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Modafinil Monotherapy in Poststroke Depression

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Although the incidence of cerebrovascular disease has stabilized, the number of stroke survivors increases as the acute management of stroke improves.¹ Poststroke depression is common; the risk for major depression is 10%–25%, while the risk for minor depression is 10%–40%.² Poststroke depression is associated with excess disability, poor rehabilitation outcomes, greater morbidity and mortality, and suicidality.³ These complications may be addressed with pharmacotherapy.⁴

Modafinil, a wakefulness-promoting agent, is approved by the Food and Drug Administration for narcolepsy.⁵ There are case reports of off-label use of modafinil for depression, including cases of treatment resistance and severe medical comorbidity.^{6–8} Although the mechanism of action is unknown, the drug has norepinephrine agonist properties in the anterior hypothalamus.⁹ We report a case of poststroke depression that was responsive to modafinil treatment.

Case Report

Ms. A, an elderly woman, came in with a worsening headache that progressed to acute loss of consciousness. Her medical history included hypothyroidism, hyperlipidemia, hypertension, and abdominal hernia repair. She had a history of bipolar I disorder treated with lithium carbonate, 600 mg/day. Her other medication was levothyroxine, 100 µg/day. The results of serum chemistries, a CBC, and measurements of thyroid-stimulating hormone and T₄ levels were found to be within normal limits.

A computerized tomography (CT) scan showed a rup-

tured berry aneurysm on the basilar tip, so Ms. A underwent endovascular coiling. Her level of consciousness continued to deteriorate. A repeat CT scan showed frontal lobe hydrocephalus; a right frontal ventriculostomy was performed and allowed to drain for 1 week. Postoperatively, Ms. A gradually regained consciousness but was disoriented and could not follow directions. An MRI performed 16 days after presentation showed a coiled aneurysm at the basilar tip, an intraventricular hemorrhage with a right frontal ventricular peritoneal shunt, a right frontal hematoma, a complex aneurysm of the left posterior communicating artery, and irregularities in the left proximal communicating and middle cerebral arteries. Twenty-four days after Ms. A's initial presentation, she began inpatient rehabilitation, where she was described as "apathetic and lethargic," with poor participation in physical therapy. There were no reported symptoms of mania, anxiety, or psychosis.

Ms. A was evaluated by the psychiatric consultation-liaison service. She was alert but disoriented to person, place, and time. Her affect was flat. She did not engage in conversation and had sparse spontaneous speech. She was unable to complete any components of the Folstein Mini-Mental Status Examination (MMSE). She reported no suicidality or hallucinations. She was started on a trial of modafinil, 100 mg/day; lithium was discontinued. After the third dose, she became more alert and spontaneously engaged in conversation. An MMSE after 10 days of modafinil therapy revealed a score of 21. She was able to tolerate physical therapy and was subsequently discharged from rehabilitation 1 week early because of her functional gains.

Two weeks after discharge, Ms. A's mood symptoms were stable. She did not appear to be apathetic or to display vegetative symptoms, and she engaged in conversation spontaneously. There were no signs of mania or hypomania. However, she and her family noted continued deficits of her memory to which she required prompting. She was able to bathe, dress, and feed herself, but she required supervision. Her next score on the MMSE was 20.

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Discussion

This case report represents the first use of modafinil for poststroke depression, to our knowledge. Antidepressants have been the most studied treatment for poststroke depression, and most studies show similar effectiveness among several antidepressants.³ However, recent literature suggests that tricyclic antidepressants may be more effective than serotonin reuptake inhibitors for poststroke depression.¹⁰

There have been no randomized controlled trials of psychostimulants for poststroke depression. Nevertheless, there is a small body of literature advocating their use.^{11–13} Grade et al.¹⁴ recently published a randomized controlled study evaluating the effectiveness of methylphenidate over a 3-week period during early poststroke recovery. They randomly assigned 21 patients to treatment and placebo groups. The methylphenidate group was started on an initial dose of 5 mg/day, which was gradually increased to 30

mg/day. The patients taking methylphenidate scored lower on the Hamilton Depression Rating Scale and the Zung Self-Rating Depression Scale. Although the study did not specifically use poststroke depression as a criterion for participation, the results suggest that treatment with psychostimulants may expedite recovery from depressive symptoms. These results are consistent with a previous double-blind study showing that amphetamine use significantly accelerated recovery with physical therapy in poststroke patients.¹⁵

The choice of modafinil in the treatment of poststroke depression is appealing since it combines the benefits of both wakefulness-promoting agents and antidepressants. Modafinil provides noradrenergic modulation, which may be beneficial in poststroke depression,¹⁰ without the potential abuse associated with methylphenidate.^{16,17} There is a more favorable side effect profile, with less hypertension, tachycardia, insomnia, and anxiety than with methylphenidate.¹⁸ Modafinil for poststroke depression is worthy of further investigation in double-blind, placebo-controlled trials.

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