Comparison of carbamazepine and lithium in the prophylaxis of bipolar disorders: a meta-analysis

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Authors' objectives
To assess whether carbamazepine is as effective as lithium in the prophylaxis of bipolar disorders.

Searching
A manual and computerised bibliographic search from 1970 to 1993 was undertaken. No search terms were stated.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) with double blinding, which compared carbamazepine with lithium and allowed statistical treatment, were included.

Specific interventions included in the review
Lithium and carbamazepine.

Participants included in the review
Patients with bipolar disorders on American Psychiatric Association DSM-III criteria. Some primary studies also included patients with schizoaffective, schizophreniform and unipolar disorders.

Outcomes assessed in the review
The length of time in remission and the failure rate (relapse or recurrence) were assessed.

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

Assessment of study quality
A checklist of 16 quality criteria was applied. The criteria addressed: adequate description of patients; use of diagnosis criteria; confirmation of diagnosis by independent assessors; homogeneity of diagnosis; selection bias; concomitant psychotropic treatment; description of side effects; relevance of dependent variable; at least one dependent variable directly reflecting patients' psychiatric conditions; length of follow-up; frequency of patient assessment; compliance checking; drop out rate; statistical analysis of major hypotheses; multivariate methods for two or more dependent variables. The authors do not state how the papers were assessed for quality, or how many of the authors performed the quality assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
A combined p-value and a weighted combined p-value were calculated to take into account the quality scores of individual studies.

How were differences between studies investigated?
Statistical tests of heterogeneity were applied to the effect sizes and the significance tests of the primary studies (both were heterogeneous). Differences in study design, patient selection and outcome measures were also explored.

**Results of the review**

Four RCTs involving 206 patients were included.

One study (the only one which used additional time in remission as an outcome measure) found a significant difference in favour of lithium, while three studies (all of which used the proportion of failures as an outcome measure) found no significant difference. The combined weighted p value was 0.15 (combined weighted standard deviation was 1.04).

**Authors' conclusions**

Carbamazepine has not yet conclusively demonstrated its prophylactic efficacy with samples of affective patients not selected for any particular characteristic such as cycle length of lithium non-response. Thus lithium should remain the preferred treatment for prophylaxis. Studies with sufficient statistical power and a sensitive outcome measure are needed. Additional research is also needed to determine whether carbamazepine affects clearly defined clinical patterns or stages of the course of affective disorders.

**CRD commentary**

The search strategy was rather restrictive and the search terms used were not given. It is unclear whether decisions about the relevance and quality of studies, or data extraction, were checked by independent reviewers. The four studies included in this review varied in their patient selection, study design and execution so statistical combination may not have been appropriate. Statistical tests for heterogeneity were not carried out so results may have been prone to bias. The drop out rates in three of the four included studies were high (over 25%, and in one case 68% after 12 months). As the authors point out, the statistical power of the included studies was weak, and did not allow the gap between "lack of significant difference" and "equal efficacy" to be bridged. The authors' conclusions are suitably cautious given the above limitations.

**Implications of the review for practice and research**

The effectiveness of carbamazepine as a prophylactic agent for unselected people with bipolar disorder is not proven, and its relative effectiveness in comparison with lithium is not clear. Further research is needed to address the question of the effectiveness of carbamazepine as a prophylactic for people with bipolar disorder.

**Bibliographic details**


**PubMedID**

7788131

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Bipolar Disorder /drug therapy /psychology; Carbamazepine /adverse effects /therapeutic use; Double-Blind Method; Humans; Lithium Carbonate /adverse effects /therapeutic use; Randomized Controlled Trials as Topic; Treatment Outcome

**AccessionNumber**

11995002092
Date bibliographic record published
02/10/1995

Date abstract record published
02/10/1995

Record Status
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.