Review: limited evidence to support pharmacological therapy for amphetamine withdrawal

**QUESTION**

**Question:** Is pharmacological therapy, alone or in combination with psychosocial treatment, effective for amphetamine withdrawal?

**Outcomes:** Discontinuation rates, average global state score (eg, Clinical Global Impression), average score on withdrawal symptomatology assessments (eg, Amphetamine Withdrawal Questionnaire), average score in craving rating scales (eg, Questionnaire for Evaluating Cocaine Craving and Related Responses) and patient satisfaction (measured by type and number of adverse events).

**METHODS**

**Design:** Systematic review with meta-analysis.

**Data sources:** The Cochrane Central Register of Controlled Trials, MEDLINE, PsycINFO and CINAHL (searched from inception to 1 May 2008). Reference lists of identified studies and conference proceedings were hand searched.

**Study selection and analysis:** Two independent reviewers appraised the studies and selected randomised controlled trials comparing any kind of pharmacological treatment, alone or in combination with a psychosocial treatment, placebo or any psychosocial treatment for amphetamine withdrawal. Studies of other drugs in addition to amphetamine were included provided >50% of participants were withdrawing from amphetamine and there was separate reporting for amphetamine. Heterogeneity was assessed using $\chi^2$ tests. Relative risk and number needed to treat were calculated for dichotomous outcomes and weighted mean difference (WMD) calculated for continuous data using the fixed effects model.

**MAIN RESULTS**

Four studies ($n = 125$; 88% male) met the inclusion criteria. Two studies compared amineptine (300 mg daily) with placebo in inpatients at a drug dependence centre who met DSM-IV criteria for amphetamine withdrawal, and two studies compared mirtazapine (15–60 mg, titrated to need) with placebo in participants who also had an Amphetamine Withdrawal Questionnaire score of $\geq 10$. Treatment duration was 2 weeks in all studies. Any active treatment significantly decreased the risk of discontinuation compared with placebo (four randomised controlled trials (RCTs), 125 participants; relative risk 0.52, 95% confidence interval (CI) 0.29 to 0.94; $p = 0.08$). Amineptine significantly improved global state on the Clinical Global Impressions scale compared with placebo (2 RCTs; WMD $-0.49$, 95% CI $-0.80$ to $-0.17$; $p = 0.002$) but mirtazapine did not (1 RCT; WMD 0.30, 95% CI $-0.22$ to 0.82; $p = 0.25$). One amineptine study and one mirtazapine study found no significant effect of treatment on average withdrawal symptom scores (2 RCTs, 74 participants; SMD $-0.08$, 95% CI $-0.54$ to 0.38). One amineptine study found no significant effect on average craving score compared with placebo.

**CONCLUSIONS**

There is limited evidence of effect for treatments of amphetamine withdrawal. Amineptine reduced treatment discontinuation rates and improved clinical presentation compared with placebo but had no effect on reducing withdrawal symptoms or craving, and is currently not available for use. There is little evidence of any benefit of mirtazapine.

**ABSTRACTED FROM**


**Correspondence to:** Steven J Shoptaw, Department of Family Medicine, University of California, 10880 Wilshire Boulevard, Suite 540, Los Angeles, CA 90024, USA; sshoptaw@mednet.ucla.edu

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