

Pharmacokinetic and Pharmacodynamic Properties of Lisdexamfetamine in Adults with Attention-Deficit/Hyperactivity Disorder

Adler Lenard A., Alperin Samuel, Leon Terry, and Faraone Stephen V..

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ABSTRACT

Background:

Lisdexamfetamine (LDX) is a prodrug and consists of an active moiety, d-amphetamine, bound to lysine. Clinically, d-amphetamine becomes available postcleavage of the prodrug in the blood stream. Clinical effects of LDX in attention-deficit/hyperactivity disorder (ADHD) have been shown to persist up to 14 hours; however, pharmacokinetic (PK) data of LDX and amphetamine in ADHD adults are not currently available.

Objectives:

(1) To examine PK data of LDX and d-amphetamine in plasma and (2) to compare such PK data with Time-Sensitive ADHD Symptom Scale (TASS) ratings (PK vs. pharmacodynamic [PD]).

Methods:

Plasma d-amphetamine/LDX levels and TASS ratings were obtained immediately before morning dosing and then 0.5, 1, 2, 4, 6, 8, 10, and 12 hours postdosing in 21 adults with ADHD treated with 5 weeks of single-blind LDX up to 70 mg/day (after 1 week single-blind placebo). ADHD Rating Scale scores were obtained at the beginning of the visit, before morning dosing.

Results:

LDX levels peaked at 1.5 hours after administration (T_{max}) and then rapidly declined (levels were negligible at 6 hours and area under the plasma concentration versus time curve, $AUC = 45.9$, $C_{max} = 25.0$, and half-life [$t_{1/2}$] = 0.5 hours). Levels of d-amphetamine peaked at (T_{max}) 4.4 hours and then slowly declined ($AUC = 641.6$, $C_{max} = 67.9$, and $t_{1/2} = 17.0$ hours). No statistically significant correlations were seen between d-amphetamine levels and TASS scores.

Conclusions: (1) Prodrug LDX levels peaked fairly rapidly and declined, while d-amphetamine levels peaked 3 hours later than LDX levels and persisted throughout the day and (2) the absence of PK/PD correlations between PK data and TASS ratings may be due to the subjects being tested in a controlled nonattention demanding environment.