Meta-analyses of mood stabilizers, antidepressants and antipsychotics in the treatment of borderline personality disorder: effectiveness for depression and anger symptoms

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CRD summary
This review found that, in short-term studies, mood stabilisers were associated with the largest reduction in anger/aggression in borderline personality disorder; antidepressants and antipsychotics were also effective. The three classes of drug had less effect on depression. These conclusions are supported by the results presented, but should be interpreted with some caution given the possibility of publication bias.

Authors' objectives
To determine whether mood stabilisers, antidepressants and antipsychotics are efficacious for depression and anger symptoms in borderline personality disorder.

Searching
MEDLINE (to May 2007), PsycINFO (to July 2005) and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception. References of original papers and review articles were screened. Search terms were reported. The review was restricted to peer reviewed, published English language studies.

Study selection
Randomised, double-blind placebo controlled trials that evaluated mood stabilisers, antidepressants or antipsychotic agents in patients where all, or the majority of participants, were diagnosed with borderline personality disorder were eligible for inclusion. Trials had to report parametric data (numeric observations with a mean and standard deviation) on anger or depressive symptoms to be included.

All trials used structured diagnostic assessment to make the diagnosis of borderline personality disorder, but specific tools used varied across trials. Most trials only included patients with borderline personality disorder. Some trials also included patients with comorbid disorders (range 0 to 100%). Specific interventions evaluated in the included trials were mood stabilisers (carbamazepine, divalproic acid, lamotrigine and topiramate), antidepressants (amitriptyline, fluoxetine, fluvoxamine, phenelzine and tranylcypromine) and antipsychotics (aripiprazole, haloperidol, olanzapine and trifluoperazine). Treatment duration ranged from five to 24 weeks, drop-out rates ranged from 5 to 65%, the proportion of patients in psychotherapy ranged from 0 to 100% and 73% of patients were women. Most trials excluded patients with alcohol and substance abuse, suicidality and self-harm behaviours. In included trials, measures of depression included the Hamilton Rating Scale for Depression, Symptom Checklist-90, Beck Depression Inventory and measures developed by the study authors; measures of anger included the Symptom Checklist-90 Hostility, Overt Aggression Scale-Modified, State-Trait Anger Expression Inventory, Anger Out, and the Profile of Mood States Anger. Most trials lasted 12 weeks or less.

Two reviewers independently assessed studies for inclusion. Disagreements were resolved through consensus.

Assessment of study quality
Two reviewers independently assessed study quality according to the following criteria: blinding of randomisation, comparability of treatment and control groups at entry, use of intention-to-treat analysis, blinded outcome assessment. Trials were assigned a score out of 4 based on the number of items fulfilled. Disagreements were resolved through consensus.

Data extraction
Two reviewers independently extracted data on number of participants, mean and standard deviation (SD) for treatment and control groups and used this to calculate effect sizes (ES) together with 95% confidence intervals. Disagreements were resolved through consensus. Where multiple measures were reported within the same study, preference was given to well-known and validated measures obtained by the investigators, rather than self-report measures. Intention-to-treat
Methods of synthesis
Pooled effect sizes were estimated using random-effects models, separately for each class of drug. Heterogeneity was assessed using the Q statistic. Publication bias was assessed using a funnel plot.

Results of the review
Eighteen randomised controlled trials (RCTs) were included (n=735 patients). Fourteen trials achieved a score of 3 or 4 points on the quality assessment, four trials received a rating of 2 points. Ten studies did not use an intention-to-treat analysis.

Mood stabilisers (ES -1.75, 95% CI -2.77 to -0.74; seven RCTs), antidepressants (-0.74, 95% CI -1.27 to -0.21; seven RCTs) and antipsychotics (-0.59, 95% CI -1.04 to -0.15; eight RCTs) were all associated with significant beneficial effects on anger and depression. Mood stabilisers (ES -0.63, 95% CI -0.99 to -0.27; four RCTs) and antidepressants (ES -0.37, 95% CI -0.69 to -0.05; seven RCTs) were also associated with significant beneficial effects on depression but antipsychotics were not (six RCTs).

Authors' conclusions
There were large variations between trials of anger reduction, but significant effect sizes were found for all three drug-types (mood stabilisers, antidepressants and antipsychotics). Mood stabilisers were associated with the largest reduction in anger/aggression but effects appear to have been limited to short-term use. The three classes of drug had less effect on depression.

CRD commentary
The review addressed a focused question supported by clearly defined inclusion criteria. The literature search was adequate for published studies, but restriction to published English language studies raised the possibility of language and publication bias; this was assessed in the review. Appropriate steps were taken to minimise bias and error at all stages of the review process. Study quality was assessed using appropriate criteria, but results were only presented as summary quality scores and were not considered in the synthesis of results. Data were pooled using appropriate methods and results were clearly presented on forest plots. Although the authors stated that heterogeneity was assessed, the results of this were not reported. However, differences between trials were discussed and considered when interpreting the pooled estimates. As the authors acknowledged, the trials excluded several groups of patients, so the results may not be generalisable to the usual group of patients with borderline personality disorder. The authors' conclusions are supported by the results presented, but should be interpreted with some caution given the possibility of publication bias.

Implications of the review for practice and research
Practice: The authors stated that mood-stabilisers should be considered a first-line therapy for individuals with borderline personality disorder.

Research: The authors stated that large-scale double-blind placebo trials of the major mood stabilisers and antipsychotics should be done; drug-drug comparisons between the mood stabilisers are required as are double-blind trials of current psychotherapies with and without medication.

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