Meta-analysis of clinical trials with copolymer 1 in multiple sclerosis
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Authors' objectives
To evaluate the efficacy of glatiramer acetate (copolymer 1) in relapsing-remitting multiple sclerosis (MS).

Searching
MEDLINE and EMBASE were searched from January 1966 to May 1999) using the following keywords: 'multiple sclerosis', 'optic neuritis', 'copolymer', 'glatiramer acetate', 'relapse', 'disability', 'progression', 'review' and 'trials'. The reference lists of all retrieved papers were scanned for additional references. Additional searches focused on conference proceedings, personal contacts (for unpublished papers) and ongoing trials.

Study selection
Study designs of evaluations included in the review
Placebo-controlled randomised controlled trials (RCTs). Both included studies were double-blind.

Specific interventions included in the review
Copolymer 1 versus placebo. Both included trials were of a 20 mg/day dose of copolymer 1.

Participants included in the review
People with clinically or laboratory-supported definite MS with relapsing-remitting course. No data were given on the patient demographics.

Outcomes assessed in the review
The number of patients with relapses (exacerbations) and the number of worsened patients of at least one point of disability (unconfirmed progression) were assessed.

How were decisions on the relevance of primary studies made?
Every report was independently scrutinised by the three reviewers and assessed for entry into the review. Any discrepancies were resolved by consensus.

Assessment of study quality
The methodological quality of the studies was assessed by looking at methods of randomisation, use of blinding techniques (double-blind versus unblind studies) and description of withdrawals and drop-outs. The authors do not state how the papers were assessed for quality, or how many of the reviewers performed the quality assessment.

Data extraction
Two independent reviewers extracted data from each article onto a prepared form, and any discrepancies were resolved by consensus.

Methods of synthesis
How were the studies combined?
The common Peto odds ratio (OR) and 95% confidence interval (CI) were calculated using a fixed-effect model.

How were differences between studies investigated?
Heterogeneity was assessed using the chi-squared test for homogeneity.
Results of the review
Two double-blind RCTs were included (n=299).

Exacerbation: at 12 months, data favour copolymer 1 (OR 0.17, 95% CI: 0.05, 0.51, p=0.002)), while at 24 and 35 months the effect was not significant.

Progression: copolymer 1 significantly decreased the odds of progression at 24 months (OR 0.57, 95% CI: 0.34, 0.95, p=0.031) and 35 months (OR 0.50, 95% CI: 0.28, 0.90, p=0.019). Heterogeneity was not noted in either result.

Authors’ conclusions
These data suggest that copolymer 1 represents an alternative to interferon treatment in relapsing-remitting MS, although further evidence of efficacy is required to justify its use in clinical practice.

CRD commentary
The review inclusion criteria are clearly stated, as are many aspects of the systematic review process (e.g. number of reviewers involved). The literature search seems comprehensive and efforts were made to locate unpublished studies, although it is not stated whether language restrictions were applied. A quality assessment was carried out but the results were not reported; however the results may not be important as both included studies were randomised, double-blind and placebo-controlled. Study details were not well-presented and, as the number of patients experiencing an outcome in each group was not stated, it is unclear whether the OR or the relative risk would have been the more appropriate summary statistic.

The authors’ conclusions are suitably cautious given the limitations mentioned above.

Implications of the review for practice and research
Practice: The authors state that further evidence of efficacy (clinical and paraclinical) is required to justify the use of copolymer 1 in clinical practice.

Research: The authors state that further evidence of efficacy (clinical and paraclinical) is required to justify the use of copolymer 1 in clinical practice.

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