Quetiapine for the treatment of behavioural and psychological symptoms of dementia (BPSD): a meta-analysis of randomised placebo-controlled trials

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CRD summary
The authors concluded that, using the Neuropsychiatric Inventory and the Clinical Global Impression of Change scale, quetiapine was statistically more effective than placebo for the behavioural and psychological symptoms of dementia in elderly people; the clinical significance of the effects was questionable. Limitations to the review methods mean that the reliability of the authors’ conclusion is unclear.

Authors’ objectives
To evaluate the efficacy of quetiapine for the behavioural and psychological symptoms of dementia in elderly people.

Searching
MEDLINE articles from 1950 to 2009, Cochrane Central Register of Controlled Trials (CENTRAL) and PsycINFO were searched. Search terms were reported. Poster presentations from the International Psychogeriatric Association were handsearched; several National trial registries were checked; and the manufacturer was contacted for trials of quetiapine for dementia.

Study selection
Eligible for inclusion were double-blind randomised controlled trials (RCTs) of quetiapine, compared with placebo. Participants could have any type of dementia, and be living in any clinical setting. The primary outcome was the behavioural and psychological symptoms of dementia, measured with the Neuropsychiatric Inventory (NPI). The secondary outcome was these symptoms, measured with the Clinical Global Impression of Change (CGI-C).

In the included trials, the type of dementia varied and the disease stage was moderate to severe (Mini Mental State Examination score 4.8 to 19.2). Where reported, participants were out-patients or from residential settings; most were women; and their mean age ranged from 73.8 to 83.2 years. Their mean baseline NPI scores ranged from 25.1 to 43.4. Most trials were conducted in the USA. The quetiapine daily dose ranged from zero to 600mg, and most trials included people who were taking acetylcholinesterase (ACE) inhibitors. Trials lasted from six to 12 weeks.

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

Assessment of study quality
The authors did not report any formal quality assessment of included trials.

Data extraction
The data were extracted to calculate mean differences and 95% confidence intervals for the outcomes of interest. The authors did not state how many reviewers extracted these data. Any unpublished or missing data for the NPI and CGI-C were sought from the trial authors.

Methods of synthesis
Weighted mean differences were calculated in fixed-effect meta-analyses, and 95% confidence intervals were presented. Statistical heterogeneity was assessed using $I^2$.

Results of the review
Five trials (1,118 participants; range 40 to 421) were included in the review.

Compared with placebo, quetiapine significantly improved the NPI score (WMD -3.05, 95% CI -6.10 to -0.01; five trials; $I^2=0$) and the CGI-C score (WMD -0.31, 95% CI -0.54 to -0.08; five trials; $I^2=7\%$). Despite statistical significance, the authors proposed that the clinical significance of these changes was questionable.
There was no evidence of statistical heterogeneity across the trials, but one trial was a significant outlier, with the highest baseline total NPI score for the quetiapine group (43.4) and the shortest trial period (six weeks). The meta-analysis suggested that placebo had a comparable clinical effect to quetiapine.

Authors’ conclusions
Quetiapine was statistically more effective than placebo for the behavioural and psychological symptoms of dementia as measured by the NPI and CGI-C, but the improvements were small and their clinical significance was questionable.

CRD commentary
The review question was clear, and the inclusion criteria were sufficiently specified to allow replication. Various data sources were searched, and attempts were made to locate unpublished data. The review process was not reported, making it difficult to determine whether steps were taken to minimise error and bias. The absence of a formal quality assessment means that the reliability of the included trials is unclear.

Trial details were presented and statistical heterogeneity was not significant, even though clinical heterogeneity was evident. Based on the statistical heterogeneity, the method of synthesis was appropriate. Most of the trials did not include NPI as a primary outcome, and the samples were small in two of the trials, which could reduce the reliability of the findings. Some of the authors’ conclusions (in relation to the superiority of other drugs) were not substantiated by the placebo-controlled trials in this review.

The authors' conclusion reflects the evidence presented, but method limitations make the reliability of this conclusion unclear.

Implications of the review for practice and research
Practice: The authors stated that the available literature did not support the use of quetiapine for the behavioural and psychological symptoms of dementia. The increased attention that patients received in the placebo groups suggested that this was an important part of the overall management of the condition.

Research: The authors suggested that research should evaluate the effects of interventions on the separate domains of the NPI.

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