sexual functions of the patients following modafinil treatment, particularly for the purpose of augmenting antidepressant treatment. Controlled studies are needed to determine the possible effects of modafinil on sexual functions, especially on sexual functions in patients with major depression.

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