Letter to the Editor

Augmentation With Modafinil to Achieve Remission in Depression: A Case Report

Sir: Depression, with a prevalence rate from 4.8% to 9.2%, is a common illness treated by family physicians.[1] Over the last 20 years, a number of antidepressants have become available for physicians to treat patients with depression. Approximately 50% to 60% of patients will respond to treatment[2]; however, only about half of those patients responding to treatment will achieve remission.[3] Clinicians are then left to treat a large number of patients who have responded to initial treatment but continue to experience depressive symptoms that interfere with their level of functioning. A case is presented of a patient diagnosed with depression, taking 2 antidepressants, who had previously failed augmentation with lithium and levothyroxine, but achieved remission with the addition of modafinil.

Case report. Ms. A, a 30-year-old woman, was referred by her family physician for consultation on antidepressant treatment strategies. She had been diagnosed 3 years before with major depressive disorder, recurrent per DSM-IV criteria.[4] On initial evaluation, she reported a number of depressive symptoms including decreased sleep, decreased libido, poor concentration, anhedonia, and low energy. Her medical history was unremarkable, and a psychiatric review of systems was significant for the lack of past or present suicidal ideation and lack of psychotic symptoms or manic symptoms. In the past, she had taken sertraline, up to 200 mg/day, for about 9 months, eventually augmented with levothyroxine, 0.05 µg/day. At the time of consultation, she was taking bupropion sustained release, 150 mg b.i.d., over the last year augmented with lithium, 300 mg t.i.d., for 4 months. She denied the use of alcohol, illicit substances, tobacco, and herbal products. Laboratory studies showed a lithium level of 0.6 mmol/L; thyroid-stimulating hormone (TSH) of 3.13 µIU/mL; and fasting glucose, blood urea nitrogen, and creatinine levels all within normal limits. A urine pregnancy test was negative. An initial Hamilton Rating Scale for Depression (HAM-D)[5] score was 18, with a significant complaint of low energy. Ms. A was concerned about a 20-lb (9-kg) weight gain she associated with the lithium and asked to discontinue this medication as she felt no better since its addition. Based on the thinking that her low energy could be due in part to poor sleep, zaleplon, 10 mg, was added, and the patient was instructed on sleep hygiene techniques. Within several days, she reported improved sleep, yet continued to experience residual low energy. She agreed to the addition of venlafaxine extended release started at 37.5 mg/day and eventually titrated to 225 mg/day. At a month's time, her HAM-D score had dropped to 12, but she continued to experience low energy and poor concentration. A second TSH, complete blood count, and pregnancy test were within normal limits or negative. Ms. A consented to a trial of modafinil, 200 mg/day, and within 1 week of treatment, she reported vastly improved energy and concentration. After 2 weeks, the HAM-D score had dropped to 4, and at 6 months, Ms. A remains in full remission.

Modafinil is a medication approved by the U.S. Food and Drug Administration to treat excessive daytime sleepiness associated with narcolepsy. Its mechanism of action is unknown, but appears to be distinct from amphetamine and methylphenidate in that it does not seem to mediate wakefulness via dopaminergic mechanisms.[6] Although the patient had never been treated with more standard psychostimulants, she had been taking bupropion for an adequate length of time and did not appear to benefit from the activating effects of bupropion's stimulation of the dopaminergic system.[7] It was felt that her continued low energy could be treated successfully as reported by Menza et al.[6] in a case series of 7 patients whose presentation was similar to that of this patient. By improving her energy, her overall sense of improvement undoubtedly contributed to achieving remission.

Although single case reports should be interpreted with caution, patients with depression and continued low energy may constitute a particular group who might benefit from a similar augmentation strategy. Further studies are warranted in a more controlled manner to determine the effectiveness of modafinil augmentation of antidepressants.

Conclusions and opinions expressed are those of the author and do not necessarily reflect the position or policy of the U.S. Government, Department of Defense, Department of the Army, or the U.S. Army Medical Command.

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