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Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

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Background

Stroke is a major cause of adult disability. The 2012 Cochrane Review of SSRIs for stroke recovery demonstrated positive effects on recovery. We updated this review in 2019 because a large trial of fluoxetine for stroke recovery (Fluoxetine or Control Under Supervision, FOCUS) was published in December 2018.

Objectives

To determine if SSRIs are more effective than placebo or usual care at improving outcomes in people less than 12 months post-stroke, and to determine associations with adverse effects.

Search methods

We searched several electronic databases up to July 2018, trials registers and grey literature.

Selection criteria

We selected all randomized controlled trials (RCTs) of any SSRI treatment versus no usual care or placebo recruiting patients who had had a stroke in the previous year. Trials had to collect data on at least one of our primary (disability score or independence) or secondary outcomes (impairments, depression, anxiety, quality of life, fatigue, healthcare cost, death, adverse events and leaving the trial early).

Data collection and analysis

Two review authors independently extracted data and assessed risk of bias. We calculated standardised mean differences (SMDs), and risk ratios (RRs) as appropriate. We restricted the primary analysis to studies at low risk of bias.

Main results

We identified a total of 63 eligible trials recruiting 9168 participants. About half the trials required participants to have depression to enter the trial. The duration, drug, and dose varied between trials. Meta-analysis of the three trials at low risk of bias found no effect of SSRI on disability score (SMD −0.01; 95% CI −0.09 to 0.06; P = 0.75; 2 studies, 2829 participants) or independence (RR 1.00; 95% CI 0.91 to 1.09; P = 0.99; 3 studies, 3249 participants) (see Figure). We downgraded both these outcomes for imprecision.

Figure: Forest plot of the outcome independence; comparing SSRIs with usual care or placebo. CI indicates confidence interval.

SSRIs reduced the depression scores but increased gastrointestinal side effects. When all trials were included irrespective of risk of bias, SSRIs reduced disability scores but not dependence.

Authors' conclusions and implication

There is no reliable evidence that SSRIs should be used routinely to promote recovery after stroke.

Implications for research

This review will be updated again when two large ongoing trials are published in 2020.

Disclosures

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GM, MD, MH, EL, and GJH are investigators and grant holders for three large trials of fluoxetine for stroke recovery.

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This paper is based on a Cochrane Review published in The Cochrane Library 2019, Issue 11 (see www.thecochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and The Cochrane Library should be consulted for the most recent version of the review.

Reference

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Figure: Forest plot of the outcome independence; comparing SSRIs with usual care or placebo. CI indicates confidence interval.

Study or Subgroup	SSRI Events	SSRI Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chollet 2011	15	57	5	56	0.8%	2.95 [1.15, 7.56]
FOCUS Trial Collaboration 2018	572	1553	588	1553	98.7%	0.97 [0.89, 1.07]
Marquez Romero 2013	8	14	3	16	0.5%	3.05 [1.00, 9.31]
Total (95% CI)		**1624**		**1625**	**100.0%**	**1.00 [0.91, 1.09]**
Total events	595		596			

Heterogeneity: Chi² = 9.23, df = 2 (P = 0.010); I² = 78%

Test for overall effect: Z = 0.02 (P = 0.99)