
Suicidal risks during treatment of bipolar disorder patients with lithium versus anticonvulsants

Baldessarini RJ, Tondo L

CRD summary

The authors concluded that the few studies that compared suicide risks during long-term lithium treatment with anticonvulsant treatment in patients with bipolar disorder were methodologically limited, but favoured lithium. The limited search, absence of a validity assessment and pooling of data from diverse studies, mean that the authors' conclusions may not be reliable.

Authors' objectives

To compare suicide risks during long-term lithium treatment with anticonvulsants in patients with bipolar disorder.

Searching

MEDLINE was searched. Search terms were reported but search dates were not. In addition, reference lists of identified reports were screened.

Study selection

Studies that directly compared long-term (at least six months) lithium treatment with anticonvulsants in patients diagnosed with bipolar disorder were eligible for inclusion. Bipolar disorder had to be diagnosed using modern Diagnostic and Statistical Manual of mental disorders-III/IV (DSM-III/IV) or International Classification of Diseases-9/10 (ICD-9/10) criteria. Eligible studies had to report at least one risk or attempt of suicide in at least one treatment arm.

The included studies were randomised controlled trials (RCTs) and chart reviews that compared lithium with the anticonvulsants carbamazepine, divalproex and lamotrigine; some studies also included a placebo treatment arm. The authors stated that most observations of suicide acts were incidental, unplanned or assessed retrospectively.

The authors did not state how papers were selected for the review.

Assessment of study quality

The authors did not state that they assessed validity.

Data extraction

For each study, the number of suicide acts was extracted for each treatment group, and suicide rates calculated as a percentage per year. Relative risks (RR) and risk differences (RD) were also calculated.

Two reviewers independently extracted data.

Methods of synthesis

Pooled relative risks and risk differences, with 95% confidence intervals (CI), were calculated using a random-effects model, with and without adjustment of numerators for unbalanced exposure time. The incidence rate, with 95% confidence intervals, was also calculated using pooled raw data. Sensitivity analysis was conducted by re-analysing data after omitting one study that appeared to be a significant outlier.

Results of the review

Six studies with control groups were included in the review (n=28,405 patients). These included three RCTs (n=538 patients) and three chart reviews (n=27,867 patients).

The weighted average duration of treatment was 30.9 months for lithium and 19.1 months for anticonvulsants. The

average crude pooled rates of suicide acts were 0.3% per year in lithium-treated groups and 0.9% per year in anticonvulsant-treated groups.

Anticonvulsant treatment was associated with a significantly increased risk of suicide acts compared with lithium treatment (RR with adjustment for unequal exposure times 2.86, 95% CI 2.29 to 3.57; RR without adjustment 1.85, 95% CI 1.46 to 2.35).

Sensitivity analysis omitting one study that appeared to be a significant outlier showed similar results.

Authors' conclusions

Studies that compared suicide risks during lithium treatment with those during anticonvulsant treatment were rare and methodologically limited, but the results favoured lithium treatment.

CRD commentary

The review question was clearly stated and inclusion criteria were defined for participants, intervention, control treatment and outcomes. However, suicide acts were not defined and criteria for study design were broad. Limiting the search to one database plus references raised the potential for publication bias and the omission of other relevant studies. It was not clear if any attempts were made to minimise language bias. Methods were used to minimise reviewer errors and bias in the extraction of data, but it was not clear whether similar steps were taken in study selection.

Study validity was not assessed, so results from these studies and any synthesis may not be reliable. No information was provided about participants. Two of the three RCTs evaluated lamotrigine and all three chart reviews included both valproate/divalproex and carbamazepine. Pooling data from studies of different designs (RCTs and chart reviews) without separately analysing RCTs was not appropriate. In the chart reviews, there may have been differences between treatment groups that influenced the results.

The limited search, absence of a validity assessment and pooling of data from diverse studies mean that the authors' conclusions may not be reliable.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that in future studies that evaluate long-term mood-stabilising drugs in patients with bipolar disorder, suicide acts should be assessed, as well as long-term morbidity. Further evaluation of divalproex is required.

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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.