Prophylactic mirtazapine may help to prevent post-stroke depression in people with good cognitive function


Q Does treatment with mirtazapine after an ischaemic stroke prevent onset of depression?

Methods

- **Design:** Randomised controlled trial.
- **Allocation:** Not reported.
- **Blinding:** Not blinded.
- **Follow up period:** 360 days.
- **Setting:** Stroke unit in academic medical centre in Ludwigshafen, Germany.
- **Patients:** Seventy people who had suffered an ischaemic stroke, confirmed by MRI or CT scan. People were excluded if they were currently using antidepressants, were depressed in the two weeks before stroke, were less than 18 years old, pregnant or breastfeeding, or had dysphasia that would interfere with psychiatric testing.
- **Intervention:** Treatment was 30 mg of mirtazapine once daily at bedtime and commenced one day after the occurrence of stroke. People in the control group were given neither mirtazapine nor placebo.
- **Outcomes:** Major depressive episode (DSM-IV and score ≥16 on Hamilton Rating Scale for Depression (HAM-D)); occurrence determined by semistructured interview and severity using HAM-D.
- **Patient follow up:** 89% after 360 days.

Main results

The study found that significantly fewer people in the treatment group developed depression after their ischaemic stroke compared with those who did not take mirtazapine during follow up (major depressive episode: 2/35 [5.7%] with treatment vs 14/35 [40%] without treatment; p = 0.001, OR 0.069, 95% CI 0.012 to 0.389). Severity of stroke (NIHSS score) was significantly related to odds of depression (OR 1.22, 95% CI 1.04 to 1.45, no further details), although age and sex had no effect.

Conclusions

Mirtazapine prevents depression in people with ischaemic stroke.

Notes

The study was not placebo controlled and participants were not blinded to treatment, which may have introduced a bias in favour of active treatment. More than 90% of people screened for recruitment were not enrolled as participants. Exclusion criteria included inability to give informed consent, aphasias that interfered with recruitment or assessment, and haemorrhagic stroke. Results may not, therefore, generalise to all patients with stroke.

Commentary

Post-stroke depression (PSD) is common and underreported. PSD may be seen up to seven years after stroke and it may lead to worse outcomes. However, early treatment may improve outcomes. Major depression after stroke is less common than depressive symptoms. Meta-analysis of antidepressant treatment in stroke has not shown consistent results but does not address early, “prophylactic” treatment. A frontal executive hypo-arousal hypothesis has been suggested. Increasing serotonergic activation might alleviate such under-arousal, although several studies suggest a more psychological than neurological basis for PSD.

This study addresses acute, reactive symptoms within the first year after stroke and does not address the impact of treatment on functional outcomes or quality of life, nor whether “prophylactic” treatment is superior to treatment in response to symptoms. It does not have the breadth of population to warrant the general acceptance of mirtazapine for all stroke patients. The inclusion criteria and baseline data suggest that the bulk of the sample was cognitively intact with significant residual deficits and thus may be prone to reactive depressions. The study nicely shows that mirtazapine (and close clinical monitoring) is effective for depressive symptoms in this type of stroke patient. However, the results do not generalise—the strict inclusion criteria employed by the study mean that prophylactic effects in a general stroke population cannot be reasonably addressed. The authors mention, but discount, the possibility of placebo effects, which is surely an overstatement given their design, which was unblinded and did not include a placebo arm. These methodological weaknesses are likely to have overplayed the benefits of mirtazapine.

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