Effectiveness of pharmacotherapy for severe personality disorders: meta-analyses of randomized controlled trials

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CRD summary
This review assessed the effectiveness of drug therapy on groups of symptoms in patients with severe personality disorder, concluding that mood stabilisers deserved greater consideration, but caution was needed. There were some methodological limitations and the authors’ recommendation for caution in interpreting the findings was appropriate.

Authors’ objectives
To assess the effectiveness of pharmacotherapy on specific groups of symptoms in patients with severe personality disorder.

Searching
PubMed, PsycINFO, PiCarta, the Cochrane Library, and Web of Science databases were searched for relevant publications from 1980 to December 2007. The search terms were reported and reference lists of relevant articles and books were manually searched.

Study selection
Double-blind placebo randomised controlled trials (RCTs) were eligible if they assessed the effects of antipsychotics, antidepressants, and mood stabilisers on specific symptoms, grouped by domain, in patients with well-defined borderline personality disorder and/or schizotypal personality disorder, diagnosed using the Diagnostic and Statistical Manual (DSM) of mental disorders version III or later. Trials that focused on the treatment of a comorbid Axis I disorder, such as psychotic, affective, and anxiety disorders, were excluded. The symptom domains were: cognitive-perceptual, impulsive-behavioural dyscontrol, and affective dysregulation. Global functioning was measured.

The included trials were conducted in in-patient and out-patient settings and lasted between five and 26 weeks. Antipsychotics (flupentixol, thiopropazine, trifluoperazine, haloperidol, risperidone, olanzapine, and aripiprazole), antidepressants (mianserin, tranylcypromine, desipramine, amitriptyline, phenelzine, fluoxetine, and fluvoxamine), and mood stabilisers (carbamazepine, lithium, valproate, topiramate, and lamotrigine) at varying doses were compared with placebo, which was not defined. A variety of measurement tools were used to assess the symptoms and only those that could be assigned to the symptom domains were included.

The authors did not state how many reviewers screened trials for inclusion.

Assessment of study quality
The authors did not state that they formally assessed trial quality, but all trials were double-blind and the dropout rates were recorded, where possible.

Data extraction
Three reviewers extracted the mean scores at the beginning and end of treatment and extracted or calculated their associated standard deviations. For each study, the standardised mean difference between the active treatment and placebo was calculated using Cohen's d. The trial authors were contacted for further information, where necessary and discrepancies were resolved by consensus.

Methods of synthesis
A fixed-effect model, or a random-effects model where there was evidence of statistical heterogeneity, was used to calculate the overall standardised mean differences, corrected for small sample sizes, and their 95% confidence intervals, grouped by type of pharmacotherapy. Statistical heterogeneity was assessed using the Cochran Q and the I² tests.
Results of the review

Thirty-two relevant RCTs were identified and 21 (19 publications) were included in the meta-analyses (n=837 patients; range 16 to 72). The dropout rates ranged from 3% to 63%.

Antipsychotics: (six RCTs, n=307) Compared with placebo, antipsychotics had a statistically significant greater effect on cognitive-perceptual symptoms (SMD 0.56, 95% CI 0.05 to 1.07; five RCTs), on the affective dysregulation symptom of anger (SMD 0.69, 95% CI 0.16 to 1.22; four RCTs), and global functioning (SMD 0.37, 95% CI 0.12 to 0.62; five RCTs), but there was evidence of statistical heterogeneity for all comparisons ($I^2$=70% or 79%). There were no statistically significant differences for impulsive-behavioural dyscontrol symptoms and affective dysregulation symptoms of depressed mood, anxiety, and mood lability.

Antidepressants: (seven RCTs, n=278) Antidepressants were statistically significantly more effective than placebo on the affective dysregulation symptoms of anxiety (SMD 0.30, 95% CI 0.02 to 0.59; five RCTs) and anger (SMD 0.34, 95% CI 0.03 to 0.65; four RCTs). There was no evidence of statistical heterogeneity ($I^2$=0%), for either comparison. No statistically significant differences were found in global functioning, cognitive-perceptual symptoms, impulsive-behavioural dyscontrol symptoms, and the affective dysregulation symptoms of depressed mood and mood lability.

Mood stabilisers: (eight RCTs, n=252) Mood stabilisers were statistically significantly more effective than placebo in impulsive-behavioural dyscontrol symptoms (SMD 1.51, 95% CI 0.42 to 2.59; $I^2$=90%; six RCTs), affective dysregulation symptoms of depressed mood (SMD 0.55, 95% CI 0.21 to 0.90; $I^2$=0%; five RCTs), anxiety (SMD 0.80, 95% CI 0.38 to 1.21; $I^2$=0%; three RCTs), and anger (SMD 1.33, 95% CI 0.43 to 2.22; $I^2$=89%; seven RCTs), and in global functioning (SMD 0.79, 95% CI 0.38 to 1.19; $I^2$=0%; three RCTs). There were no statistically significant differences in cognitive-perceptual symptoms.

Authors' conclusions

The findings cast doubt on the usual drug treatments and suggested that mood stabilisers could be effective for some symptom domains, but they needed to be interpreted with caution as there were some methodological limitations.

CRD commentary

The review question and supporting inclusion criteria were clearly defined. The literature search was comprehensive, but limited to published articles and relevant data might have been missed. The authors did not formally assess the trial quality, which makes it difficult to determine the reliability of the findings, and there was high attrition in some trials. Three authors extracted the data independently, but it was unclear whether this was the process for study selection, which means that reviewer error and bias cannot be ruled out. Few patient characteristics were reported, so it was unclear whether the patients were comparable at baseline. There was evidence of methodological and statistical heterogeneity for some comparisons and it might not have been appropriate to pool these data. The authors acknowledged some limitations with the included trials, including small samples, short trial durations, the combination of psychotropic drugs into three global classes, the use of different measurement tools, and the high attrition rates.

The authors' conclusions seem to have reflected the evidence. The potential for bias and the limitations of the included trials mean that their recommendation to interpret the findings with caution should be heeded.

Implications of the review for practice and research

Practice: The authors stated that their findings did not support the Practice Guideline for the Treatment of Patients with Borderline Personality Disorder published by the American Psychiatric Association. Serious side-effects of the psychotropic drugs needed to be taken into account in clinical practice.

Research: The authors stated that well-conducted trials with sufficient participants and better outcome measures were needed. Analyses should compare the traditional versus atypical antipsyhcotics, and tricyclic antidepressants or monoamine oxidase inhibitors versus selective serotonin reuptake inhibitors or other second-generation antidepressants, to help develop new treatment guidelines.
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