Feasibility and effectiveness of treatments for post-stroke depression in elderly inpatients: systematic review

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Authors' objectives
To determine the feasibility (absence of contraindications or unacceptable side-effects and study completion rates) and effectiveness (reduction of depression or symptoms) of treatments for post-stroke depression in elderly medical inpatients.

Searching
MEDLINE was searched from January 1987 to August 1997 using the keywords ‘depression or depressive disorder’ (exploded) and ‘aged’. The bibliographies of the retrieved articles were also examined. Articles not published in English or French were excluded, as were review articles, meta-analyses, duplicate publications, editorials and letters.

Study selection
Study designs of evaluations included in the review
The review was limited to longitudinal studies. The included studies were randomised controlled trials (RCTs) and prospective and retrospective cohort studies.

Specific interventions included in the review
The inclusion criteria specified that the studies must examine treatment(s) for depression, singly or combination, including pharmacological, psychological or other e.g. electroconvulsive therapy (ECT). The pharmacologic interventions included in the review were heterocyclic drugs, with or without selective serotonin re-uptake inhibitors (SSRIs), SSRIs alone, psychostimulants and ECT. These interventions were compared with each other, with placebos, or with no treatment groups.

Participants included in the review
Post-stroke patients (minimum age 55 years or mean age 65 and over) admitted to the medical, geriatric or rehabilitation service (excluding surgical or psychiatric units) were eligible for inclusion. Nineteen to 79% of the patients in the included studies had a stroke in the left hemisphere alone. The mean time interval between the stroke and treatment ranged from 30 to 300 days.

Outcomes assessed in the review
To be included, the studies had to report a diagnosis of depression and/or a depression symptom level, with depression diagnosed by accepted criteria such as the American Psychiatric Association's Diagnostic and Statistical Manual (DSM) or Hamilton Depression Rating Scale. The other outcomes recorded included activities of daily living and function, frequency of contraindications, and unacceptable side-effects that required the treatment to be discontinued.

How were decisions on the relevance of primary studies made?
The articles were screened by one reviewer, based on the title and/or abstract. A final decision for inclusion was made independently by two reviewers against the inclusion criteria for the review.

Assessment of study quality
The criteria used to assess the validity of the RCTs were randomisation, double-blinding, description of withdrawals and drop-outs, and comparability of the treatment and control groups at the beginning of the study. It appears that no validity criteria were applied to cohort studies. Information on the quality criteria (for RCTs) were abstracted independently by two reviewers.
Data extraction
One reviewer extracted data on the stroke location and the length of time between the stroke and treatment. All other data were abstracted independently by two reviewers using a prepared form. These data included: study design and duration; population from which the sample was selected; age and gender of the patients; criteria for depression; type of treatment; the number of patients enrolled and completing the study; description of the treatment and control groups; measures of depression; frequency of contraindications to treatment; frequency of unacceptable side-effects requiring discontinuation of treatment; and rates of moderate to marked improvement and/or treatment. Any discrepancies were resolved by consensus or a third reviewer.

Methods of synthesis
How were the studies combined?
The studies were tabulated by type of treatment and discussed and compared in the narrative. No formal pooling occurred; this was possibly due to the small number of studies with useable data. The methods for assessing publication bias were not discussed. Studies were discussed within each of the four types of interventions (heterocyclic drugs, with or without SSRIs, psychostimulants, or ECT).

How were differences between studies investigated?
The sources of heterogeneity were not discussed in detail, but the authors do state that there were no associations between either stroke location or time interval and the feasibility or effectiveness of the treatments.

Results of the review
Thirteen studies (410 participants) were included: 4 RCTs (142 participants), one non-randomised controlled trial (48 participants) and 8 cohorts (220 participants).

The rates of moderate to marked improvement in the participants on heterocyclics (nortriptyline, trazadone, imipramine plus mianserin, and a ‘mixture of heterocyclics’) ranged from 36 to 75%, compared with 16 to 44% in the comparison groups (no treatment in 3 studies, placebo and desipramine plus mianserin). A statistically-significant reduction in depressive symptoms was reported in 2 of the 3 RCTs, the non-randomised controlled trial and one of the 2 cohort studies. In addition, there was a significant improvement in activities of daily living in one RCT. The rates of discontinuation due to side-effects ranged from 0 to 45% in the participants on heterocyclics, and from 0 to 100% in the comparison groups.

The 2 studies of SSRIs (one RCT comparing citalopram with placebo and one non-randomised trial comparing fluoxetine with no treatment) reported a significant reduction in depressive symptoms. The RCT reported a moderate to marked improvement in 62% of the patients in the intervention group, compared with 29% in the placebo group. Drop-outs due to side-effects were 12% (intervention) compared with 3% (control).

The 5 cohort studies (one prospective, 4 retrospective) of psychostimulants reported rates of improvement in depression of 40 to 80% (there were no placebo or ‘no treatment’ groups). The one retrospective cohort study of ECT reported a 95% rate of improvement. Drop-outs due to side-effects ranged from 4 to 18%.

The evidence suggested that there were contraindications to treatment for 83% of the patients in a group to receive heterocyclics (imipramine or desipramine plus mianserin), compared with 11% of those in a group to receive SSRIs. No information was presented on contraindications to treatment in patients who were to receive either a psychostimulant or ECT.

The overall inter-rater agreement concerning relevance (based on a sample of 39 titles and abstracts) was 100%. The agreement between abstractors for information relating to study setting, type of treatment, and the four criteria of methodological quality was 77%, 88%, and 62 to 100%, respectively.

Authors' conclusions
The limited evidence suggests that SSRIs, psychostimulants or ECT are feasible treatments for post-stroke depression in...
elderly in-patients. Heterocyclics are less feasible due to the high frequency of contraindications. All of the treatments, including heterocyclics, appear to be at least moderately effective in the short term.

**CRD commentary**
The authors posed a broad question in a selected group of post-stroke patients with depression. They acknowledged that their search strategy was limited in that it searched one electronic database over a period of ten years, using limited search terms, for articles in only two European languages. It is possible that some studies eligible for the review were not identified.

Attention was given to assessing the quality of the RCTs included in the review, but not the cohort studies. The authors mentioned that although most studies used the American Psychiatric Association's DSM criteria to diagnose major depression, most did not use a structured interview schedule or describe how the criteria were applied. More information on these issues, as well as participant characteristics (e.g. age, gender, and period of intervention), from the individual studies would be useful. It is not possible to determine the longer-term effects of the anti-depressive therapies from this review. The main outcome measure, a moderate to marked improvement following the intervention, did not appear to have been decided in advance of the data collection process. The outcome measures from the primary studies were not reported.

The authors acknowledged that the presence of publication bias was not assessed, and that this bias is likely given that all the included trials reported positive results. Only four of the thirteen studies in this review were RCTs. Overall, these problems make it very difficult to assess whether the four groups of interventions are indeed effective in depressed elderly people who have suffered from a stroke. The authors' conclusions are inappropriate given the limited evidence available, as presented in this review.

**Implications of the review for practice and research**
**Practice:** The authors state that the limited evidence suggests that SSRIs, psychostimulants or ECT are at least modestly effective in the short term.

**Research:** The authors state that more research is needed to determine which treatments or combinations of treatments are most effective for depressed post-stroke in-patients in the long term.

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