
LETTER TO THE EDITORS

Baclofen as a Cocaine Anti-Craving Medication: A Preliminary Clinical Study

The lack of success in finding an effective pharmacological treatment for cocaine abuse may, in part, be due to the drug's apparent action on multiple and specific neurotransmitter systems, as well as the episodic nature of cocaine itself. Cocaine craving is frequently cue-induced, and appears to be accompanied by increases in dopamine and noradrenaline release, as well as cortical arousal and increased metabolism in the frontal cortex, induced by catecholamines and probably also glutamate. Conceptually, a medication that inhibits the release of these neurotransmitters should prevent cocaine binges and drug use relapse. Baclofen, a GABA_B receptor agonist that inhibits the release of several neurotransmitters, including dopamine, noradrenaline, 5HT, and glutamate (Huston et al. 1995; Hojck and Holopainen 1992), may be a promising candidate.

The manner in which baclofen indirectly affects dopaminergic and other reward system pathways provides attractive theoretical rationale for evaluating the medication as a potential cocaine pharmacotherapy. Preclinical studies have shown that baclofen, through inhibition of somatodendritic dopamine release, prevents development of cocaine-induced behavioral sensitization and abolishes the motor-stimulant actions of cocaine (Kalivas and Steward 1991). Baclofen was recently shown to attenuate the reinforcing effects of cocaine in rats (Roberts et al. 1996). Other studies suggest that baclofen may be a fast acting treatment for the affective state that occurs during cocaine abstinence (Andrews and File 1993a,b; Krupitsky et al. 1993) and, hence, may promote greater engagement in psychosocial treatment. Still, it remains to be demonstrated whether these preclinical and theoretical attributes of baclofen work in humans to block cocaine craving and, perhaps, prevent relapse to cocaine use.

In anticipation of a large clinical trial of baclofen for treatment of cocaine dependence, the Los Angeles Ad-

diction Treatment Research Center, in downtown Los Angeles, California, has completed a preliminary treatment program using baclofen, open label, as a cocaine anti-craving pharmacotherapy. Ten cocaine abusing males were treated with baclofen, 60 mg per day (20 mg t.i.d.), and three times a week group counseling (M, W, F). After an initial evaluation, including physical examination and laboratory testing, patients were inducted onto oral baclofen over three days to 60 mg per day. At each clinic visit, patients provided urine samples to be analyzed for cocaine. To monitor for safety, patients also met with the physician once a week to receive their medication and, if deemed necessary, undergo additional laboratory tests. A manualized program, developed by Rawson and colleagues (1995) at the Matrix Center, served as a format for the group counseling sessions, which taught skills for initiating abstinence and preventing relapse.

Patients ranged in age from 24 to 61 years (average = 39.1) and averaged 12.7 years of education. Seven were married or separated and three had never married. Four patients were unemployed, four worked at blue-collar jobs, and two held clerical positions. Reported involvement with cocaine ranged from 1.9 to 18 years (average = 10.0), with one to ten years of heavy use (average = 7.1). The longest period of reported continuous cocaine abstinence ranged from 0 to 210 days, with seven patients admitting to 30 or fewer days of abstinence in the year prior to treatment. Three patients reported having 1 to 3 alcohol containing drinks per month, three reported having 5 to 10 drinks once per week, and four reported having 5 to 14 drinks per day. Four patients acknowledged daily or monthly marijuana use.

Patients who complained of side effects could have their medication dosage reduced. One patient's dose was reduced to 40 mg per day (20 mg b.i.d.) through the

seventh week and then to 20 mg per day (morning only) for the remaining 11 weeks of treatment due to complaints of headache. Another patient's dose was reduced to 30 mg per day (10 mg t.i.d.) for three weeks due to multiple somatic complaints, but his dose was increased back to 60 mg per day after he was found to be using cocaine regularly. A third patient was treated with 60 mg per day on Fridays and Saturdays, 30 mg per day on Sundays, and no medication on weekdays (Mon–Thurs) due to complaints of drowsiness that interfered with his occupation as a truck driver. Overall, patients appeared to tolerate the medication well and none had clinically significant changes in lab values during the treatment period. Five experienced mild side effects, most commonly nausea, nightmares, headache, sedation, and dizziness, consistent with information provided in the package insert. Two patients discontinued baclofen after experiencing nightmares involving cocaine use.

Patients generally reported decreased cocaine craving and reduction in cocaine use, which was verified by urinalysis. Urine samples negative for cocaine for the ten patients ranged from 0% to 98%, with an average of 60.8%. Continuous cocaine abstinence averaged 4.8 weeks (range = 0–14 wks) and treatment length for the group averaged 10.3 weeks (range = 1–17 wks). Nine patients used cocaine at least once during treatment, but none reported lasting or deleterious effects attributable to cocaine/baclofen interaction. Of the four patients who were asked, none experienced any subjective differences in their cocaine "highs" while taking baclofen.

Overall, we believe this initial clinical experience suggests that baclofen is a well tolerated and safe medication that may effectively help to retain patients in treatment for clinically relevant periods and reduce their cocaine use. However, it still needs to be determined if this is due to baclofen's specific action in suppressing cocaine craving or to a possible general anxiolytic effect. In future studies, we plan to examine whether baclofen attenuates anxiety states during cocaine treatment. Meanwhile, from these preliminary results, it appears that baclofen is worth further evaluation, under controlled conditions, as a pharmacotherapy for cocaine dependence.

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