Differential effectiveness of antipsychotics in borderline personality disorder: meta-analyses of placebo-controlled, randomized clinical trials on symptomatic outcome domains

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CRD summary
The review concluded that drug therapy tailored to well-defined symptom domains can have beneficial effects on cognitive-perceptual symptoms, anger and mood liability in borderline personality disorder but wide and long-term use remained controversial. The authors overall conclusions reflect the evidence presented. However, wide variation between pooled studies and a lack of quality assessment should be borne in mind.

Authors' objectives
To evaluate the effectiveness of antipsychotic medication on specific symptomatic outcome domains in patients with well-defined borderline personality disorder (BPD).

Searching
PubMed, PsycINFO, PiCarta, The Cochrane Library and Web of Science were searched for publications between 1980 and January 2011. Search terms were not reported. Reference lists of related studies were scanned. Language restriction was not reported.

Study selection
Randomised placebo controlled trials (RCTs) of psychotropic medication in adult patients with well-defined borderline personality disorder were eligible for inclusion. Borderline personality disorder needed to be defined by Diagnostic and Statistical Manual of Mental Disorders (DSM) third edition, DSM-III-Revised or DSM-IV. Studies that focused on pharmacotherapy in other DSM personality disorders were excluded. Studies with a primary focus on treatment of a comorbid Axis I disorder such as psychotic, affective or anxiety disorders were excluded. If the measurement of instrument could not be assigned properly, it was eliminated from analysis.

Outcomes of interest were cognitive-perceptual symptoms, impulsive behavioural dyscontrol, affective dysregulation (depressed mood, anxiety, anger, mood liability) and global functioning.

Antipsychotic medication used included flupentixol, thiothixene, trifluoperazine, haloperidol, olanzapine, aripiprazole, ziprasidone and quetiapine at various doses. Intervention duration varied from five weeks to 26 weeks. Settings included in-patient and outpatient clinics.

The authors did not state how many reviewers were involved in study selection.

Assessment of study quality
There was no formal validity assessment.

Data extraction
Data were extracted into a standard form. For continuous outcome measures, the mean symptoms scores and corresponding standard deviation (SD) or standard error (SE) were recorded. Where applicable, standard error was converted into standard deviation. Where outcomes were not fully reported, missing data were requested from the trial authors. Standardised mean differences (SMD) between groups that used active agents and placebo controls were calculated. Effect sizes were corrected for small sample sizes.

It appeared that more than one reviewer extracted data as the authors stated that any differences were resolved in consensus.

Methods of synthesis
A fixed-effect model was used to combine studies and calculate standardised mean differences with associated 95% confidence intervals (CIs). Where there was statistical variation (Cochrane's Q p<0.05) between studies a random-
effects model was used. Statistical heterogeneity was assessed using \( I^2 \) (\( \leq 25\% \) was considered low heterogeneity, 25\% to 50\% moderate heterogeneity and >50\% high heterogeneity).

**Results of the review**

Eleven placebo-controlled randomised controlled trials were included in the meta-analysis (1,155 participants, range 24 to 314). Losses to follow-up ranged from 7\% to 57\%; most studies reported more than 30\%.

There were small but significant benefits for use of psychotic medication compared to placebo for cognitive-perceptual symptoms (SMD 0.23, 95\% CI 0.11 to -0.35, \( I^2=44\% \); nine RCTs), anger (SMD 0.39, 95\% CI 0.18 to 0.60, \( I^2=56\% \); nine RCTs), mood lability (SMD 0.20, 95\% CI 0.07 to 0.33, \( I^2=0\% \); five RCTs) and global functioning (SMD 0.25, 95\% CI 0.03 to 0.47, \( I^2=61\% \); eight RCTs).

There were no significant differences between use of antipsychotics and placebo for impulsive behavioural dyscontrol (10 studies, \( I^2=52\% \)), depression (seven studies, \( I^2=76\% \)) and anxiety (six studies, \( I^2=52\% \)).

**Authors’ conclusions**

Drug therapy tailored to well-defined symptom domains can have beneficial effects in borderline personality disorder. At short term, antipsychotics can have significant effects on cognitive-perceptual symptoms, anger and mood lability but wide and long-term use of antipsychotics in these patients remains controversial.

**CRD commentary**

The review question and inclusion criteria were clear. It was not reported whether searches were limited by language. It appeared that more than one reviewer was involved in data extraction (not stated explicitly) but not in study selection. No formal quality assessment was reported so the quality of the included trials was unclear. Publication bias was not reported.

Appropriate statistical techniques were used but the authors acknowledged that it was unclear whether pooling of different drug classes, dosages, duration of intervention and clinical settings (in-patient and outpatient) was appropriate. Significant heterogeneity in anger and global functioning was not explored.

Many of the included studies were conducted in outpatient settings which the authors noted have low compliance. This may affect the generalisability of the results to everyday clinical practice.

The authors acknowledged the limitations of this review and their overall conclusions reflect the evidence presented. However the wide variation between the pooled studies and lack of quality assessment should be borne in mind.

**Implications of the review for practice and research**

The authors did not state any implications for practice and further research.

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