Maintenance treatment of major depression: a review of the literature

Blacker D

Authors' objectives
To assess the efficacy of maintenance treatments for major depressive disorder (MDD).

Searching
The literature search began with the American Psychiatric Association's references from "Practice Guideline for Major Depressive Disorder in Adults" covering the period 1971 through 1991, and extended the search of the MEDLINE database through 1992 using the search terms 'affective disorder', 'major depression', 'depressive disorder', 'seasonal affective disorder', 'melancholia', 'unipolar depression', 'endogenous depression', 'dysthymic disorder', 'postpartum depression', 'pseudodementia', 'antidepressant drugs', 'trycyclic antidepressive agents', 'monoamine oxidase inhibitors', 'lithium', and 'electroconvulsive therapy'.

An additional search of MEDLINE was conducted using the term 'depression, prevention and control' for the years 1991-1994. Additional journals were scanned from January 1992 through December 1994 for relevant articles. The search was restricted to English language publications.

Study selection
Study designs of evaluations included in the review
Randomised clinical trials with at least 20 patients per cell which were not limited to sub-populations such as children or adolescents, the elderly, or the medically ill.

Specific interventions included in the review
Lithium (0.5-1.4 mEq/L), amitriptyline (AMI) (60-230 mg/ml), imipramine (IMI) (50-200 mg/day, median 125 mg/day), IMI (150 mg/day or as tolerated, with a mean of 132 mg/day) plus lithium (0.6-0.9 mEq/L) until patients were stable, Interpersonal Therapy (IPT) (weekly for 12 weeks, then bi-weekly for 8 weeks, and then monthly) and placebo.

Participants included in the review
Patients undergoing maintenance therapy for MDD who had a previous history of one or more episodes of depression.

Outcomes assessed in the review
Prevention of future episodes of MDD (defined as a syndrome marked by depressed (or sometimes irritable) mood accompanied by typical neuro-vegetative changes, without regard to a specific set of diagnostic criteria).

How were decisions on the relevance of primary studies made?
The author does not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
No formal assessment of quality was undertaken, although several methodological issues that should be considered were discussed.

Data extraction
The author does not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative review which discussed the study design, content, results and methodological drawbacks of each study.

How were differences between studies investigated?
There was no investigation of differences between the studies.

Results of the review
Four comparative studies (RCTs) randomised 788 participants. In addition the recommendations of the American psychiatric Association (APA) and the Agency for Health Care Policy and Research were evaluated in the discussion.

In the first study, differences were non significant between lithium and amitryptyline, but statistically significant between drug and placebo (p = 0.025). Observed relapse rates were quite high.

In the second study, the investigators concluded that IMI and lithium were better than placebo in the long-term treatment of MDD.

In the third study, the authors concluded that IMI was better than lithium in patients with severe illness, and that a combination regimen offered no advantages. In the fourth study, Kaplan-Meier curves showed IMI with or without IPT-M to be the best maintenance treatment consistently over the 3 years of follow-up, followed by IPT-M with or without placebo, and then placebo.

The APA guidelines note that various antidepressants and lithium have been shown to be effective and IMI at the usual acute therapeutic dose has been documented effective for up to 5 years. The full acute dose may not be necessary but should be used if it does not cause undue side effects. Maintenance electroshock therapy (generally about one treatment per month) is also noted to be appropriate for some patients.

The AHCPR guidelines favour medication for maintenance treatment and generally sees psychotherapy as adjunctive. It is recommended that individuals with a lifetime history of three episodes be maintained on a full therapeutic dose of an antidepressant for a period of 1 to several years after the most recent episode.

Authors' conclusions
There is support for the benefits of maintenance treatment for MDD, especially with antidepressant medications, in patients with frequent episodes.

CRD commentary
The author has stated the research question and inclusion and exclusion criteria. The literature search is good, but it was limited to English language publications and excluded unpublished data so it is not clear whether additional relevant studies may have been missed.

The author has not made any formal quality assessment of the included trials and does not report how the data was extracted for the review. This missing data makes it difficult to replicate the review. It is also not possible to evaluate the review for biases in the authors' selection, inclusion and evaluation of the individual studies. The data was pooled in a narrative format focusing on common categories of study and patient characteristics, and interventions. The author has reported individual results as the conclusions drawn by the original researchers and discusses and summarises these in the review.

It is difficult to evaluate the results of the review based on the narrative discussion, but the conclusions appear to be reported without bias.

Implications of the review for practice and research
Practice: The authors do not state any implications for practice.
Research: The author states that further research is needed concerning the optimal doses of antidepressant medications, particularly SSRIs, and the frequency and type of psychotherapy during the maintenance phase. The author also states that this might include attention to cost-effectiveness as well as efficacy.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.