Early Antidepressant Treatment Is Effective for Post-Stroke Depression

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Major depression is twice as likely to develop in post-stroke patients (approximately 20%) than in nonstroke patients of the same age.¹ Other psychiatric symptoms that are also more common in post-stroke patients include minor depression, anxiety, anger, and inappropriate or excessive laughing or crying (emotional incontinence).²

Two explanations for the high frequency of depression in the post-stroke period (up to 40% of patients if one includes all forms of depression) usually are put forth. The first suggests that clinical depression is a psychological reaction to the debility and other symptoms of the stroke; the second focuses on the physical damage to the brain that affects not only physical functioning but also parts of the brain or transmitters vital to mood regulation.

The link between stroke and depression may be established before a stroke occurs. During a 13-year follow-up study of 1703 persons, those with a history of depressive disorder were 2.6 times more likely to have a stroke than those without the disorder, even after controlling for heart disease, hypertension, diabetes, and current and previous use of tobacco.³

Whatever the connection between stroke and depression, the combination worsens prognosis. In persons with acute stroke, depression has been associated with poorer cognitive and physical recovery. Morris and colleagues⁵ studied a consecutive series of 103 patients approximately 2 weeks after stroke and found that those with either major or minor depression were 3.4 times more likely to die during the 10-year follow-up than those without depression. This relationship was independent of other major risk factors, such as age, sex, social class, type of stroke, lesion location, and level of social functioning.

Fortunately, treatment with antidepressants early in the post-stroke period is often helpful. Double-blind studies of the use of nortriptyline,⁶ citalopram,⁷ sertraline,⁸ and other antidepressants have shown efficacy in treating persons with post-stroke depression.

In addition, a 12-week regimen of fluoxetine or nortriptyline during the first 6 months post-stroke significantly increases the rate of survival for both depressed and nondepressed patients.⁹ In this study, an intention-to-treat analysis showed that 42 (59.2%) of the 71 patients randomly assigned to receive antidepressants were alive at the 9-year follow-up compared with 12 (36.4%) of the 33 patients who received placebo. Of the patients who completed the 12-week treatment protocol (N = 81), 36 (67.9%) of the 53 patients who received antidepressants were alive at the 9-year follow-up compared with 10 (35.7%) of the 28 patients who received placebo. The probability of survival was significantly greater in the patients who received antidepressant treatment (P = .004). As the study authors noted, it is surprising that a mere 12 weeks of antidepressant treatment early in the post-stroke period had such a profound effect on survival rates 9 years later. Indeed, the Kaplan-Meier survival analysis indicated that the benefit of antidepressant use was not apparent until the third year of the study, long after the completion of the short-term antidepressant treatment.

Post-stroke patients not only are at increased risk for an early death but often have ongoing problems with mental function. Executive functioning, in particular, is impaired in most people who have had a stroke. This impairment interferes with a person’s response to unfamiliar or complex situations and may slow rehabilitation and psychosocial readaptation. However, a recent placebo-controlled trial of 12 weeks of antidepressant treatment in the immediate post-stroke period
showed an improvement in executive function.\textsuperscript{10} At the end of treatment, there was no difference between the patients in the antidepressant group and those in the placebo group. However, 21 months after the end of treatment, the placebo group showed further deterioration of executive function, whereas the antidepressant group showed clear and significant improvement independent of depressive symptoms.

Although the benefit of antidepressants in physical and cognitive recovery is well established, the mechanism is not entirely clear. Spalletta and colleagues\textsuperscript{11} postulated that the etiology and treatment of post-stroke depression is best explained by the inflammatory cytokine hypothesis of depression: the production of proinflammatory cytokines resulting from brain ischemia in cerebral areas may cause a depressive syndrome that can continue for years. All antidepressant medications, independent of their mechanism of action, are able to oppose, to some extent, the effects of proinflammatory cytokines on the brain.\textsuperscript{12} For example, Musselman and colleagues\textsuperscript{13} observed that depressive symptoms in persons treated with interferon alfa can be attenuated with paroxetine. An even more popular explanation involves the relatively new idea that neurogenesis is crucial for the antidepressant effect.\textsuperscript{14} Very simply, the administration of antidepressants enhances the development of immature neurons and promotes the survival and function of adult neurons by increasing brain-derived neurotrophic factor.

### Conclusion

Antidepressant treatment early in the post-stroke period is indicated for any person with depressive symptoms. Antidepressants may even be beneficial for post-stroke patients without depression, but this practice lacks sufficient outcome data.

### References:

**References**


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