Attention-deficit hyperactivity disorder in children and youth: a quantitative systematic review of the efficacy of different management strategies

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Authors' objectives
To obtain estimates of the relative efficacy of three main treatment strategies for attention-deficit hyperactivity disorder (ADHD) in children and youths (aged less than 18 years).

Searching
The following databases were searched: from 1981 to August 1997, Current Index to Journals in Education (CIJE), HealthSTAR, MEDLINE, and PsycINFO; from 1988 to August 1997, EMBASE; from 1990 to August 1997, OCLC ArticleFirst via FirstSearch; and from 1995 to August 1997 Current Contents. The search terms used were listed in the manuscript. Additional studies were identified by examining the Cochrane Database of Systematic Reviews, by handsearching bibliographies from key textbooks and reviews published in major journals from 1995 onwards, and by contacting several drug manufacturers (Novartis, SmithKline Beecham, and Abbott).

Study selection
Study designs of evaluations included in the review
Randomised controlled studies with a publication date of 1981 or later were included

Specific interventions included in the review
A course of at least one week of stimulant medication administered on consecutive days or a course of psychosocial intervention. The specific interventions examined by the included studies were methylphenidate (MPH), dextroamphetamine (DAS), pemoline, multicomponent cognitive-behavioural therapy, teacher component cognitive-behavioural therapy, cognitive-behavioural therapy, attention control plus MPH, cognitive therapy plus placebo drug, cognitive therapy plus stimulant medication, attention control with placebo drug, parent training plus MPH, parent training plus placebo drug, placebo, and no therapy. The dosage level used in medication-only studies ranged from 0.45 to 1.27 mg/kg daily and the duration of follow-up ranged from 7 to 120 days. For studies of behavioural and combination therapy the follow-up ranged from 3 months to 'present'. The duration of behavioural therapy varied in all the intervention groups.

Participants included in the review
The participants considered were aged up to 18 years with a diagnosis of attention-deficit disorder (ADD), ADD-hyperactivity, or ADHD made in an explicit and reproducible way with no coexisting diagnosis. Diagnoses were based on the criteria of the American Psychiatric Association (see Other Publications of Related Interest no.1). The age of the participants in the included studies ranged from 4 to 17 years. The proportion of male participants, where stated, ranged from 69 to 100%.

Outcomes assessed in the review
The outcomes were measured by a teacher or parent using a behaviour rating scale in a form suitable for meta-analysis. The scales completed by the teachers were the Abbreviated Conners Teacher Rating Scale, the Child Attention Profile Questionnaire, IOWA Conners Teacher or Parent Rating Scale, the Revised Behaviours Problems Checklist, and the ADD-H Comprehensive Teacher Rating Scale. The parents completed the Home Situations Questionnaire, the Abbreviated Conners Parent Rating Scale (or Hyperactivity index), the Revised Behaviours Problems Checklist, and IOWA Conners Teacher or Parent Rating Scale.

How were decisions on the relevance of primary studies made?
The titles or abstracts of all potentially eligible studies were reviewed against the inclusion criteria. Potential or definitely eligible studies were retrieved and reviewed in detail by two different reviewers, and any disagreements settled by consensus.
Assessment of study quality
The validity was assessed using the scoring system developed by Jadad et al. (see Other Publications of Related Interest no.2), which included the assessment of randomisation, double-blinding, and description of withdrawals. Scores ranged from 0 to 5, with scores less than 3 indicating poor quality. Two reviewers assessed the methodological quality, and any differences in scoring were settled by consensus.

Data extraction
The authors do not state how many of the reviewers performed the data extraction. Data were extracted for six areas: study characteristics, e.g. design; characteristics of the participants, i.e. age and gender; intervention characteristics, i.e. details of the treatment; patient attrition; adverse treatment reactions; and main outcome measurements. All the data extracted for the outcome measurements were rechecked against the original articles at the time of data entry. For medication studies, the standardised unit of mg/kg daily was adopted. The drug effect from only one dose level was considered for each study.

Methods of synthesis
How were the studies combined?
The DerSimonian and Laird method (see Other Publications of Related Interest no.3) was used to calculate either a weighted mean difference (WMD) or standardised mean difference (SMD) for each outcome. A random-effects model was used because of heterogeneity across a range of variables. Forest plots were presented in the manuscript. The stimulant drugs were analysed collectively. For the analysis of medication-only effects, data from two of the parallel-group trials were included with the crossover studies. A sensitivity analysis was undertaken to compare the difference in efficacy between medication-only studies with a poor quality score (less than 3) and those with scores of 3 and above.

