Adjunctive quetiapine for serotonin reuptake inhibitor-resistant obsessive-compulsive disorder: a meta-analysis of randomized controlled treatment trials


CRD summary
The authors concluded that there was limited evidence that adjunctive quetiapine is effective for patients with obsessive-compulsive disorder who are unresponsive to serotonin re-uptake inhibitors. The conclusions about limited evidence appear to reflect findings from three small studies, but poor reporting of the review methods and differences between the included studies make it difficult to assess their reliability.

Authors' objectives
To evaluate the effects of adding quetiapine to the treatment of patients with obsessive-compulsive disorder (OCD) who are unresponsive to serotonin re-uptake inhibitors (SRIs).

Searching
EMBASE, MEDLINE, PsycINFO and the Cochrane Library were searched. Neither the search dates nor the search terms were reported.

Study selection
Double-blind, placebo-controlled randomised controlled trials that evaluated the effects of adding quetiapine to the treatment of patients with OCD who were unresponsive to SRIs were eligible for inclusion. Patients were diagnosed using the American Psychiatric Association's DSM-IV OCD criteria.

The primary review outcome was change from baseline in the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) total score. The secondary review outcomes were: responder rates (as defined by individual studies); changes in baseline depression scores (Hamilton Depression Scale or Montgomery Asberg Depression Rating Scale); change from baseline in the Sheehan Disability Scale score; number of patients leaving the the study early and number leaving due to adverse events and; number of serious adverse events.

In the included studies, treatment duration ranged from 6 to 16 weeks, the maximum quetiapine dose was 300 or 400 mg/day, mean baseline Y-BOCS scores ranged from 24.1 to 28.2, and the mean age ranged from 31.8 to 37.9 years across treatment groups. Approximately 60% of all participants were female. Some of the included studies excluded patients with co-morbid axis one pathology including tic disorders; one did not.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Studies were assessed for double-blind randomisation, intention-to-treat analysis and the reporting of means and standard deviations.

The authors did not state how the validity assessment was performed.

Data extraction
One reviewer extracted data on an intention-to-treat basis as relative risks (RRs) and standardised mean differences (SMDs) with 95% confidence intervals (CIs).

Methods of synthesis
The SMDs and RRs from individual studies were pooled statistically; the methods used were not reported.

Statistical heterogeneity was assessed by examining forest plots and using the $\chi^2$ test. Where heterogeneity was found, potential sources were examined.
Results of the review
Three double-blind RCTs (n=102) were included.

All of the studies used intention-to-treat analysis and reported means and standard deviations for continuous outcomes.

Adjunctive quetiapine was associated with a statistically significant reduction in Y-BOCS score from baseline compared with placebo (SMD -0.55, 95% CI: -0.96, -0.15, p=0.008). Statistically significant heterogeneity was found (p=0.02). The exclusion of one study removed the heterogeneity; the authors stated that this study may be responsible for the overall treatment effect.

There were no significant differences between adjunctive quetiapine and placebo in responder rates or any other secondary outcomes.

Authors' conclusions
There was limited evidence that adjunctive quetiapine was effective for SRI-unresponsive patients with OCD.

CRD commentary
Although the inclusion criteria were not explicitly stated, the review question was fairly clear and primary and secondary outcomes were clearly defined. It was difficult to distinguish inclusion criteria for the study design from the characteristics of the included studies. Several relevant sources were searched, but the search strategy was not described fully and no attempts to minimise either language or publication bias were reported. A single reviewer extracted the data; this lack of duplication suggests the potential for reviewer error and bias. The methods used to select studies and assess validity were not described, so it is not known whether any efforts were made to reduce errors and bias. Validity was assessed using specified criteria and the results of this assessment reported. The data were pooled, statistical heterogeneity was assessed, and potential sources of heterogeneity were examined. The authors acknowledged that the heterogeneity in the analysis of the primary outcome limited the clinical significance of the treatment effect.

Conclusions about limited evidence appear to reflect findings from three small studies, but incomplete reporting of the review methods and differences between the included studies make it difficult to assess their reliability.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further research is required to determine whether the clinical efficacy of adjunctive quetiapine is due to changes in extracellular dopamine levels.

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