Sustained release dextroamphetamine (15–30 mg but not 30–60 mg) improved retention in patients with cocaine dependence


QUESTION: In patients with cocaine dependence, is sustained release dextroamphetamine more effective than placebo for improving retention?

Design
Randomised (allocation concealed*†), blinded (patients, clinicians, data collectors, and data analysts), placebo controlled trial with 12 weeks of follow up.

Setting
Department of Psychiatry and Behavioural Sciences at the University of Texas-Houston, Houston, Texas, USA.

Patients
128 patients (mean age 36 y, 79% men) with cocaine dependence who were in good medical health without other psychiatric diagnoses (except nicotine dependence), as determined by the Structured Clinical Interview for DSM-IV (SCID). Follow up at study end was [24%†; all patients were included in the retention analysis.

Intervention
Patients were allocated to dextroamphetamine sulphate, 15 mg for 28 days then doubled to 30 mg for 56 days (n=47†); dextroamphetamine sulphate, 30 mg for 28 days and then doubled to 60 mg for 56 days (n=46†); or to placebo (n=35†). Patients received dextroamphetamine sulphate sustained release regimen once within 2 hours of awakening, and once 6 hours later. Dosing was supervised in the clinic only on the 2 visit days each week. Patients also received behavioural therapy once weekly.

Main outcome measures
Retention and side effects. Other assessed outcomes, which included use of cocaine, compliance, and depression (Beck Depression Inventory [BDI]), had <80% follow up.

Main results
Retention was best for the 15–30 mg group followed by the placebo group, and worst for the 30–60 mg group (p < 0.001). Study completion rates for 15–30 mg, 30–60 mg, and placebo groups were 40%, 9%, and 23%, respectively (table). Few side effects varied when intake values were used as covariates; varying with increasing dose were sleeping, fever, mouth or tongue twitch, and dizziness (p values < 0.05).

Conclusions
In patients with cocaine dependence, sustained release dextroamphetamine was more effective than placebo for improving retention at doses of 15–30 mg, but detrimental to retention at doses of 30–60 mg. The improvement in retention was not clinically significant.

*See glossary.
†Information provided by author.

<table>
<thead>
<tr>
<th>Outcome at 12 weeks</th>
<th>Comparison</th>
<th>Event rates</th>
<th>RBI (95% CI)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study completion</td>
<td>15–30 mg v placebo</td>
<td>40% v 23%</td>
<td>77% (-9 to 261)</td>
<td>Not significant</td>
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<tr>
<td></td>
<td>RBR (CI)</td>
<td>NNH</td>
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<tr>
<td>30–60 mg v placebo</td>
<td>9% v 23%</td>
<td>62% (-10 to 87)</td>
<td>Not significant</td>
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</tr>
</tbody>
</table>

†Abbreviations defined in glossary; RBI, RBR, NNT, NNH, and CI calculated from data supplied by author.

COMMENTARY
Management of patients with cocaine dependence poses substantial difficulties for addiction treatment services. The trial by Grabowski et al assessed the effectiveness of a substitute stimulant agonist for improving retention rates and reducing cocaine abuse. However, because substitute stimulant agonists carry a substantial risk of side effects (both physical and psychological), prescribing them needs to carry with it a favourable balance of risk for the individual patient treated.

In this study, although all patients fulfilled a DSM-IV diagnosis of cocaine dependence, and received daily dextroamphetamine medication, only 23.4% of the study group reported daily consumption of cocaine, and 28.7% reported cocaine use only once a week or less. The authors rightly point out that inclusion criteria for subsequent studies should include both criteria for cocaine dependence and criteria for frequency of use. When patients with no cocaine use during the study were removed from the data, a trend towards fewer cocaine positive urine samples in the higher dose dextroamphetamine group was identified in line with the predictions.

It is clear from the results of this study that, contrary to expectations, an increased dose of substitute agonists on a daily basis had a detrimental effect on retention, and worsened the side effect profile, but resulted in the greatest improvement in depression scores after dose doubling. However, retention was best in the group on the lower dose of dextroamphetamine. It should also be noted that consumption of dextroamphetamine was supervised only on 2 days a week, that only >80% of those on active treatment had amphetamine positive urine screens, and that no anxiety scores were measured during the study although they are important. Blood pressure did not increase substantially, but there was a moderate dose related increase in heart rate. Few patients withdrew from the study as a result of medication side effects and for those who completed the study, dose related side effects were observed.

Practitioners treating patients with cocaine dependence will be informed by the content of this paper despite the limitations identified by the authors. It is noteworthy that dosing with substitute dextroamphetamine did not lead to substantial side effects irrespective of dose and therefore a further study of substitute agonist treatment for cocaine dependence (with daily supervised consumption of the substitute agonist) would be welcomed.

Judy Myles, MBBCH, FRCPsych
Bristol Specialist Drug Service
Bristol, UK

Source of funding: National Institute on Drug Abuse.
For correspondence: Dr J Grabowski, University of Texas-Houston, Houston, Texas, USA. john.grabowski@uh.edu
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