Efficacy, Acceptability, and Tolerability of Lisdexamfetamine, Mixed Amphetamine Salts, Methylphenidate, and Modafinil in the Treatment of Attention-Deficit Hyperactivity Disorder in Adults: A Systematic Review and Meta-analysis

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Abstract

OBJECTIVE:
Psychostimulants are the first-line treatment in adults with attention-deficit hyperactivity disorder (ADHD). This meta-analysis aimed to evaluate the efficacy, acceptability, and tolerability of lisdexamfetamine (LDX), mixed amphetamine salts (MASs), modafinil (MDF), and methylphenidate (MPH) in comparison with placebo.

DATA SOURCES:
We systematically searched PubMed/MEDLINE and Clinicaltrials.gov in May 2016, along with CENTRAL and EU Clinical Trials Register in February 2016, for the randomized, double-blind, placebo-controlled, parallel-group clinical trials conducted on adults diagnosed with ADHD.

STUDY SELECTION AND DATA EXTRACTION:
Substantial comorbidity, substance abuse or dependence, and nonpharmacological interventions represented grounds for exclusion. Published reports were the sole source for data extraction. Improvement in ADHD symptoms was the primary outcome. Random-effects model meta-analysis was applied to calculate the standardized mean difference (SMD) with 95% CIs.

DATA SYNTHESIS:
The search retrieved 701 records, of which 20 studies were eligible for analysis. High effect size (expressed as SMD) in reducing ADHD symptoms was observed for LDX (-0.89; 95% CI = -1.09, -0.70), whereas MASs (-0.64; 95% CI = -0.83, -0.45) and MPH (-0.50; 95% CI = -0.58, -0.41) reduced symptoms moderately compared with placebo. No efficacy was shown for MDF (0.08; 95% CI; -0.18, 0.34). Relevance to Patient Care and Clinical Practice: In this meta-analysis, the efficacy, tolerability, and acceptability of psychostimulants were compared with that for placebo. Five of the included trials have not been evaluated in any of the previously published meta-analyses.

CONCLUSIONS:
The results suggest that LDX has the largest effect size and has a promising potential for treating adults with ADHD.