Clinical efficacy of piracetam in cognitive impairment: a meta-analysis

Authors' objectives
To evaluate the clinical efficacy of piracetam in ageing and dementia. The authors set out to update an existing meta-analysis from the Cochrane Collaboration (see Other Publications of Related Interest).

Searching
UCB's database (containing all of UCB's products) was searched. The database is updated weekly from sources including Biosys, Caplus, Drugu, EMBASE, Kuest-Eplus, Lifesci, MEDLINE and SciSearch. This search was complemented by a complete list of UCB internal reports and protocols. Studies reported between 1972 and the first half of 2001 were sought.

Study selection
Study designs of evaluations included in the review
Parallel-group, double-blind, placebo-controlled trials were eligible for inclusion.

Specific interventions included in the review
Piracetam for the treatment of dementia and cognitive impairment. The included studies, all of which were placebo-controlled, used doses of piracetam ranging from 2.4 to 8.0 g/day for durations of 6 to 52 weeks.

Participants included in the review
Trials of patients with age-related cognitive disorders or of degenerative dementias in the elderly were eligible for inclusion. Studies of patients with cognitive impairment or dementia due to other specific causes (including vascular accidents, electroconvulsive therapy and head injury) were excluded. The diagnoses of participants in the included studies included psych-organic syndrome, cerebral arteriosclerosis and dementia syndromes, disorders of senescence, moderately severe organic psychosyndrome, mild mental deterioration, cerebral sclerosis, dementia (senile or arteriosclerotic), mild primary degenerative dementia, and organic brain syndrome.

Outcomes assessed in the review
Studies reporting an overall clinical global impression of change (CGIC) by the investigator, which was rated independently from psychometric testing, were eligible for inclusion. CGIC was dichotomised into 'improved' or 'no change/worse'.

How were decisions on the relevance of primary studies made?
The retrieved articles were reviewed by two independent pairs of reviewers (one from an independent consultant company and one from UCB). The selection of studies was independent of their results.

Assessment of study quality
The authors do not report a formal method for assessing validity. However, the studies were assessed for blinding and method of randomisation. The retrieved articles were reviewed by two independent pairs of reviewers (one from an independent consultant company and one from UCB). The selection of studies was independent of their results.

Data extraction
The retrieved articles were reviewed by two independent pairs of reviewers (one from an independent consultant company and one from UCB). The categories of data extracted included drug dosage and duration, outcome assessment performed and diagnosis.
Methods of synthesis
How were the studies combined?
Both fixed-effect (Peto's method) and random-effects models were used to evaluate pooled odds ratios (ORs), along with 95% confidence intervals (CIs). A Mantel-Haenszel estimation of the fixed-effect was performed in order to check the robustness of the results. The numbers-needed-to-treat (NNT) were also calculated. Estimates were first calculated on the basis of the 'observed cases' population, which included the cases and data as previously reported for the study. A second analysis was performed on the larger 'as randomised' population, in which all the patients who had been excluded from the 'observed cases' analysis (including drop-outs) were allocated to the category of 'no change/worse'.

How were differences between studies investigated?
Differences between the studies were assessed using the chi-squared test. A sensitivity analysis was performed by excluding the two studies that contributed most to the heterogeneity statistic.

Results of the review
A total of 19 studies involving 1,488 participants were included.

There was evidence of heterogeneity in the results from the individual studies (chi-squared 58.23, d.f.=18, p<0.001).

Estimates using 'as observed' data.

The ORs for improvement in the piracetam group compared to placebo (19 studies) were 3.35 (95% CI: 2.70, 4.17) and 3.31 (95% CI: 2.64, 4.14) when using the fixed-effect models of Peto and Mantel-Haenszel, respectively. Using the random-effects model, the OR was 3.20 (95% CI: 2.05, 4.99, p<0.001) and the NNT was 3.9 (95% CI: 2.8, 6.3). When the 2 studies that contributed most to the heterogeneity statistic were removed, the OR for improvement in the piracetam group compared to placebo (17 studies) was 2.50 (95% CI: 1.96, 3.17) using the fixed-effect model (Peto); the NNT was 4.6 (95% CI: 3.7, 6.1).

Results computed on the basis of the larger 'as randomised' population were very similar for each of the analyses (including the sensitivity analysis).

Authors' conclusions
The authors conclude that while there may be problems in meta-analyses and the interpretation of the statistical results, the results of this analysis provide compelling evidence for the global efficacy of piracetam in a diverse group of older people with cognitive impairment.

CRD commentary
The review question was clearly stated and was supported by inclusion criteria relating to the interventions, participants, study design and outcomes. Heterogeneity was appropriately assessed and the studies were quantitatively pooled using suitable methods. The meetings when the report was written were sponsored by UCB and three of the review authors worked as consultants for UCB, in relation to anti-dementia drugs. There is, therefore, a possible conflict of interest. In light of this, the authors' conclusions should be viewed with caution.

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

Research: The authors state that in order to confirm the findings of their meta-analysis, prospective, double-blind, placebo-controlled studies, using modern diagnostic and efficacy measures, should be conducted.

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Other publications of related interest

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.