How were differences between studies investigated?
Differences between the studies were investigated narratively and by statistical analysis (chi-squared test).

Results of the review
Twenty-six studies (999 participants) were included: 19 studies (all drug-treatment studies) used a crossover design and 7 studies used a between-patients parallel design.

The methodological quality scores ranged from 0 to 5 with 17 studies scoring at least 3. There was substantial heterogeneity among the studies analysed with respect to quality, design, sample size, patients' characteristics, interventions, outcome measures, and follow-up.

Medication versus placebo.
The overall SMD using the teacher rating scales (18 studies, 1,317 participants; some participants counted twice on account of the study designs) was -1.028 (95% confidence interval, CI: -1.212, -0.843; chi-squared 35.33, d.f.=17).

The overall SMD using the parent rating scales (13 studies, 1,135 participants; some participants counted twice on account of the study designs) was -0.859 (95% CI: -1.140, -0.578; chi-squared 52.58, d.f.=12).

Psychological or behavioural therapy versus control or no comparison.
The overall SMD using the teacher rating scales (2 studies, 36 participants) was -3.777 (95% CI: -8.064, +0.510; chi-squared 1.96, d.f.=1).

The overall SMD using the parent rating scales (1 study, 26 participants) was -0.488 (95% CI: -1.270, -0.294).

Combination therapy (medication plus behavioural therapy) versus control or comparison.
The overall WMD using the teacher rating scales (2 studies, 36 participants) was -3.777 (95% CI: -8.064, +0.510; chi-squared 1.96, d.f.=1).
The overall WMD using the parent rating scales (2 studies, 36 participants) was -7.345 (95% CI: -12.289, -2.401; chi-squared 1.63, d.f.=1).

Combination therapy versus medication.

The overall WMD using the teacher rating scales (3 studies, 76 participants) was 1.285 (95% CI: -0.717, +3.286; chi-squared 1.15, d.f.=2).

The overall WMD using the parent rating scales (2 studies, 38 participants) was -0.460 (95% CI: -3.861, +2.942; chi-squared 0.30, d.f.=1).

Combination therapy versus psychological or behavioural therapy.

The overall WMD using the teacher rating scales (3 studies, 68 participants) was -2.006 (95% CI: -4.174, +0.163; chi-squared 1.44, d.f.=2).

The overall WMD using the parent rating scales (2 studies, 39 participants) was -5.911 (95% CI: -8.631, -3.190; chi-squared 0.22, d.f.=1).

Authors' conclusions
Stimulant medications were found to be an effective treatment strategy for ADHD in children and youth. However, it may be difficult to assess the relative benefits of behavioural interventions alone, and combined medication and behavioural therapy, because of the paucity of nonmedical studies. In addition, the considerable heterogeneity between studies, in terms of participants, interventions and outcomes, made it difficult to interpret the results.

CRD commentary
This appeared to be a well-conducted review. The aims were clearly stated and a comprehensive literature search was undertaken. However, apart from contacting the drug manufacturers, no attempt was made to locate unpublished data and therefore publication bias cannot be ruled out.

A systematic process involving two reviewers was used to assess the relevancy of the included studies. Some information was provided on the process of data extraction, but it was not stated how many reviewers were involved. Relevant details of the included studies were clearly presented in tabular format and were described in the text. The validity of included studies was assessed by two reviewers, and the differences between the studies were discussed in the narrative and analysed statistically.

The authors' conclusions appear to follow from the results. However, it may have been inappropriate to pool the results on account of the significant heterogeneity present.

Implications of the review for practice and research
Practice: The authors state that their results suggest that medical therapy is efficacious in managing children with ADHD, that nonmedical interventions used alone are not efficacious, and that combinations of medical and nonmedical therapies may be efficacious in some situations. However, they also recommend that when making health policy decisions, the findings should be interpreted with caution given the lack of good-quality studies and the significant heterogeneity between existing studies.

Research: The authors state that definitive large trials of behavioural therapies, and combinations of medication and behavioural therapies, are needed to determine the benefits of alternative treatment strategies for ADHD. They also note that future research will need to identify the best outcome measures for evaluating nonmedication therapies.

Bibliographic details

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Attention Deficit Disorder with Hyperactivity /diagnosis /therapy; Central Nervous System Stimulants /therapeutic use; Child; Child, Preschool; Combined Modality Therapy; Evidence-Based Medicine; Infant; Infant, Newborn; Psychiatric Status Rating Scales; Randomized Controlled Trials as Topic; Treatment Outcome

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