

Mirtazapine for methamphetamine use disorder: A randomised double-blind placebo-controlled trial

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Introduction: There are no approved pharmacotherapies for methamphetamine use disorder. Phase 2 trials have identified the generic antidepressant, mirtazapine, as a promising candidate. We determined the safety and effectiveness of mirtazapine as a pharmacotherapy for methamphetamine use disorder in routine clinical practice.

Methods: We conducted a Phase 3 parallel randomized double-blind placebo-controlled trial in 6 outpatient alcohol and other drug clinics in Australia (ACTRN12622000235707). Adults with moderate to severe methamphetamine use disorder (N=344) received either mirtazapine (30 mg daily/12 weeks) or equivalent placebo. The primary endpoint was the

change in days of methamphetamine use in the past 28 days from baseline to week 12. Secondary endpoints were depression, insomnia, HIV risk behavior, quality of life and methamphetamine negative oral fluid samples.

Results: Participants who received the intervention (placebo, n=167; mirtazapine, n=172) had used methamphetamine on a median (IQR) of 24 days (17-28) of the past 28 days at baseline. The mean reduction in days of methamphetamine use from baseline to week 12 was 7.0 days (of 28 days) in the mirtazapine group and 4.8 days (of 28 days) in the placebo group. The mean reduction in days of methamphetamine use from baseline to week 12 was significantly greater in the mirtazapine group than in the placebo group (mean difference of 2.2 days of 28 days, 95% CI -4.2 to -0.2 days, p=0.02). More participants on mirtazapine reported drowsiness (47% vs. 33%) and weight gain (10% vs. 3%). We found no significant effects of mirtazapine on secondary endpoints.

Discussions and Conclusions: Mirtazapine can be delivered safely in routine clinical practice to help people with methamphetamine use disorder reduce their methamphetamine use.

Implications on communities, practice, policy and/or First Nations communities: This finding has important clinical implications in the absence of any approved pharmacotherapies. Mirtazapine is an inexpensive generic medication with a well-established safety profile. It is currently indicated for depression and can be prescribed off label for methamphetamine use disorder.

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