Duration of effect of oral long-acting stimulant medications for ADHD throughout the day
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CRD summary
This review found that most long-acting stimulants conferred benefits in populations with attention-deficit/hyperactivity disorder for up to 12 hours as measured by mathematics tests. Methodological flaws and a lack of information about the quality of the studies mean that the results should be interpreted with some caution and made the reliability of the authors' conclusions unclear.

Authors' objectives
To determine the duration of effect of long-acting stimulant treatment in patients with attention-deficit hyperactivity disorder (ADHD) using analogue classroom protocols.

Searching
MEDLINE, BIOSYS and EMBASE were searched to June 2009 for relevant published studies; search terms were reported. Unpublished material was sought in the form of poster abstracts for the congresses of the American Psychiatric Association and American Academy of Child and Adolescent Psychiatry from 2006 to 2009.

Study selection
Clinical trials that assessed the efficacy of long-acting stimulants in patients with ADHD over a one-day duration were eligible for inclusion where permanent product measure of performance (PERMP) scores or other mathematics tests were the primary outcome measures. Studies were required to use analogue classroom protocols or adult workplace environments. Studies of short-acting or non-oral stimulants, non-stimulants and medications not approved by the United States Food and Drug Administration and studies that included only minimal data on efficacy were excluded from the review.

The included studies employed randomised double- or single-blind placebo-controlled designs. The age range of patients in most trials was six to 12 years. Treatments were long-acting amphetamine formulations that included lisdexamfetamine dimesylate, mixed amphetamine salts extended release, dextroamphetamine extended release and long-acting methylphenidate formulations that comprised osmotically controlled-release oral delivery systems, methylphenidate extended release, methylphenidate spheroidal oral drug absorption systems and dexmethylphenidate extended release. The treatments were all given at a range of doses. Time points for measurement of efficacy of medications were one to 14 hours post-administration. Where reported, the outcome was duration of symptom improvement.

The authors did not state how many reviewers performed the study selection.

Assessment of study quality
The authors did not report any formal assessment of methodological quality. Information was reported on study design for blinding methods, number of crossover periods and description of outcome measures used.

The authors did not state how many reviewers evaluated these quality criteria.

Data extraction
Data were extracted as reported on duration of symptom improvement in hours.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
The results of the review were summarised in a narrative synthesis.
Results of the review
Fifteen trials (n=1,172 participants) were included in the review: 378 patients (five trials) were treated with long-acting amphetamine formulations and 794 patients (10 trials) were treated with long-acting methylphenidate formulations. Two trials used single blind designs.

Efficacy in studies that examined long-acting amphetamine formulations was maintained for up to 14 hours (three trials) in children and adults with lisdexamphetamine dimesylate, for up to 12 hours in two trials of mixed amphetamine salts extended release and for four hours in one trial of dextroamphetamine extended release.

Duration of efficacy with long-acting methylphenidate formulations was maintained from one hour to 12 hours post-dosing for osmotically controlled-release oral delivery systems (four trials), 1.5 hours to 7.5 hours for methylphenidate extended release in one trial, one hour to 12 hours post-dosing for methylphenidate spheroidal oral drug absorption systems (two trials) and 30 minutes to 12 hours post-dosing for dexmethylphenidate extended release (five trials).

Authors' conclusions
Most long-acting stimulants conferred benefits on ADHD symptoms in patients across the age spectrum for up to 12 hours as measured by the permanent product measure of performance mathematics test. Formulations may differ in time to peak effect and maintenance of effect as well as magnitude of effect at different time points during the day.

CRD commentary
The review addressed a clear question. Criteria for inclusion of studies were defined. Appropriate electronic databases were searched and there were attempts to identify unpublished data. No steps to minimise errors and biases at any stage of the review process were reported. There was no formal assessment of methodological quality, which made it difficult to make a judgment on the reliability of the results of the trials. Clinical heterogeneity for the included medications justified the authors' decision to summarise the results in a narrative synthesis.

Methodological flaws in the review process may have led to errors and biases. These and the lack of information on the quality of the included studies mean that the results should be interpreted with caution and made the reliability of the conclusions unclear.

Implications of the review for practice and research
Practice: The authors stated that duration of effect was only one part of medication selection for ADHD and that efficacy, side-effects, comorbid conditions, patient preference and medication history should be integral to individualised treatment plans. Potential for abuse of stimulants should be considered by physicians when prescribing stimulant agents for ADHD, particularly in adolescents and adults.

Research: The authors did not state any implications for research.

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