DOI:10.1111/j.1365-2125.2004.02094.x

Letter to the Editors

Reboxetine may be helpful in the treatment of amphetamine withdrawal

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Illicit amphetamine use is widespread internationally [1], amphetamine and MDMA are the second most commonly used drugs in the European Union after cannabis [2]. There have been alarming epidemics of amphetamine use, particularly metamphetamines, in South-east Asian countries in the last few years. Clients undergoing withdrawal from amphetamines can pose a range of challenges to services traditionally orientated towards managing opiate or alcohol withdrawal. Not least of these challenges is the lack of an evidence-based prsecribing option. A Cochrane Review concluded that the evidence for treatment of amphetamine withdrawal is very limited and that, at present, no available treatment has been demonstrated to be effective. They further concluded that medications to be considered for further treatment studies may be those with the propensities to increase dopamine, norepinephrine and/or serotonin activities of the brain [3].

Reboxetine is the first selective and specific norepinephrine reuptake inhibitor available for clinical use [4]. Its mode of action suggests that it may be useful in treatment for amphetamine withdrawal. We therefore conducted an open label case series to make an initial assessment of its treatment potential.

Clients attending a community addiction service, with a diagnosis of amphetamine dependence syndrome and who intended outpatient detoxification from amphetamine or who had discontinued amphetamine but were experiencing mood disturbance, were offered reboxetine therapy. The case notes of all clients who had been prescribed reboxetine were later examined and their key worker interviewed. Client reports were compared with the results of urine drug screens. Other substance use did not exclude clients from the offer of reboxetine therapy. Reboxetine dosage was titrated according to tolerability.

Of 11 cases in all, two had been taking prescribed Dexamphetamine before withdrawal. The remaining nine were using illicit amphetamine, from 1 to 50 g per week. There was equal representation of oral and intravenous use of amphetamine. Other illicit or prescribed drugs were commonly used, including cannabis, opiates and benzodiazepines. Six of the 11 did not drink alcohol. In nine of the cases a detailed description of untreated amphetamine withdrawal symptoms was available. Three of the 11 clients described psychotic symptoms. The most commonly cited symptom was depression, or low mood (8/9). Other commonly described symptoms were lethargy or anergia and excessive sleep. Clients had been exposed to a mean of 1.5 different antidepressants previously (range 0-4) without reported benefit.

All but one client took a maximum dose of reboxetine 8 mg day^{-1}, five reported no resumption of amphetamine use, four reported significantly reduced use of amphetamine, and one reported abstinence after an initial return to amphetamine use. The timing of return to amphetamine use ranged from 2 weeks to 8 months. Two clients reported that they did not experience their usual withdrawal symptoms when they were taking reboxetine. One client reported that using amphetamines was unrewarding whilst taking reboxetine, as there was little or no effect. One client reported that the initial benefit of taking reboxetine had worn off after 1 month. No adverse effects were recorded for seven patients. Three clients reported urinary symptoms associated with taking reboxetine, hesitancy, frequency or nocturia. Two clients reported sweating as an adverse effect.

Therapy with reboxetine was associated with some beneficial effects in 10 cases withdrawing from amphetamine in this pragmatic case series. Reboxetine was sufficiently well tolerated for all patients to have taken it for at least 2 weeks. Almost half of the clients remained abstinent from amphetamine for the duration of clinical follow-up.

This report is of an open label case series. Apparent

treatment effects may be due to factors other than the prescription of reboxetine. Nevertheless, in a field where the scale of the problem is significant and where no other treatment has been clearly demonstrated to be effective, positive findings warrant further investigation. A randomized trial of reboxetine *vs.* placebo for the treatment of amphetamine withdrawal symptoms would be the next logical step.

References

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