Lithium treatment reduces suicide risk in recurrent major depressive disorder

Guzzetta F, Tondo L, Centorrino F, Baldessarini R J

CRD summary
This review evaluated the effect of lithium on the incidence of suicide and suicide attempts in patients with recurrent major depressive disorders. The authors concluded that treatment with lithium might reduce the rate of suicide and suicide attempts. These conclusions have to be considered with caution given the limitations of the review in terms of the literature search, potential for bias, and failure to assess study quality.

Authors' objectives
To assess the effects of treatment with lithium on suicide and suicide attempts in patients with recurrent major depressive disorder (MDD).

Searching
MEDLINE was searched from January 1966 up to April 2006; the search terms were reported. One of the co-authors provided an unpublished study.

Study selection
Study designs of evaluations included in the review
Inclusion criteria for the study design were not explicitly stated.

Specific interventions included in the review
Studies evaluating lithium were eligible. Additional treatments provided to both patients with and without lithium included antidepressants, antipsychotics, anticonvulsants or sedatives. Mean treatment duration was 4.56 years (standard deviation, SD=2.53) in patients receiving lithium and 6.27 years (SD=4.84) in the group without lithium.

Participants included in the review
Studies of patients with recurrent MDD as diagnosed by the International Classification of Diseases (ICD-9), American Psychiatric Association's DSM III/IV criteria, or equivalents were eligible for inclusion.

Outcomes assessed in the review
Studies that provided data on suicidal behaviour were eligible for inclusion. The primary outcomes reported were the rates of suicide or suicide attempts in patients with recurrent MDD.

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

Assessment of study quality
The authors did not state that they assessed validity.

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

Data were extracted to calculate rates of suicide and suicide attempts. When necessary, the authors of retrieved studies were contacted for additional information. When data were not provided on the longest likely exposure to lithium, a conservative best-estimate was used.
Methods of synthesis
How were the studies combined?
The data were pooled to calculate incidence rate ratios and their 95% confidence intervals (CIs). The random-effects model of Peto was used to calculate pooled risk ratios (RRs), while the Mantel-Haenszel method was used to impute risk differences.

How were differences between studies investigated?
A sensitivity analysis was performed by excluding individual studies one at a time. Statistical heterogeneity was visualised using a forest plot.

Results of the review
Eight studies (329 participants), of which seven were published and one unpublished, were included in the review.

Two of the 8 included studies had a randomised controlled design and one of them was a double-blind placebo-controlled study.

The pooled RR for risk of suicide attempts and suicides without versus with long-term lithium treatment was 4.24 (95% CI: 1.49, 12.0, p=0.007). The authors stated that the exclusion of individual studies in the sensitivity analysis had no impact on the final results.

Authors' conclusions
Treatment with lithium was associated with a lower risk of suicide or suicide attempts in patients with recurrent MDD.

CRD commentary
This review addressed a well-defined question that was supported by specified inclusion criteria for the interventions, participants and outcomes. Since only one relevant database was searched and it was unclear how extensively the search for unpublished studies was conducted, publication bias cannot be excluded. Publication bias was not assessed. It was not stated whether any language restrictions had been applied, therefore language bias also cannot be ruled out. It was not stated whether the study selection and data extraction processes were carried out in duplicate, so reviewer error and bias might have been introduced. No quality assessment of the included studies was reported and the potential impact of methodological flaws in the primary studies upon the reliability of the review findings cannot, therefore, be assessed; this is of particular importance given the variety of study designs included. Statistical heterogeneity was not formally tested, which makes it unclear whether the decision to combine the studies in a meta-analysis was appropriate. The authors' conclusions have to be viewed with caution given the relatively low number of patients enrolled in the included studies, as well as the methodological and reporting weaknesses of the review.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further studies are needed to confirm the efficacy of lithium in patients with recurrent MDD.

Bibliographic details

PubMedID
17388706

Indexing Status
Subject indexing assigned by NLM

**MeSH**
Antidepressive Agents /therapeutic use; Depressive Disorder, Major /complications /drug therapy /psychology; Humans; Lithium Carbonate /therapeutic use; Recurrence; Risk Assessment; Suicide, Attempted /psychology

**AccessionNumber**
12007001289

**Date bibliographic record published**
29/02/2008

**Date abstract record published**
29/02/2008

**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.