Sex differences in response to lithium treatment

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Authors' objectives
To investigate whether there are differences between the sexes in clinical response to lithium.

Searching
MEDLINE and Current Contents were searched (no dates or keywords were reported), and the reference lists of the identified reports were examined. The authors added data from their own study.

Study selection
Study designs of evaluations included in the review
The authors did not specify inclusion criteria relating to the study design, other than 'clinical trials'. They did, however, report whether the included studies were of a blinded or open design.

Specific interventions included in the review
Studies that used lithium as the primary treatment (of any duration) or permitted separate analysis of lithium-treated participants were eligible for inclusion in the review. The duration of the treatment ranged from one month to 70.8 months.

Participants included in the review
Studies of patients with major affective disorders were eligible for inclusion. Studies that either included single-sex samples not otherwise selected, or specified or permitted the determination of response rates for men and women separately, were also eligible for inclusion. All but one of the reports included in the review included data for both men and women. The patients included in the review had bipolar affective disorder (I and II, depressed and manic), or were mixed samples of patients with major affective disorders including recurrent major depression and bipolar disorder.

Outcomes assessed in the review
The outcome was response to treatment, as defined in each study.

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 reviewers performed the selection.

Assessment of study quality
The authors report whether the studies were blinded but, apart from that, they made no attempt to assess validity.

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

The data extracted were: study identification, year of publication, diagnosis, blinded or open design, duration, outcome, and the response rates for women and for men. The proportions of male and female responders to all male and female participants was also calculated.

Methods of synthesis
How were the studies combined?
An overall proportion (weighted average) was computed for the entire data set, to enable comparison with a chi-squared table; the two-tailed significance was set at a p-value of 0.05.

How were differences between studies investigated?
The authors seem to have used a chi-squared test to look for differences in the response rates between participants with bipolar disorder and mixed affective disorder, and between open and blinded and short-term and long-term studies.

Results of the review
Seventeen studies (n=1,548) were included.

Five studies were reported to be blinded and twelve were of an open design. Seven studies reported 'clinical improvement', one reported 'greater than 50% clinical improvement', four reported 'non-recurrence', one reported 'no major recurrence', one reported 'depression rating', one reported 'clinical recovery', one reported 'scale improvement' and one reported 'ill 10% or less of the time'. The heterogeneity assessment did not indicate any significant heterogeneity so all the data were pooled.

The pooled analysis yielded overall response rates of 65.6% (684 out of 1,043) in women and 61.0% (308 out of 505) in men; the difference was not statistically significant (chi-squared 3.11, d.f.=1, p=0.08).

Authors' conclusions
The results indicated little difference between the sexes in clinical response to lithium treatment of bipolar and related affective disorders.

CRD commentary
The research question and study inclusion criteria were clearly stated, but the review had several limitations. Few details of the search strategy, including whether language restrictions were applied, were provided. Also, the authors do not seem to have attempted to identify unpublished material apart from their own. This could have led to relevant studies being missed. It is unclear whether the included studies were all randomised controlled trials or varied in their design. No attempt was made to assess validity, other than to report whether the studies were blinded or not. The participants included in each study and the range of outcomes reported seem to be clinically heterogeneous, even though statistical heterogeneity was not found in the results. Given the doubts over the study designs, it seems inappropriate for the data to have been pooled. Few details of the review process were reported, e.g. how many of the reviewers selected the studies and extracted the data. In addition, while the authors report that a weighted average was calculated, they do not state how the studies were weighted.

The authors' conclusions should be treated with caution given the limitations highlighted.

Implications of the review for practice and research
Practice: The authors state that lithium maintenance treatment remains an attractive option for the treatment of bipolar disorder in women of childbearing age.

Reviewer's statement: This statement should probably be viewed with caution given the methodological limitations of the review.

Research: The authors did not state any implications for further research.

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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.