Relationship of ADHD symptoms and global illness severity in adults treated with lisdexamfetamine dimesylate.

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Abstract
The relationship between attention-deficit/hyperactivity disorder (ADHD) symptoms and global clinical assessment of functionality is complex. This post-hoc analysis explores this relationship and suggests implications for patient assessment in clinical practice. Adults with ADHD on a stable lisdexamfetamine dimesylate (LDX) dose for ≥ 6 months were enrolled in a double-blind, placebo-controlled, randomized withdrawal study. Participants entered a 3-week open-label phase continuing their prior LDX dose and were then randomized to placebo or the same LDX dose for a 6-week, double-blind, randomized withdrawal phase. ADHD symptom distribution was measured by the ADHD Rating Scale IV (ADHD-RS-IV) with Adult Prompts total score reflecting DSM-IV-TR ADHD symptom criteria and severity by Clinical Global Impressions-Severity (CGI-S) ratings at study entry and at end of study. Of 123 participants enrolled in the open-label phase, 116 were included in the randomized withdrawal phase (placebo, n = 60; LDX, n = 56). As reported in a prior publication, mean (standard deviation) ADHD-RS-IV total score change from baseline (week 3) to end of study (randomized withdrawal phase) was 16.8 (11.80) for placebo and 1.6 (8.63) for LDX. At end of study, for placebo and LDX, 5.0% and 32.1% of participants, respectively, had a CGI-S = 1, 11.7% and 35.7% had a CGI-S = 2, 11.7% and 17.9% had a CGI-S = 3, 33.3% and 7.1% had a CGI-S = 4, 35.0% and 7.1% had a CGI-S = 5, and 3.3% and 0% had a CGI-S = 6; no participants had a CGI-S = 7 (P < 0.0001). The CGI-S ratings increased (worsened) as ADHD symptom scores worsened. Post-hoc regression analysis between ADHD-RS-IV scores and CGI-S demonstrated shared variance of 47% at week 3 and 69% for both placebo and LDX at end of study. Although ADHD symptom scores demonstrate a linear relationship with global illness severity, the variance suggests that other factors not captured by symptom scales are also important in assessing patient outcomes in clinical practice. (Trial registration: ClinicalTrials.gov NCT00877487.).