Lithium is more effective than placebo for preventing all relapses in patients with bipolar but not unipolar disorder


QUESTION: In patients with recurrent mood disorder, is lithium more effective than placebo for preventing relapse?

Data sources
Published and unpublished randomised controlled trials were identified by searching the Cochrane Controlled Clinical Trials Registers; by reviewing the reference lists of all identified trials, other relevant papers, and major textbooks on mood disorder; by handsearching the journals Lithium (1990–4) and Lithium Therapy Monographs (1987–91); and through personal contact with authors of trials included in the review, with other recognised experts, and with pharmaceutical companies. This well designed review by Burgess et al addresses an important clinical question, given the recurrent nature of mood disorders. The question they ask is controversial because results showing fewer relapses in patients on lithium maintenance treatment have been criticised for bias from the effect of discontinuation. In discontinuation studies, patients who were stable on lithium for a period of time were randomised to continued lithium or placebo, often leading to an abrupt discontinuation of lithium in the placebo group. Such discontinuation has been associated with a higher rate of relapse in those stopping lithium,2 resulting in misleading differences between the 2 groups. Methodologically, one of the strengths of this review is that discontinuation studies were specifically excluded, though discontinuation of lithium in a proportion of patients in most of the remaining studies could not be excluded. This approach necessarily limits the number of studies, and hence the number of patients, included in the review, and the precision of its estimates. The conclusions of the review should be considered with these points in mind.

This review finds that evidence exists to suggest that lithium maintenance treatment reduces the overall risk of relapse in bipolar affective disorder, with 1 relapse being prevented for every 4 patients taking lithium. Whether this effect was driven more by reductions in depressive or manic relapse, or both, is statistically uncertain; the overall relapse prevention is the headline. The place of lithium maintenance treatment in unipolar affective disorder remains unclear; there were only 3 studies to include in the review. Lithium has not become established as a routine prophylactic agent in unipolar depression. The recommendation is to do more trials.

The authors also highlight the lack of data on health and social functioning, patients’ attitudes to treatment, and mortality and suicide in lithium maintenance studies to date. This review helps confirm the usefulness of lithium for treatment of bipolar affective disorder.

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COMMENTARY

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